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The neurodevelopmental continuum towards a neurodevelopmental gradient hypothesis

Summary

In contrast to the categorical approach of the current nosographic system, in the last decades increasing literature is suggesting that psychiatric disorders may be better conceptualized as a continuum, which would feature as a common basis a neurodevelopmental alteration. The "neurodevelopmental continuum" (NC) is a theoretical framework supported by several empirical evidences in multiple fields of research. The conceptual core of this model is that an alteration in brain development, the expression of which would be determined by the intertwined relationships between genetic and environmental factors, may constitute the common underpinning of different kinds of mental disorders. Moreover, the NC theory also implies that psychiatric conditions could be placed along a gradient, where autism spectrum disorder (ASD) with intellectual disabilities would be the most severe expression of an alteration of the "social brain development", followed by other DSM-5 neurodevelopmental phenotypes characterized by a milder impairment. This model would subsequently include, along a decreasing neurodevelopmental gradient, other psychiatric conditions such as schizophrenia and mood disorders as well as eating and anxiety disorders, encompassing also non-psychopathological personality traits. From a cognitive point of view, the link between neurodevelopmental alterations and vulnerability towards psychopathology could be identified in an impairment of the proprioceptive experience and of the interoceptive inference, which would prevent the patient to properly define his own subjectivity and to adequately place him-self in the relational space. The conceptual framework proposed here may allow significant changes in both research and clinical settings, eventually leading to improve therapeutic and prevention strategies.

Key words
Neurodevelopment • Autism • DSM-5 • Dimensional approach • Comorbidity

Classification of neurodevelopmental disorders in DSM-5

The fifth edition of the Diagnostic and statistical manual of mental disorder (DSM-5) defines "Neurodevelopmental disorders" (ND) as "[…] *a group of conditions with onset in the developmental period. The disorders typically manifest early in development, often before the child enters grade school, and are characterized by developmental deficits that produce impairments of personal, social, academic, or occupational functioning. The range of developmental deficits varies from very specific limitations of learning or control of executive functions to global impairments of social skills or intelligence […]"* [1].

This category in DSM-5 includes:

- intellectual disabilities;
- communication disorders;
- autism spectrum disorder (ASD);
- attention-deficit/hyperactivity disorder (ADHD);
- specific learning disorders;
- motor disorders (among them: "Tic disorders" such as "Tourette's disorder").

However, focusing on features like symptomatological severity, and overall cognitive functionality and adaptability, we may re-think the whole ND cate-

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gorization as a psychopatological continuum, where ASD with intellectual disabilities is the most severe expression of an alteration of the "social brain development" [2]. Subsequently, the other phenotypes are characterized by a milder impairment in social communication and interaction, reflecting an intermediate impact on the ability of the new born to define his own subjectivity. A task which may be summarized as the possibility to say: "I am". That is to say, the ability to reach a valid auto-representation and to develop an adequate theory of mind [3]. This is a task of utmost complexity, involving all those aspects that contribute to the ontogenesis of the Self in its subjective time and relational space. For this purpose, it is needed:

1. Fully functioning coenesthetic perception: it will allow the subject to build the experience of feeling his own body in an integrative fashion, perceiving it as one global entity, functioning under subjective control. The experience can be summarized as "I feel my own body" [4];
2. The ability to develop cognitive maps, integrating the sensorial information about the world with past experience and with the bodily representation in time and space. This includes a perceptive cycle that allow the subject "to see" as something different from the experience of his own body [5];
3. An inner representation of the ways in which others might see the subject: "to be seen". The cognitive ability "to be seen" includes several orders of consequences. First of all, there must be some kind of other object able to "see". Some kind of intentionality (thus some kind of subjectivity) must be recognized in that object. These characteristics transforms the "watching" object in a proper "other subject" different from the subject but with comparable interior states. This last feature, extremely complex, underlies the appearance, in the child, of the ability to lie [3 4 5].

Each alteration of these features may lead to a severe impairment in the way a subject perceives its own body and build the experience of the world, including that of its own position in it [4 5]. We may suppose that a severe distortion in the development of these fundamental functions of the brain would result in the conditions listed under the "ND" category of DSM-5. However, milder alterations of the same functions may not produce detectable symptoms during childhood, remaining almost silent, or at least not leading to full-blown clinical manifestations. Despite that, they may actually result in other kinds of expressions, such as milder cognitive impairment, odd thinking or bizarre behaviours, neurotic traits, relational abnormalities [2 5 6]. These features, when requiring clinical attention, may appear as a full-fledged anxiety disorder, such as social anxiety, specific phobias or panic attacks [6]. In this framework, it is noteworthy that social anxiety, as autistic-like ND, is a disorder which features, from a clinical and neurobiological point of view, an impairment in social brain [7]. Some literature has also highlighted how social anxiety disorder may mask autistic traits (AT) among females [6]. Mild alterations in neurodevelopment may also lead to an enhanced self-focus and to mental rumination, resulting in intrusive thinking and cognitive inflexibility about body health or shape: this is in line with the literature that is suggesting a significant overlap between AT and eating disorders [8], as well as hypochondria or dysmophophobia [9]. Sometimes an association with neurological soft-signs can be also detectable [10]. Recently a growing body of studies stressed the importance of investigating mild symptoms of neurodevelopmental alterations, such as AT, due to their possible role in promoting different kinds of psychiatric disorders, including suicidal ideation and behaviours [11-14]. These autistic-like mild and atypical manifestations, behavioral traits and personality characteristics, seem to be distributed along the same continuum which includes, at its extreme end, the "ND" category of DSM-5 [6].

In the last decades several psychometric scales have been developed in order to assess AT [6]. These instruments show how AT may cross the border of ASD, showing overlapping features with other ND, as well as with adult psychoses (schizophrenia and bipolar disorders) and eating disorders [6]. AT are also considered a significant vulnerability factor towards life events [6 11]. This data is of specific interest considering the well-known role of traumatic experiences in precipitating the onset of psychopathology [6 15 16], leading to hypothesize interlaced relationships between AT and post-traumatic symptoms in shaping psychopathological trajectories [6 11].

From the "Neurodevelopmental Continuum" towards a "Neurodevelopmental gradient"

Since the 70's, the conceptual framework in which the DSMs have been developed is that each clinically defined psychiatric disease should have a discrete etiological basis. However, in the last decades increasing literature is suggesting that psychiatric disorders can be better conceptualized as a "neurodevelopmental continuum" (NC) [1 6]. According to this model, similar kinds of alterations, linked to neurodevelopment, may lead to several different functional outcomes and phenotypic expressions. Such different trajectories seem to be related to both specific genetic characteristics and possible environmental influences, as well as to the timing of expression in the lifespan [6]. The NC is a theoretical framework supported by several empirical evidences in multiple fields of research [2 6]. The conceptual core of the NC model is that an alteration in brain development, determined by the intertwined relationships between genetic and environmental factors, may constitute the common underpinning of many (eventually, all) mental disorders [2 6].

Moreover, the NC theory also implies that psychiatric disorders could be placed along a gradient of decreasing

neurodevelopmental impairment. A possible model for this gradient could be understood in these terms [2 6]:

- ASD with strong cognitive deficits (Kanner's type);
- ASD without mild/no cognitive deficits (Asperger's type);
- ADHD;
- intellectual disabilities;
- schizophrenia;
- eating disorders;
- bipolar disorders;
- anxiety disorders;
- vulnerability to traumatic experiences.

According to this hypothesis, the concept of ND should be rethought, in order to include also functional psychoses (schizophrenia and bipolar disorders), and to be considered as a predisposing factor which may open the way to the onset of several other disorders, such as eating or anxiety disorders, as well as featuring a higher vulnerability to traumatic experiences[6]. It is noteworthy that in this model specific attention is paid to the expression timing of the above mentioned disorders, which should be considered within a dimensional approach. The risk for developing clinical manifestations is not homogeneous across lifetime, featuring critical periods associated to both neurobiological and environmental factors, such as life events, but also to age-related and other subject-specific conditions. E.g., a psychotic break that happens in late childhood it is different from one occurring in adult life, in both terms of possible precipitating factors and possible impacts on the personality structure [6].

Neurodevelopmental disorders beyond the borders of DSM-5

As reported above, a mild alteration in neurodevelopment may prevent the subject from building an appropriate self-representation and a satisfying relational life, which may lead to different kinds of clinical expressions [2 4 5 6]. However, generally the onset of clinical manifestations in these cases does not occur in childhood, but in adolescence, when the subject must face new challenges, with a significant impact on the global adjustment [6]. The scientific and cultural framework within we may investigate the psychogenesis of the most dramatic psychiatric disorders, such as schizophrenia, bipolar disorders but also eating disorders, should focus on the role of a deficit in the proprioceptive experience, such as deficits in "feeling" our own body and its relationship with external space and past events [4]. For example, in eating disorders and self-injuring behaviours we may hypothesize an abnormal perception of patient's own body, including an altered reactivity towards pain [17]. In particular, in line with recent hypotheses from computational psychiatry, an alteration of the interoceptive system, with an impairment of the ability of inferring one self's states (as if they were of someone else) may be a common cognitive feature of apparently different disorders such as hypochondria or dysmorphophobia [4].

According to the current theoretical and nosographic framework, the clinical expression of ND is considered firmly separated from the major clinical manifestations typical of adult life. The separation could be related to age of onset (first years of life vs adolescence or youth). However, the most striking differences lie at the level of clinical presentation: symptoms such as delusions and hallucinations are usually described in adulthood, while they are not frequent in childhood (and in particular, they are not strictly included among the manifestations of ND as reported in DSM-5). It is specifically the primacy of these psychiatric symptoms that draws a line between ND and major psychoses such as schizophrenia or mood disorders. However, this marked distinction may fade when considering the shared presence, in the above mentioned conditions, of [10 18 19]:

- cognitive impairment, which is present before (and after) psychotic breakdown;
- neurodevelopmental delays;
- neurological soft signs;
- motor abnormalities;
- a long list of supposed "comorbidities" with neurotic symptoms and psychopathic traits;
- overlapping environmental (especially when related with early brain development) and genetic risk factors.

On the other hand, the possible trajectories of the NC are not limited to full-blown psychiatric conditions [6]. From a broader point of view, they may converge in [6 11]:

- A condition of significantly higher vulnerability towards the development of full-threshold psychiatric symptoms;
- A tendency to show greater difficulties in coping with traumatic experiences, to the point that almost all life experiences would be, in some way, "traumatic". This feature may be considered as the expression of an inability to face the experience of the world, and properly adjust to it, eventually reorganizing the perception of the personal world.

The environmental factors which may open the way towards a full-blown psychosis could be associated to the challenges of entering adult life. These latters may feature the confrontation with new kinds of intimate relationships, such as the sexual ones, the adjustment to work environment, the necessity to reach higher independence in daily life [6]. A psychotic episode could precipitate the premorbid condition of vulnerability and disrupt the previous functional adjustment (which was unstable from the beginning), promoting a further disorganization of the neurobiological asset. Psychotic symptoms may persist or not as residual symptoms after recovery; nevertheless they often lead to a worsening of the neurobiological and social functioning [18].

Concluding remarks

The conceptual framework here proposed may lead to significant changes in both research and clinical settings, including therapeutic and prevention strategies. The main assumption of this model lies in the recognition of several perceptive, cognitive and motor phenotypes which may co-occur in different clinical populations, with an evolution over anamnestic history. These phenotypes seem to share etiological and pathogenetic mechanisms, while the variables influencing their outcome may be identified in:

- the specific genetic asset of each person;
- the life-long interaction with environmental factors, including therapeutic strategies and the ability of the patient to seek help.

It is also possible to observe, through the lifespan, back and forth pathways along the neurodevelopmental gradient of clinical expressions, eventually providing a theoretical basis for a better understanding of the so called "rollback phenomenon", frequently observed in clinical practice [20]. Globally, this conceptualization challenges the idea of psychiatric disorders as discrete categories. It implies a paradigm shift from the current nosographic system towards a dimensional point of view, which would place psychiatric conditions in a ND continuum where the different shapes of psychopathology might be described as expressions of a specific "neurodevelopmental gradient".

Conflict of interest

The Authors declare to have no conflict of interest.

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Original article

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Fashion industry as a source of inspiration for the 'Mental Health Department 4.0': an overview

Summary

Objectives

To investigate the topic of creativity and innovation in psychiatry, with a focus on the Italian model of the mental health department.

Methods

This overview is based on books and papers purposely extracted from the national and international literature, published in the fields of psychiatry and economics, in English and Italian, without time limits, concerning the following topics: mental health care; mental health department; big data; creativity; innovation; Industry 4.0; fashion industry.

Results

The way data are collected, analysed and used to generate predictions in the fashion industry, namely in the fast fashion, may be a source of inspiration for Italian psychiatry, to innovate the model of the mental health department (MHD). This requires the ability to collect and process big data, by means of ad hoc data centers. Also, common software is required in each branch making up the MHD. The adoption of a broader approach to clinical practice based on projects (each project representing a user, and his/her family), rather than on problems/periods of life (i.e., childhood and adolescence vs adulthood, substance misuse vs psychiatric problems, psychological discomfort vs. psychiatric disorders, etc.) may help overcome some issues traditionally affecting psychiatry, e.g., the difficulty to close the gap between adult psychiatry and child and adolescent psychiatry, the difficult relationships between psychiatry and psychology, and the controversial concept of dual-diagnosis. A project-based approach may also foster the interplay with other Agencies and with Authorities.

Conclusions

To implement the 'mental health department 4.0', at least four issues are required: the implementation of data centers; the use of the same Information and Communication Technology system in each branch of the department; the generation of just in time outputs and data driven 'empirical responses' to mental health needs; the shift from a patient-centered system to a project-centered system. All this requires liaison functions and skills, as well.

Key words

Innovation • Mental health • Mental health department 4.0 • Fast fashion • Fashion industry

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Introduction

As psychiatrist who works at the interface between psychiatry and economics, I often notice a discrepancy concerning the relationship of both disciplines with contemporaneity. As far as economics is concerned, a topic regularly addressed in papers and seminars is the so called 'Fourth Industrial Revolution', based on the concept of 'Industry 4.0'. Originally conceived in Germany in 2011, the latter represents a radical shift in the industrial production implemented by the Western economies, in partic-

ular after the end (and possibly as a response to) the Great Recession. Industry 4.0 is based on the extensive use of cyber-physical systems, which generate and process big amounts of data in a very short time [1-4].
On the other hand, medicine seems still confined to the twentieth century. It is true that significant improvements have been made with the adoption of the managerial approach to healthcare in the early 1990s. Yet, it seems that the medical model is still relying (in the most virtuous cases) on an approach to production (of health interventions, services etc.) typical of the Second and Third Industrial Revolution, not fully in line with the deep changes occurred in our societies and economies in the last decades[4]. Similar considerations may be applied to psychiatry, and to the organizational model of the mental health department (MHD), experimentally implemented in Italy during the 1970s and 1980s, then widely adopted during the 1990s and the 2000s. To fill this gap, the debate concerning Industry 4.0 and the Fourth Industrial Revolution, as well as the innovation of new production strategies adopted by creative industries (such as fashion industry), may represent a source of inspiration for health services, namely for psychiatric ones, which face a steadily increasing workload, despite the spending review implemented in our country as main response to the recent economic crisis [5 6]. In this paper I will first summarise the evolution of the MHD in Italy from Act 180/1978 to the present, and I will then address the topic of innovation in the fashion industry, particularly with respect to fast fashion. Finally, I will end proposing to implement some features of the modern creative industry in the field of psychiatry, to innovate the model of the MHD and engineer the processes occurring in it, consistently with nowadays' needs. Such new approach to psychiatric services is tentatively named 'MHD 4.0'.

Methods

This overview is based on books and papers purposely extracted from the national and international literature, published in the fields of psychiatry and economics, in English and Italian, without time limits, concerning the following topics: mental health care; mental health department; big data; creativity; innovation; fashion industry. The literature was retrieved from Scopus and Web of Science using different combinations of the following keywords: "creativity", "fashion industry", "Industry 4.0"; "innovation", "psychiatry", "mental health", "mental health department". Moreover, a manual search on Google and reference lists of identified articles was carried out, and experts in the field of Italian psychiatry and innovation were consulted. Papers were selected by the author according to their relevance for the purpose of the present overview.

1978-2018: forty years of community mental health care in Italy

A 'great divide' may be identified in the history of Italian psychiatry, represented by Act 180/1978. The latter completely changed the ways mental health care was and still is delivered in our country. The main consequence of Act 180/1978 was to stop new admissions to the psychiatric hospitals (asylums), 'total institutions' which represented the main way to treat people affected by psychiatric disorders in Italy before 1978. Act 180/1978 did not close asylums, rather it prohibited new admissions to them, and fostered the implementation of small psychiatric units within the general hospitals. It took more than twenty years to close asylums, thanks to Decree 229/1999 (the 'third reform' of the Italian National Health System).
In the years following 1978, the development of psychiatric services in Italy was heterogeneous. In some regions a complex network of territorial and hospital units was created. Such network represented the model for the MHD, lately adopted at national level. On the other hand, other regions did not implement an adequate network of services for mental health care. The corollary of this was that big inequalities affected mental health care in Italy, both from the structural and functional standpoint [7].
To overcome this limitation, a first specific Plan [7] was made (1994-1996), with the aim of developing the MHD model in the whole country within 1996, i.e., to provide all twenty regions with adequate facilities to deliver psychiatric care. The MHD represents the way psychiatric facilities are organized inside Local Health Agencies, both at territorial as well as at hospital level. It is made up of four branches: community mental health centers, acute inpatient units placed within general hospitals, day-hospital facilities and residential facilities (Fig. 1). According to the Plan, five mandatory interventions had to be implemented. First, the organizational model of the MHD on the whole national territory. Second, specific interventions to overcome the issue of people admitted to psychiatric hospitals before Act 180/1978, who were still living there in the 1990s. Third, the promotion of an information system, to monitor expenditure in the field of mental healthcare, which may further represent a basis to establish cost centers. Fourth, the identification at national level of a system of quality indicators concerning mental health care. Fifth and final, the promotion of training initiatives for professionals consistent with the aims of the Plan.
Thanks to the first Plan, the organizational model of the MHD was developed in every Italian region. On the other hand, several needs were still to be met. For example, the absence of specific attention toward psychiatric problems concerning childhood and adolescence, a lack of systematic evaluation of resources allocated to mental health care and effectiveness of the interventions

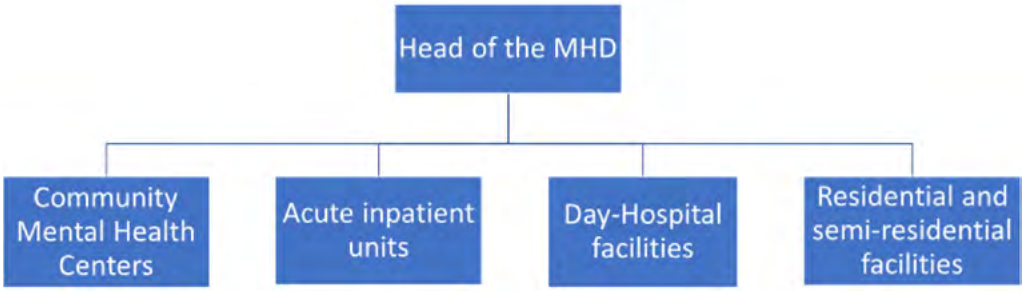

FIGURE 1. *The organizational model of the Mental Health Department (from Ministero della Salute, 1994; 1999, mod.)* [7 8].

implemented, a lack of adequate implementation of cost centers, and so forth. Therefore, another Plan (1998-2000) was made [8], which identified new aims concerning mental health care. For example, the implementation of primary, secondary and tertiary prevention programs, and of strategies to reduce suicides. This Plan confirmed the adoption of the organizational model of the MHD, and provided more details concerning role and function of the Director of the MHD, as well as of all facilities that make up the Department (Fig. 1). For each facility, detailed structural and organizational criteria were provided. Also, hints were provided concerning the relationships with universities and local authorities. It is worth noting that issues concerning Child-Adolescent Psychiatry were further developed by means of another, specific Plan [9].

To sum up, the first Plan (1994-1996) fostered the adoption of the MHD model, while the second Plan (1998-2000), provided more practical information concerning the way a MHD works, is structured and interplays with other branches of the health systems (e.g., primary care) or other Authorities. Finally, in March 2008 the Italian Ministry of Health approved the national guidance for mental health [10], that further integrate the first and second Plan.

In the light of the above, it is possible to conceive the MHD as shown in Figure I: an articulate, though static structure, featured by pros and cons. On the one hand, the organizational model of the MHD is able to cover all the areas and aims pointed out by the two Plans [7 8]. On the other, the structure is articulated and rigid, with possible problems of communication and misunderstandings between the different branches. The fact that this model is built according to static indicators (e.g., incidence and prevalence, population size, etc.) does not guarantee it is able to respond *just in time* to the actual burden of psychiatric disorders. In fact, the latter may vary quickly, depending on socio-economic changes, available resources, spending reviews, migrations, job losses, and so forth. Therefore, the model of the MHD as currently conceived seems not completely able to respond to the current state of psychiatry and its needs. To overcome such limitations, innovation is needed, though the current political and economic scenario makes it difficult. A possible solution is to look for hints for innovation in other fields, as the one of creative industry. In fact, the organizational model of the MHD as represented in Figure I is partly similar to the one of traditional fashion industry, frequently featured by a rigid separation between creative and sales units [11 12], few formal and informal contacts between the members of different units are few, and scarce amount of information directly exchanged [13].

From fast fashion to the Mental Health Department 4.0

The topic of innovation is detailed elsewhere [14-21]. For the purpose of the present paper, it is worth noting that innovation is linked to creativity [13]. The latter may be defined as "the production of novel and useful ideas in any domain" [11]. Fashion industry is part of the culture industry [22], which refers to "economic activities in which symbolic and aesthetic attributes are at the very core of value creation" [22]. Creativity and the search for novelty are essential features of the culture industry [23]. Yet, the deep changes occurred worldwide in the last decades, due to globalization, Information and Communication Technology (ICT) diffusion and, more recently, to the severe economic crisis, have fostered the search for a major integration of market knowledge into new product development processes [23 24]. An example of this is fast fashion, a production strategy adopted since the early 2000s by a group of firms such as Zara and H&M, different than the traditional production paradigm adopted by fashion industries (though the issue of anticipating and incorporating the market's needs in the implementation of new products features all industries, even those that do not adopt a fast fashion paradigm; the latter may be conceived as a specific way to face

the above mentioned contemporary challenges). Traditionally, fashion industry is featured by the production of one or two collections per year, separation of units (i.e., design, production, sales etc.) and longer times (seasons or years). Alternatively, fast fashion adopts a different production strategy, in which the collection is launched and then regularly modified according to the feedbacks of the sales. As a result, collections are changed every two weeks, and in a single year up to 12-24 collections may be produced and sold. It is therefore fundamental that design, production and marketing are tied together. Design is 'inspired' by what the market requires most in a certain period, and production has to quickly respond to both creative inputs and market requirements. What is typical of the fast fashion model is that shops are owned by the firm, because selling points are conceived as antennas, able to capture what products are sold most and provide the core of the creative industry (i.e., the design unit) with a big amount of data. In this model, products, namely clothes, may be conceived as probes, launched to collect data from the market. This provides the products with two different meanings. On the one hand, products are goods to sell, to generate a profit. On the other, they are a source of information. To sum up, the success of this model is based on three elements: data collection, data analysis and interpretation, and ability to test the hypothesis derived from the two previous points [25].

Collection and processing of data are key-issues of fashion industry, namely fast fashion, as well as the majority of industries in the Fourth Industrial Revolution. In this phase of capitalism, data are conceived as 'the new oil'. Therefore, data centers are the core of every type of industry, as well as Agencies operating in the healthcare field. Another key-issue is the use of data to generate new ideas to translate into new products as far as possible. This model of 'empirical response' to the market seems useful for healthcare systems as well, particularly for psychiatric services, to innovate the MHD. In this field, private profit may be replaced by the concept of efficiency. Therefore, following the metaphor of products as 'goods and probes', everything is done within a public service may be conceived at the same time as health intervention and source of information (data).

The idea of developing data centers within the MHDs is not new; it is consistent with the two above-mentioned Plans [7 8]. Yet, a hint for the innovation of MHDs is to develop data centers able to manage big data by means of specific algorithms, as currently done by social networks such as Facebook or big companies as Amazon. This also requires a radical shift: to conceive everything is done within a MHD as *a source of data*, in the same way as fast fashion considers products as probes, launched to gather data. This structural and functional organization may provide the management of the MHD with information that might be quickly implemented in the clinical practice, with a reduction of the lead time. Of course, it is necessary that all branches of the MHD use the same ICT system and software, to speed up communication, collaboration and integration between the parts.

A final step toward the MHD 4.0 is the implementation of a (clinical) project-centered system, rather than a patient-centered system. To better understand this issue, an example is useful. A patient-centered system means that the user is the 'unit of analysis' and of interest. All is planned around the person: family interventions, medical interviews, nurses' interventions, vocational rehabilitation, and so forth. Yet, this approach mirrors the bio-medical model focused on the disease (in this case, the psychiatric disorder), and the individual as person affected by it. On the one hand, such approach is useful, particularly when the workload does not exceed the professional group's capacity and resilience (i.e., those featuring the multidisciplinary équipe, made up of psychiatrists, nurses, educators, mental health technicians etc.). On the other hand, the patient-based model has some limitations, that become evident particularly with respect to the several branches making up the MHD. In fact, traditional issues concerning psychiatric services are represented by the transition from child-adolescent psychiatry to adult psychiatry, or the situation of a user that belongs at the same time to the caseload of two services, e.g., adult psychiatry and substance misuses services, as in the case of *dual diagnosis*. In such condition, as well as in others, the traditional MHD model, static, vertical, rigid, and patient-centered shows all its limitations.

A project-based approach postulates that multidisciplinary mini-équipes are built around the project, rather than the patient. The project starts when users or relatives meet (*even virtually*) any MHD facility for the first time. From that moment on, they will be part of the caseload of the Department, rather than to a single branch of it. Therefore, it is not the user that moves from one branch to another, according to his/her needs; rather, it is the équipe composition that changes, according to the user's needs, and moves, following the person. Also, it is not necessary that a user (i.e., a person affected by one or more psychiatric disorders) contacts the MHD. The project may start even when a user refuses to attend the community mental health service or other facilities. A corollary of all this is that case management and integration skills are required, a topic addressed in the next paragraph.

Table I summarizes the main features required by the MHD 4.0, shown in Figure II. As noticeable, the core of such model is the data center, rather than the top management. The center should be a multidisciplinary unit,

TABLE I. *Features of the Mental Health Department 4.0.*

Feature/action	Aim
Use the same ICT system and software	To foster quick communication, collaboration and integration between the branches of the MHD
Implementation of data centers	Data collection; development of specific algorithms for data analysis; generation of 'empirical responses' *(see text for details)*
Everything is a source of data	To improve data collection (quality and quantity)
Development of specific algorithms	To analyze and process big data
Shift from a patient-centered system to a project-centered system.	To reduce the gap between the branches of the MHD

made up of statisticians, engineers and mental health professionals (e.g., psychiatrists and nurses), specifically with clinical and liaison skills. It is fundamental that health professionals that participate to the data center be regularly in touch with the clinical practice, to properly interpret data analyzed by the algorithm.
It is important to acknowledge that previous experiences of integration within the MHD are reported in literature [26-29]. What the MHD 4.0 adds is the implementation and integration of cyber-physical systems to gather, manage and analyze big amount of data concerning clinical practice in psychiatry, to generate predictions with respect to incidence and prevalence of psychiatric disorders, as well as to the workload of the Department. The ultimate goal of this is to increase the efficiency of the health system.

Integration within the Mental Health Department 4.0

The engineering of processes within the MHD 4.0 requires adequate integrating skills and functions. Case management is an issue frequently referred to, and extensive literature is available on this topic [30]. This paragraph focuses on *liaison skills*, a transversal topic concerning case-management as well as communication between different professionals and integration of the several branches of the MHD. Again, fashion industry provides us with hints and suggestions [13].
Integration may be defined as the collaboration between professionals who work in differentiated units aiming "to achieve unity of effort" [31]. On the other hand, differentiation may be defined as "the status of segmentation of the organizational system into subsystems" [31]. In the organizational system of the MHD, sub-systems are represented by its four branches (Fig. 1). As in the fashion industry, even in the MHD knowledge integration mechanisms may be formalized, semi-formalized or informal. In the MHD, formal integration mechanisms are, for example, meetings between the managers of specific units; semi-formalized integration mechanisms may be represented by training courses and initiatives for the personnel. Finally, informal integration mechanisms may be represented by information or knowledge exchange between colleagues who meet in situations outside working hours. The three levels of integrations are featured by different cognitive distance and levels of time constraint [13]. Therefore, knowledge intermediaries are important actors within the organization (peculiarly in the fashion industry), able to reduce the cognitive distance between members of different units. The latter may present different ways of understanding and interpreting their experiences. Therefore, facilitators and translators are needed to bridge the cognitive distance, and foster integrations between different units [32 33]. Two types of knowledge intermediary may be identified: "knowledge facilitators" and "knowledge translators". The former are individuals who transfer knowledge across syntactic "unproblematic" boundaries among organizational units, while the latter are individuals who enable the flow of knowledge by removing semantic barriers [13 32-34].
From the current organization of MHDs as displayed in Figure 1, the importance of facilitators and translator roles in fostering the communication between each branch of the MHD stems out. It may be assumed that many cas-

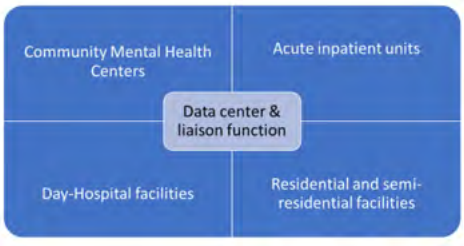

FIGURE 2. *The organizational model of the "Mental Health Department 4.0".*

es of "difficult patients" or difficult relationships between branches may be due to reduced/absence of integrative function, linked to a reduced facilitator/translator role. Therefore, it is essential to identify the mental health professionals who may exert this specific function as knowledge facilitators/translators, i.e., the integration between different units. On the other hand, it should be bared in mind that in psychiatry this role is not always represented or exerted by a specific professional, distinguished by the other mental health professionals. Besides being conceived as a professional role, it may also be conceived as a *function*, or a skill that each mental health professional should display in certain circumstances. With respect to this, it might be argued that this is typical of consultation-liaison psychiatry. Yet, rather than a sub-specialty, the latter should be conceived as a *forma mentis*, i.e., an attitude required in every field of psychiatry, and by every mental health professional [35]. This is a noticeable difference between fashion industry and the MHD 4.0. In fact, while in the fashion industry liaison roles are formalized, in psychiatry such roles may be displayed by all professionals (at least, in certain circumstances).

The last years have been featured by a severe economic crisis, with noticeable mental health outcomes for both the population and the mental health services [5 36-38]. Moreover, austerity measures were implemented, with noticeable consequences for the Italian National Health Service [6]. One of the strengths of the present paper is to suggest an organizational model that may help increase the efficiency of the MHD, in times of reduced funding and increased workload. Despite this, some major limitations of the present overview need to be acknowledged. First, due to the methods adopted, it is possible that not all relevant papers on the topic were included, since literature was not systematically investigated. Despite this, it was possible to address the topic of innovation in psychiatry, as well as the possibility to look for sources of innovation in other fields, such as the one of creative industry. Second, this paper mainly deals with issues concerning Italian psychiatry: therefore, it is possible that the findings here presented might be of limited interest for clinicians or researchers working in other countries. Yet, innovation remains a fundamental topic in Italy, concerning both the private and public sector. Third, in the present study the original model of the MHD as detailed in the two Plans was considered [7 8]. It could be argued that more articulated models are currently implemented, that address substance misuse, child and adolescence, and psychological issues by means of specific and integrated facilities [39]. Yet, the organizational model of the MHD 4.0 could be potentially applied even in the most advanced types of mental health care services. Fourth, this overview provided mainly speculations concerning the MHD 4.0, though no evidence or practical experience were provided. To overcome this major limitation, further studies are needed, to test the usefulness of the organizational model here proposed.

Conclusions

The present paper summed up the development of the MHD model, and suggested possible ways to innovate it, inspired by some features of production and management of innovation processes typical of the fashion industry, as well as by Industry 4.0. As a consequence, it was proposed to name this process of innovation 'MHD 4.0'. The latter may be helpful for users, families and services. The users and their family may receive more effective and tailored interventions, and may be actively involved by means of all technologies available in the contemporaneity (smartphones, apps, Social networks, etc.). Even professionals working in the MHD or at the interface with it may better their working conditions. Yet, it should be remembered that the balance between flexibility and precarity, and between smart work and increased workload is not an easy one. What may sound appealing for the organization might not be the same for workers. Moreover, some work features in the 21st century may turn into risk factors for burnout syndromes and depressive disorders[4]. Creativity may help, both to look for innovation as well as to foster health promotion and protection of both users and personnel. Not surprisingly, fashion industry was considered a source of innovation for the MHD. In fact, psychiatry as well may be conceived as a particular type of "creative industry", in which creative processes should be elicited and managed, since creativity, when appropriately guided and applied, is the main avenue toward mental health.

Conflict of interest

The Author declare to have no conflict of interest.

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Headache in paediatric and adult patients with Gilles de la Tourette syndrome

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Abstract

Objective

Gilles de la Tourette syndrome (GTS) is a neuropsychiatric disorder characterized by multiple motor and vocal tics and commonly associated with co-morbid conditions. Despite early reports of increased prevalence of headache in both children and adults with GTS, little is known about the nature of this co-morbidity. We conducted a collaborative study based in specialist clinics to compare the prevalence and characteristics of headache in paediatric and adult patients with GTS.

Methods

We assessed a total of 140 patients with GTS for the presence and characteristics of headache: 109 children and adolescents (age range 6-17 years) and 31 adults (age range 18-55, randomly selected from a clinical sample of 200 patients) seen at specialist clinics. A further comparison was performed between the group of adults with headache (n =15) and a subgroup of gender-matched children with headache (n =16).

Results

In our study, the prevalence of headache was 48.4% in adults with GTS and 22.9% in children with GTS (p = 0.01). Adults with GTS presented with higher tic severity and poorer quality of life compared to younger patients (p = 0.01). There was a significant difference in the headache types: tension type headache was significantly more commonly reported by adults with GTS, whereas migraine was significantly more commonly reported by children with GTS (p = 0.02). Adults with GTS and co-morbid headache consistently presented with higher tic severity and poorer quality of life compared to children with GTS and co-morbid headache (p = 0.01).

Conclusions

Headache is confirmed as a relatively common co-morbidity of GTS, particularly in adult patients seen at specialist clinics. The higher prevalence of headache in adults with GTS (especially tension-type headache) compared to younger patients could be related to higher tic severity and poorer quality of life in our adult clinical sample. If replicated, these findings can inform clinical practice in guiding targeted screening and management interventions for headache in patients with GTS across the lifespan.

Key words

Gilles de la Tourette syndrome • Tics • Headache • Children • Adults

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Introduction

Gilles de la Tourette syndrome (GTS) is a complex neurodevelopmental disorder characterized by the chronic presence of multiple motor tics plus at least one vocal tic [1 2]. The majority of patients with GTS present with co-morbid behavioural problems, especially obsessive-compulsive disorder (OCD) and attention-deficit and hyperactivity disorder (ADHD), as well as frequent affective symptoms and impulsivity [3]. Relatively little is known about the neurological co-morbidities of GTS, despite previous reports of neurological soft signs [4] and increased risk for common neurological conditions such as epilepsy [5]. The results of preliminary studies exploring the occurrence of headache in both children [6-8] and adults [7] with GTS

have raised the possibility of an increased risk across the lifespan. In order to better understand the relationship between GTS and headache, we conducted a collaborative study across specialist clinics to compare the prevalence and characteristics of headache in paediatric and adult patients with GTS.

Methods

A total of 140 patients with GTS were recruited for the present study. One hundred and nine children and adolescents with GTS (age range 6-17 years) were recruited from the specialist movement disorders clinics of the Child Neuropsychiatry Unit, University of Insubria (Varese, Italy), the 'C. Besta' Neurological Institute (Milan, Italy), and the University of Pavia (Pavia, Italy). Moreover, 31 adult patients with GTS (age range 18-55) were randomly selected from a larger clinical sample of 200 patients seen at the specialist Tourette syndrome clinic, Department of Neuropsychiatry, National Centre for Mental Health (Birmingham, United Kingdom).

All patients provided informed consent to participate in the study and were clinically evaluated by a neuropsychiatrist with experience in GTS, who collected a comprehensive medical and family history and reviewed comorbid diagnoses, including OCD and ADHD. The patients were assessed using the Diagnostic Confidence Index (DCI)[9], a clinician-rated measure of lifetime likelihood of GTS diagnosis in patients presenting with tic symptoms, based on the presence of specific clinical characteristics (including waxing and waning course, presence of premonitory urges, tic suppressibility) and selected complex tics (including coprolalia, echolalia, echopraxia, and palilalia). In total, the DCI covers 27 clinical features associated with GTS, all of which have a corresponding weighted score. The total DCI score is expressed as a percentage, with higher scores indicating higher confidence that the patient has GTS. In addition, the severity of tic symptoms was assessed using the Yale Global Tic Severity Scale (YGTSS) [10], a clinician-rated scale assessing the severity of both motor and vocal tics across five different domains: number, frequency, intensity, complexity, and interference. Each of these is scored from 0 to 5, and combined to produce a global tic severity score. An additional measure of overall impairment, which addresses functioning in social, academic and occupational environments, is scored from 0 to 50. These two scores are combined to produce the total YGTSS score, ranging from 0 to 100, with higher scores indicating increased tic severity. The Visual Analogue Scale (VAS) of the age-specific versions of the Gilles de la Tourette Syndrome-Quality of Life scale (GTS-QOL) was used to evaluate patient perception of health-related quality of life (HR-QOL) in both children and adults with GTS [11 12]. Self-rated VAS scores range from 0 to 100, with 100 indicating the highest possible satisfaction with life. Finally, all patients underwent a comprehensive neurological examination and were screened for the diagnosis of headache according to the clinical criteria detailed in the third edition of the International Classification of Headache Disorders (ICHD-3) [13].

Both clinician-rated and self-rated scores obtained from all young and adult patients were described and compared. Statistical analyses were performed using the PASW (SPSS) Statistics version 17.0.3 (IBM, New York, USA): Chi-Square analysis was used for categorical data, whereas continuous variables were assessed with parametric (Student t) and nonparametric (Mann-Whitney U and Wilcoxon) tests. P values inferior to 0.05 were considered statistically significant.

Results

Our clinical samples consisted of 31 adults with GTS (mean age 31.6 years, sd 10.0) and 109 children and adolescents with GTS (mean age 12.0 years, sd 2.7). The proportion of female patients was higher in the adult group compared to the children group (29.0% and 17.4%, respectively), although the difference was not statistically significant ($p = 0.15$). Likewise, there were no statistically significant differences in age at tic onset (8.3 years, sd 4.5 *versus* 6.2 years, sd 2.2; $p = 0.27$), family history of tics (48.4 *versus* 60.6%; $p = 0.23$), or psychiatric co-morbidities (OCD: 32.3 *versus* 33.0%; $p = 0.94$; ADHD: 29.0 *versus* 41.3%; $p = 0.22$), with the exception of depression (45.2 *versus* 8.3%; $p = 0.01$). The proportion of patients taking pharmacotherapy for their tic disorder was higher in the adult group compared to the children group (54.8 and 35.8%, respectively), although the difference was not statistically significant ($p = 0.06$). Likewise, there were no statistically significant differences in the proportions of patients taking typical antipsychotics (19.4 *versus* 24.8%; $p = 0.53$), atypical antipsychotics (32.3 *versus* 27.5%; $p = 0.61$), and alpha2-agonists (16.1 *versus* 6.4%; $p = 0.09$). Adults with GTS presented with higher tic severity and lower HR-QOL compared to younger patients. Specifically, the adult group had significantly higher YGTSS scores (61.2, sd 15.6 *versus* 50.6, sd 16.6; $p = 0.01$), as well as higher DCI scores (73.2, sd 21.6 *versus* 63.5, sd 16.3; $p = 0.05$), whereas comparison of self-report VAS scores showed that overall satisfaction with life was significantly lower in the adult group (55.2, sd 22.8 *versus* 69.8, sd 21.0; $p = 0.01$).

The adult cohort was characterised by a higher prevalence of headache (48.4 *versus* 22.9%; $p = 0.01$). A further comparison was performed between the group of adults with headache and a subgroup of gender-matched children with headache. With regard to headache type,

tension type headache was significantly more commonly reported by adult patients with GTS (p = 0.02), whereas migraine was significantly more commonly reported by children and adolescents with GTS (p = 0.02). Comparison of the headache characteristics (frequency and duration of headache episodes) between young and adult patients with GTS revealed no statistically significant differences between the two age groups. Adults with GTS and co-morbid headache consistently presented with higher tic severity (p = 0.01) and lower HR-QOL (p = 0.01) compared to children and adolescents with GTS and co-morbid headache (Table I).

TABLE I. *Comparison of young and adult patients with GTS and headache.*

Patient characteristics	Children (n = 16)	Adults (n = 15)	p value
Age (mean, sd)	12.0 (2.7)	31.6 (10.0)	0.01*
Female gender (n, %)	5 (31.2)	5 (33.3)	0.90
Age at tic onset (mean, sd)	6.1 (1.7)	8.9 (5.5)	0.13
Family history of tics (n, %)	9 (56.3)	6 (40.0)	0.37
OCD (n, %)	6 (37.5)	5 (33.3)	0.81
ADHD (n, %)	7 (43.8)	5 (33.3)	0.55
Depression (n, %)	3 (18.8)	6 (40.0)	0.19
Pharmacotherapy (n, %)	10 (62.5)	11 (73.3)	0.52
- Typical antipsychotic (n, %)	3 (18.8)	5 (33.3)	0.35
- Atypical antipsychotic (n, %)	8 (50.0)	7 (46.7)	0.85
- Alpha2-agonist (n, %)	1 (6.2)	4 (26.7)	0.12
YGTSS total (mean, sd)	47.8 (12.6)	60.8 (14.4)	0.01*
GTS-QOL VAS (mean, sd)	75.4 (19.7)	52.3 (22.1)	0.01*
DCI (mean, sd)	64.3 (19.5)	74.6 (20.2)	0.23
Headache type			
Migraine	11 (68.8)	4 (26.7)	0.02*
- Migraine with aura	3 (18.8)	1 (6.7)	0.25
- Migraine without aura	8 (50.0)	3 (20.0)	0.08
Tension type headache	5 (31.2)	11 (73.3)	0.02*
Headache frequency			
< 1/month	2 (12.5)	1 (6.7)	0.58
1-3/month	4 (25.0)	4 (26.7)	0.92
1/week	3 (18.8)	5 (33.3)	0.36
2-3/week	6 (37.5)	2 (13.3)	0.12
> 3/week	1 (6.2)	3 (20.0)	0.26
Headache duration			
< 30 minutes	3 (18.8)	2 (13.3)	0.68
30-60 minutes	3 (18.8)	2 (13.3)	0.68
1-2 hours	5 (31.2)	1 (6.7)	0.08
3-5 hours	2 (12.5)	3 (20.0)	0.57
6-12 hours	2 (12.5)	5 (33.3)	0.17
13-24 hours	1 (6.2)	2 (13.3)	0.50

**p < 0.05*

Abbreviations: GTS, Gilles de la Tourette syndrome; OCD, obsessive-compulsive disorder; ADHD, attention-deficit and hyperactivity disorder; YGTSS, Yale Global Tic Severity Scale; GTS-QOL VAS, Gilles de la Tourette Syndrome-Quality of Life Visual Analogue Scale; DCI, Diagnostic Confidence Index.

Discussion

The results of our study confirmed that headache is a relatively common problem in patients with GTS, particularly in adults seen at specialist clinics [6-8]. In our clinical samples, headache was reported in about 48% of adults with GTS and 23% of children and adolescents with GTS, suggesting that screening for headache and treatment interventions might be appropriate in this patient population across the lifespan.

In our study, the higher prevalence rate of headache (especially tension-type headache) in older patients could be related to the higher tic severity in the adult group. Overall, specialist clinics for adult patients with GTS tend to be accessed by the subpopulation of patients with persistently severe GTS throughout adulthood. Moreover, the smaller sample size in the adult group could have led to an overestimation of the prevalence of headache in this age group. Finally, our adult sample reported poorer HR-QOL and showed a trend towards a higher prevalence of co-morbid affective symptoms, compared to the younger sample. Our findings could complement the results of a recent study on a large sample of 401 patients with headache suggested that psychiatric symptoms and social stressors were associated significantly more often with tension-type headache than with migraine [14].

Our findings are in line with the results of previous studies suggesting a possible association between GTS and migraine. The hypothesis of a shared pathophysiological basis is in line with the available evidence of altered serotonin metabolism in both conditions [6 7]. A shared disturbance in the extrapyramidal system has also been proposed, based on neuroimaging findings about the involvement of basal ganglia-thalamocortical circuitries [15]. More recently, large scale genetic studies have found evidence for shared hereditability of GTS and migraine [16 17].

The main limitations of the present study include sample size (relatively small in both groups), generalisability (limited by referral bias across specialist clinics), and inter-rater reliability (potentially sub-optimal). Our findings prompt further research into the link between GTS and headache. Specifically, replication of our results on the differential prevalence and characteristics of headache in patients with GTS across the lifespan could inform more targeted screening and treatment interventions. This is particularly relevant as pharmacological studies have identified medications, such as the antiepileptic drug topiramate, that are effective in the treatment of both headache (migraine prophylaxis) and GTS (tic control) [18]. Finally, further research is needed to test the existing hypotheses on the possibility of shared underlying mechanisms between GTS and headache.

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Conflicts of interest

The Authors declare to have no conflict of interest.

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Original article

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The Inter-Rater Reliability and convergent validity of the Italian translation of the Structured Clinical Interview for the DSM-5 Alternative Model of Personality Disorders Module III in a psychotherapy outpatient sample

Summary

Objectives

The present study aimed at assessing the inter-rater reliability of the Italian translation of the Structured Clinical Interview for the DSM–5 Alternative Model of Personality Disorders Module III (SCID-5-AMPD-III), the convergent validity of the SCID-5-AMPD-III personality disorder (PD) diagnoses with respect to the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5) Section II PD diagnoses, and the frequency of multiple PD diagnoses in a clinical sample of adult participants who were voluntarily asking for psychotherapy.

Methods

We relied on a pairwise interview design to assess the inter-rater reliability of the SCID-5-AMPD-III PD diagnoses in a sample of 84 adult clinical participants (53.6% female; participants' mean age = 36.42 years, SD = 12.94 years) who voluntarily asked for psychotherapy treatment.

Results

Our findings showed that the SCID-5-AMPD-III PD diagnoses were provided with adequate inter-rater reliability (median Cohen's k = .83). Convergent validity data for the SCID-5-AMPD-III PD diagnoses were also encouraging (median Cohen's k = .54). Substantial agreement was observed between the SCID-5-AMPD-III and the SCID-5-PD on the frequency of multiple PD diagnoses (Cohen's k value = .62).

Conclusions

Our data support the hypothesis that the SCID-5-AMPD-III PD diagnoses are provided with adequate inter-rater reliability and convergent validity with SCID-5-PD diagnoses, at least among Italian clinical adult participants.

Key words

Structured Clinical Interview for the *DSM-5* Alternative Model of Personality Disorders Module III • SCID-5-AMPD Module III • Inter-Rater Reliability • Adult Clinical Participants

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Introduction

To overcome the difficulties (e.g., lack of empirically validated cut-offs, high co-occurrence rates among PDs, within-PD heterogeneity) with the categorical model of personality disorders (PDs; see [1], for a review), the Fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-5* [2]) provided the Alternative Model of Personality Disorder (AMPD) in Section III, "Emerging Measures and Models" (pp. 761-781), while retaining the criteria for categorical personality disorder (PD) diagnoses listed in *DSM-IV* Axis II [3] in *DSM-5* Section II.

The *DSM-5* AMPD adopts a dimensional conceptualization of personality pathology, which is based on two main criteria: (A) personality-functioning impairment, and (B) personality-trait pathology. Personality-functioning impairment (i.e., Criterion A) considers two higher order domains: (a) self, including the two subdomains of identity and self-direction; and (b) interpersonal, including the two subdomains of empathy and intimacy [2]. Criterion B, personality-trait pathology, is based on a hierarchical trait model with five dysfunctional personality domains and 25 dysfunctional personality traits. A score of 2 (i.e., moderate impairment) or greater on the Level of Personality Functioning Scale (LPFS [2]) was considered suggestive of clinically-relevant personality-functioning impairment.

The LPFS assesses impairments of 12 subdomains of personality functioning organized within four main domains: identity, self-direction, empathy, and intimacy [2]. LPFS scores range from *0 (little or no impairment)* to *4 (extreme impairment)*; the threshold for PD diagnosis is set at LPFS Level 2 *(moderate impairment)*, as this was intended to maximize the sensitivity and specificity of PD identification 4. Rather, to assess *DSM-5* AMPD Criterion B, a dimensional model of pathological personality traits was constructed along with a corresponding instrument named the Personality Inventory for *DSM-5* (PID-5 [5]). The presence of a LPFS score ≥ 2 and one or more dysfunctional personality traits listed in the *DSM-5* AMPD Criterion B were deemed to be necessary for the PD Trait-Specified (PD-TS) diagnosis 2.

As Clark and colleagues [6] acutely pointed out, the *DSM-5* AMPD could have been conceptualized as purely dimensional, with a PD diagnosis specified by individuals' domains and severity of both their personality-functioning impairment and their pathological trait(s). According to this perspective, only PD-TS diagnosis would be necessary to fully capture individuals' unique characteristics [6]. Indeed, a substantial body of literature documented that PDs are likely to be dimensional in nature [7]; however, to ease the transition to the new conceptualization, the *DSM-5* Personality and PD Work Group derived a hybrid model by mapping six of the *DSM-5* Section II PD categorical diagnoses – namely, Antisocial, Avoidant, Borderline, Narcissistic, Obsessive-Compulsive, and Schizotypal PDs – using the *DSM-5* AMPD model of impairment in personality functioning and dysfunctional traits [6].

Four disorders were excluded from this hybrid model on the basis of the simplicity of their trait component (e.g., histrionic PD is essentially captured by emotional lability and attention seeking) and limited empirical validity [6 8]. Finally, a diagnosis of PD-TS was provided to denote personality trait-and-functioning pathology in the absence of one of the six specified PDs.

For each of the six PD diagnosis, the *DSM-5* AMPD [2] indicates the moderate or greater typical impairment in personality functioning, manifested by characteristic difficulties in two or more of the identity, self-direction, empathy and intimacy areas, as well as pathological personality traits that should be elevated in order to meet criteria for diagnosis. Individuals who have a pattern of impairment in personality functioning (i.e., Criterion A) and maladaptive traits (i.e., Criterion B) that matches one of the six defined personality disorders should be diagnosed with that PD [2]. For instance, typical features of Narcissistic PD are variable and vulnerable self-esteem, with attempts at regulation through attention and approval seeking, and either overt or covert grandiosity [2]. Difficulties characterizing Narcissistic PD are apparent in identity, self-direction, empathy, and/or intimacy (i.e., Criterion A), along with specific maladaptive traits (Attention Seeking and Grandiosity) in the domain of Antagonism [2].

A number of psychometrically-sound measures were developed to provide self-reports (e.g., [9-12]) and clinicians ratings [13 14] of the *DSM-5* AMPD Criterion A. The PID-5 was provided with strong empirical support (e.g., [15]) and cross-cultural validity [16] as a measure of the *DSM-5* AMPD Criterion B domains and traits.

Although the LPFS represented a synthesis of clinician-administered measures for assessing personality functioning into a composite model [4], different from the PID-5 for Criterion B, no method provided a comprehensive assessment of the proposed constructs (Morey, 2018).

Moreover, as Morey [12] nicely pointed out no instrument was designed to simultaneously assess both Criterion A and Criterion B of the *DSM-5* AMPD, while also evaluating the six categorical PD diagnoses that were retained in the *DSM-5* AMPD. With this purpose in mind, First and colleagues [17] developed the Structured Clinical Interview for the *DSM-5* Alternative Model for Personality Disorders (SCID-5-AMPD [17]).

The SCID-5-AMPD is a semi-structured diagnostic interview to guide the assessment of the severity of impairment in personality functioning according to the LPFS (assessed in SCID-5-AMPD Module I), the 25 pathological personality trait facets (assessed in SCID-5-AMPD Module II), as well as the six specific personality disorders and the PD-TS diagnosis (assessed in SCID-5-AMPD Module III). Therefore, a unique component of SCID-5-AMPD is its Module III (SCID-5-AMPD-III), which facilitates the evaluation of the specific diagnoses listed in *DSM-5* AMPD allowing to assess Criterion A (required impairments in personality functioning) and Criterion B (required pathological personality trait facets) for each of the six specific diagnoses of the AMPD [17]. If full criteria are not met for any of the specific PDs, PD-TS diag-

nosis is considered based on a determination of at least moderate impairment in personality functioning from the Criterion A assessments and the presence of at least one pathological personality trait based on the Criterion B trait evaluation [17].

The modular format of the SCID-5-AMPD allows the researcher or clinician to focus on those aspects of the AMPD of most interest [17]. For instance, Christensen and colleagues [18] focused on the SCID-5-AMPD Module I and examined the reliability of its Norwegian translation showing that it was provided with adequate interrater reliability with intraclass correlation coefficient (ICC) values ranging from .89 to .95 for LPFS domains (ICC = .96 for the LPFS total score), at least when it was assessed relying on the video-recording method. Moreover, ICC ranging from .59 to .90 were observed for LPFS domains (LPFS total score ICC value = .75) when the SCID-5-AMPD Module I test–retest reliability was assessed according to a short term (maximum interval between interviews = 2 weeks) design [18].

Notwithstanding Christensen and colleagues' [18] encouraging findings, to the best of our knowledge, no further study examined the psychometric properties of the SCID-5-AMPD. Moreover, although numerous previous studies have examined the convergence between the AMPD proposed trait facets (i.e., Criterion B) and the Section II PDs they are meant to capture [19] (see [20] for a meta-analysis), a lesser number of studies (e.g., [21]) examined the degree to which the proposed *DSM-5* AMPD diagnoses converge with *DSM-5* Section II PD diagnoses. Indeed, the relevance of this issue should not be neglected since the six categorial PD diagnoses were retained in the *DSM-5* AMPD with the aim of easing transition to the new conceptualization of practitioners who were used to rely on the *DSM-IV* axis II/ *DSM-5* Section II categorical PD diagnoses. Despite its immediate clinical pragmatic usefulness, this issue may be helpful in order to start evaluating the potential challenges (e.g., [22,23]) inherent to current categorical approaches to PD diagnosis, including AMPD (e.g., Clark et al., 2015). For instance, Clark and colleagues [6] provided convincing evidence that the proposed PD-TS diagnosis may offer a more straightforward method to PD diagnosis than relying on specific PDs with unique trait criterion sets, also removing the dependency on fallible PD constructs with questionable validity support (see also [20]).

Starting from these considerations, we designed the present study with three major purposes. First, we aimed at assessing the inter-rater reliability of AMPD diagnoses as they were assessed by the Italian translation of the SCID-5-AMPD Module III in a clinical sample of adult participants who were voluntarily asking for psychotherapy. We also assessed the convergent validity of the SCID-5-AMPD-III PD diagnoses with respect to the *DSM-5* Section II PD diagnoses that were based on the Italian translation [24] of the Structured Clinical Interview for *DSM-5* Personality Disorders (SCID-5-PD [25]). Finally, the base rate estimates of the six SCID-5-AMPD-III categorical PD consensus diagnoses and the corresponding SCID-5-PD-III categorical PD diagnoses was computed; moreover, the base rate estimate for any SCID-5-AMPD-III categorical PD diagnosis was compared to the base rate for any categorical SCID-5-PD.

In the present study, we relied on a pairwise interview design to assess the inter-rater reliability of the SCID-5-AMPD-III (as well as SCID-5-PD) diagnoses. Participants were administered the second interview roughly 48 hours after the first interview; the interview order was randomized and counterbalanced. For each participant, two raters were randomly extracted to administer the SCID-5-AMPD-III, and two different raters were randomly extracted to administer the SCID-5-PD. For both interviews, each rater acted as interviewer and observer roughly the same number of times. Each SCID-5-AMPD-III interview was rated independently by the corresponding interviewer and observer; an identical procedure was used for the SCID-5-PD ratings. For each participant, the SCID-5-AMPD-III was administered and scored by raters who were blind to the SCID-5-PD rating; similarly, the SCID-5-PD was administered and scored by raters who were blind to the participant's SCID-5-AMPD-III ratings.

Methods

Participants

The sample was composed of 84 adult participants who were consecutively admitted to the Clinical Psychology and Psychotherapy Unit of San Raffaele Turro Hospital from December 2018 to July 2019. Forty-five (53.6%) participants were female and 39 (46.4%) were male; participants' mean age was 36.42 years, *SD* = 12.94 years. Forty-two (50.0%) participants were single, 36 (42.8%) participants were married, 5 (6.0%) participants were divorced, and one (1.2%) participant was widow. Twelve (14.3%) participants had junior high school degree, 50 (59.5%) participants had high school degree, and 22 (26.2%) participants had university degree. Thirty-two (38.1%) participants received at least one *DSM-5* Section II non-PD psychiatric diagnosis; in this sample, depressive disorders (*n* = 16, 19.0%) and substance abuse disorders (*n* = 16, 19.0%) were the most frequently diagnosed *DSM-5* Section II non-PD psychiatric diagnosis. *DSM-5* Section II non-PD psychiatric diagnoses were assessed by trained clinical psychologists during their initial assessment interviews; since *DSM-5* Section II non-PD psychiatric diagnoses were not the

primary focus of this research, they were used mainly for descriptive purposes in the current study.
All participants were admitted to the Clinical Psychology and Psychotherapy Unit in order to receive psychotherapy treatment for interpersonal difficulties and/ or problems with behavior and emotional regulation on a strictly voluntary basis; inpatient participants were referred to the Unit by the clinicians who were following them in treatment. Potential participants were screened for the following exclusionary criteria: (1) age less than 18 years; (2) IQ less than 80; (3) diagnosis of schizophrenia, schizoaffective disorder, schizophreniform disorder, or delusional disorder according to *DSM-5* diagnostic criteria; (4) diagnosis of dementia or organic mental disorder according to DSM-IV diagnostic criteria; (5) education level lower than elementary school, and (6) the absence of acute symptom remission. All participants in the current research passed this screen. Participants with psychiatric disorder diagnoses were administered the SCID-5-AMPD-III and the SCID-5-PD after acute symptom remission according to the judgment of the clinicians who were following them in treatment to avoid confounding effects of non-PD psychiatric disorders on these measures [26].

Procedures

All participants volunteered to take part in the study after being presented with a detailed description and all were treated in accordance with the Ethical Principles of Psychologists and Code of Conduct; none of the participants received an incentive, either directly or indirectly for participating, and were administered all measures as part of their routine clinical assessment. Participants were administered the SCID-5-AMPD-III and the SCID-5-PD as part of routine clinical assessment and blind to the aim of the present study; interviewers (PsyD trainee) were also kept blind to the aim of the study (they were required to perform pairwise interviews with independent rating as part of their routine training). Since 10 graduate psychologists in their first year of training as clinical psychologists (PsyD) trained in administering the SCID-5-AMPD and SCID-5-PD participated in the present study, we used a pairwise interview design in order assess the inter-rater reliability of the SCID-5-AMPD diagnoses. Raters were paired randomly. Each rater served approximately equally as interview and observer. The participant attribution to interview-observer pairs was randomized by consecutive admission.

Measures

Structured Clinical Interview for the DSM-5 Alternative Model for Personality Disorders Module III (SCID-5-AMPD-III [17])

The SCID-5-AMPD-III is a semi-structured interview that allow to assess the six specific PDs and PD-TS that are included in the *DSM-5* AMPD. After the *General Overview* for the SCID-5-AMPD, Module III began with eight *Preliminary Questions About View of Self and Quality of Interpersonal Relationships*; then, the interviewer had to continue with the assessment of Criterion A and Criterion B for each of the six specific *DSM-5* AMPD PDs; afterward, the assessment of the two personality trait facets not associated with any specific personality disorder (Submissiveness and Distractibility) needs to be carried out. Finally, suggested interview questions are provided to assist the interviewer in determining whether the General Criteria for PDs are met. For those individuals who have a pattern of impairment in personality functioning and maladaptive traits that does not meet the diagnostic criteria for one or more of the six defined PDs, the interviewer considers whether the diagnosis of PD-TS applies. Finally, the interviewer uses the LPFS for rating the interviewee's level of functioning according to the interviewer's overall judgment regarding the level of functioning. In line with SCID-5-PD, the order of *DSM-5* AMPD PDs assessment in the SCID-5-AMPD is different from the order of presentation in *DSM-5* AMPD to avoid assessing the more challenging personality disorders first (e.g., Antisocial PD).

Structured Clinical Interview for DSM-5 Personality Disorders (SCID-5-PD 25)

The SCID-5-PD is a 119-item semi-structured interview designed to assess the 10 *DSM-5* PDs in Clusters A, B, and C. In the present study, the SCID-5- PD was preceded by the administration of its self-report screening questionnaire (SCID-5-SPQ). SCID-5-PD enables direct probing of negative SCID-5-SPQ answers when this is considered clinically relevant for assessing the 10 *DSM-5* PDs. Previous studies [24] showed that the Italian translation of the SCID-5-PD was provided with adequate psychometric properties.

Data analysis

Cohen's *k* coefficient was used to assess the interrater reliability of SCID-5-AMPD-III (and SCID-5-PD categorical diagnoses). Cohen's *k* coefficient was computed only for those PDs that were diagnosed at least five times by either interviewer or observer. Intraclass correlation coefficient was computed as an index of inter-rater reliability for the number of SCID-5-AMPD-III categorical PDs. In the present study, odds ratio (OR) was used as a measure of association for SCID-5-AMPD-III PD diagnoses. The inter-rater reliability of the individual criteria of the SCID-5-AMPD-III PD diagnoses was evaluated calculating Cohen's linearly weighted *k* coefficient (k_w). Cronbach's α coefficient was used to assess the internal consistency reliability of the SCID-5-AMPD-III and SCID-5-PD diagnoses. Finally, the McNemar test was computed to test the difference between paired proportions (i.e., the base

rate estimate for any PD diagnosis between SCID-5-AMPD-III and SCID-5-PD interviews).

Results

The frequencies, base rate estimates, agreement indices and inter-rater reliability coefficient (Cohen's *k*) values for the SCID-5-AMPD-III categorical diagnoses are summarized in Table I. As it can be observed in Table I, Cohen's *k* values indicate that all SCID-5-AMPD-III PD diagnoses could be safely reproduced across independent raters. Only two participants received a SCID-5-PD Schizotypal PD diagnosis by either Rater 1 or Rater 2; thus, Cohen's *k* coefficient could not be computed. Rather, the PD-TS diagnosis is included only in the SCID-5-AMPD-III. The intraclass *r* value for the number of SCID-5-AMPD-III categorical PDs that were diagnosed by Rater 1 (*M* = 1.15, *SD* = 1.07) and Rater 2 (*M* = 1.14, *SD* = 0.95), respectively was .84, 95% CI = .77, .90. The average administration time for the SCID-5-AMPD-III was 99.40 minute, *Mdn* = 90.00 minutes, *SD* = 15.45 minutes.

The inter-rater reliabilities (i.e., Cohen's linearly weighted *k* coefficient values) for the individual criteria of the SCID-5-AMPD-III PD diagnoses are summarized in Table II. As shown in Table II, good-to-excellent agreement [31 32] was observed for the large majority (i.e., 94.6%) of SCID-5-AMPD-III indicators. In the present study, the inter-rater reliability estimate (i.e., Cohen's k_{w} coefficient) of the Level of Personality Functioning Scale score between Rater 1 (*Mdn* = 2.00, *SD* = 0.90) and Rater 2 (*Mdn* = 2.00, *SD* = 0.86) was .87, $p < .001$.

Considering the SCID-5-AMPD-III PD consensus diagnoses, the average co-occurrence rate estimates (i.e., the average rate of co-occurrence of each SCID-5-AMPD-III PD with all the remaining five SCID-5-AMPD-III PD diagnoses) were 28.20, 31.10, 20.70, 27.60, 35.00, and 16.00% for Avoidant PD, Obsessive-Compulsive PD, Narcissistic PD, Borderline PD, Antisocial PD, and Schizotypal PD, respectively (median co-occurrence rate = 27.90%). Significant associations were observed between Avoidant and Borderline PDs, OR = 3.69, 95% CI = 1.19, 11.41, Narcissistic and Borderline PDs, OR = 3.33, 95% CI = 1.20, 9.17, and Borderline and Antisocial PDs, OR = 6.25, 95% CI = 1.35, 28.98 (Tab. III).

Discussion

To the best of our knowledge, the present study represents the first attempt at testing the psychometric properties of the SCID-5-AMPD-III. Confirming and extending previous findings on the SCID-5-AMPD Module I [18], our data seemed to show that the SCID-5-AMPD-III is provided with adequate inter-rater reliability, at least in a study group of Italian participants who voluntarily asked for psychotherapy treatment. Convergent validity data for the SCID-5-AMPD-III PD diagnoses were also encouraging, particularly when compared to

TABLE I. *The Structured Clinical Interview for DSM-5 Alternative Model of Personality Disorders – Module III: Personality Disorder Diagnosis Base Rate Estimates, Agreement Indices, Inter-Rater Reliability Coefficient (Cohen's k) Values, and Structured Clinical Interview for DSM-5 Personality Disorders Cohen's k Values (n = 84).*

	Rater 1		Rater 2		Agreement Indices and Inter-Rater Reliability coefficients								SCID-5-PD
SCID-5-AMPD-III PD Diagnoses	*N*	%	*N*	%	O-	E-	O+	E+	O	E	*k*	95% CI	*k*
Avoidant	17	20.2	16	19.0	98.5	67.2	94.1	10.9	98.8	68.4	.96	.89, 1.00	1.00
Obsessive-Compulsive	8	9.5	13	15.5	93.4	77.6	61.5	6.3	94.1	78.0	.73	.51, .95	.56
Narcissistic	29	34.5	28	33.3	91.4	49.3	84.0	20.4	94.1	55.2	.87	.76, .98	.78
Borderline	21	25.0	18	21.4	92.5	62.3	77.3	13.0	94.1	64.3	.83	.69, .97	.89
Antisocial	7	8.3	4	4.8	96.3	87.7	57.1	3.1	96.4	87.7	.71	.40, 1.00	.92
Schizotypal	5	6.0	6	7.1	98.7	87.7	83.3	3.4	98.8	87.8	.90	.71, 1.00	--
Trait-specified	17	20.2	17	20.2	91.4	66.3	70.0	11.3	92.9	67.7	.78	.61, .95	--
Mdn	--	--	--	--	93.4	67.2	77.3	10.9	94.1	68.4	.83	.69, .98	.89
Any PD diagnosis	63	75.0	67	79.8	81.0	12.6	94.0	63.0	95.2	64.9	.86	.74, .99	.82

Note. SCID-5-AMPD-III: Structured Clinical Interview for DSM-5 Alternative Model of Personality Disorders – Module III; SCID-5-PD: Structured Clinical Interview for DSM-5 Personality Disorders; PD: Personality Disorder; k: Cohen's k; O-: Percentage of Observed Negative Agreement; E-: Percentage of Expected Negative Agreement; E+: Percentage of Expected Positive Agreement; O+: Percentage of Observed Positive Agreement; O: Percentage of Observed Agreement; E: Percentage of Expected Agreement; 95% CI: 95% confidence interval for SCID-5-AMPD-III Cohen's k ; --: statistic not computed; Mdn: median value.

TABLE II. *Structured Clinical Interview for DSM-5 Alternative Model of Personality Disorders: Individual Criterion A and Criterion B Indicator Inter-Rater Reliability Index (i.e., Cohen's linearly weighted k Coefficient) Values (n = 84).*

Criterion A	k_w	Criterion B	k_w
Avoidant PD		**Avoidant PD**	
Identity	.81	Anxiousness	.69
Self-direction	.76	Withdrawal	.71
Empathy	.72	Anhedonia	.73
Intimacy	.63	Intimacy avoidance	.73
Obsessive-compulsive PD		**Obsessive-compulsive PD**	
Identity	.74	Rigid perfectionism	.64
Self-direction	.75	Perseveration	.70
Empathy	.66	Intimacy avoidance	.69
Intimacy	.67	Restricted affectivity	.67
Narcissistic PD		**Narcissistic PD**	
Identity	.68	Grandiosity	.72
Self-direction	.63	Attention Seeking	.69
Empathy	.56		
Intimacy	.61		
Borderline PD		**Borderline PD**	
Identity	.78	Emotional lability	.64
Self-direction	.72	Anxiousness	.52
Empathy	.69	Separation insecurity	.70
Intimacy	.64	Depressivity	.64
		Impulsivity	.76
		Risk taking	.73
		Hostility	.65
Antisocial PD		**Antisocial PD**	
Identity	.68	Manipulativeness	.73
Self-direction	.68	Callousness	.72
Empathy	.71	Deceitfulness	.82
Intimacy	.75	Hostility	.63
		Risk Taking	.61
		Impulsivity	.56
		Irresponsibility	.74
Schizotypal PD		**Schizotypal PD**	
Identity	.75	Cognitive dysregulation	.64
Self-direction	.66	Unusual beliefs	.72
Empathy	.70	Eccentricity	.67
Intimacy	.79	Restricted affectivity	.70
		Withdrawal	.65
		Suspiciousness	.75
		Other Criterion B Traits	
		Submissiveness	.63
		Distractibility	.68

Note. *PD: Personality Disorder; k_w: Cohen's linearly weighted k coefficient; all k_w ps <.001.*
The internal consistency reliability coefficient (i.e. Cronbach's a) values, base rate estimates, agreement indices, and convergent validity coefficient (i.e., Cohen's k) values of the SCID-5-AMPD-III and SCID-5-PD consensus diagnoses are summarized in Table III. On average, the convergent validity between SCID-5-AMPD-III PD diagnoses and SCID-5-PD diagnoses was moderate, with a median k value of .54. According to SCID-5-AMPD-III, 24 participants (28.6%) received two or more PD diagnoses, whereas 18 participants (21.4%); the corresponding Cohen's k value was .62, 95% CI = .43, .81. In our sample, the average number of SCID-5-AMPD-III PD diagnoses was 1.17 (SD = 1.06), whereas the mean number of SCID-5-PD diagnoses was 0.94 (SD = 0.90), with a convergent validity estimate (intraclass r coefficient) of .73, 95% CI = .61, .81. Interestingly, the base rate estimate for any PD diagnosis was not significantly different between SCID-5-AMPD-III and SCID-5-PD interviews, McNemar test 2-tailed p >.34. Thus, our data seemed to suggest that relying on the SCID-5-AMPD-III or on the SCID-5-PD does not result in an increased overall rate of PD diagnoses.

TABLE III. *Structured Clinical Interview for DSM-5 Alternative Model of Personality Disorders-Module III and Structured Clinical Interview for DSM-5 Personality Disorders Consensus Diagnoses: Internal Consistency Reliability Coefficient (i.e., Cronbach's a) Values, Base Rate Estimates, Agreement Indices, and Convergent Validity Coefficient (i.e., Cohen's k) Values (n = 84).*

	SCID-5-AMPD-III			SCID-5-PD			Agreement indices						Convergent validity	
PD diagnoses	α	*N*	%	α	*N*	%	O-	E-	O+	E+	O	E	*k*	95% CI
Avoidant	.87	17	20.2	.76	8	9.5	88.2	73.6	47.1	6.9	89.3	74.1	.59†	.35, .82
Obsessive-compulsive	.79	9	10.7	.42	8	9.5	86.4	81.6	21.4	5.3	86.9	81.8	.28*	.00, .59
Narcissistic	.85	30	35.7	.77	34	40.5	76.3	44.7	64.1	23.4	83.3	52.7	.65†	.48, .82
Borderline	.87	21	25.0	.87	19	22.6	88.2	61.5	66.7	13.5	90.5	63.7	.74†	.57, .91
Antisocial	.93	8	9.5	.85	7	8.3	91.3	83.6	36.4	4.7	91.7	83.7	.49†	.16, .81
Schizotypal	.86	5	6.0	.71	2	2.4	94.0	91.9	16.7	1.7	94.1	92.0	.26*	.00, .70
Mdn	.86	--	--	.77	--	--	88.2	77.6	41.8	6.1	89.9	78.0	.54†	.26, .81
Any PD diagnosis	--	64	76.2	--	60	71.4	63.0	14.9	85.1	58.4	88.1	68.2	.69†	.52, .86

Note. SCID-5-AMPD-III: Structured Clinical Interview for DSM-5 Alternative Model of Personality Disorders – Module III; SCID-5-PD: Structured Clinical Interview for DSM-5 Personality Disorders; PD: Personality Disorder; a: Cronbach's a; k: Cohen's k; O-: Percentage of Observed Negative Agreement; E-: Percentage of Expected Negative Agreement; E+: Percentage of Expected Positive Agreement; O+: Percentage of Observed Positive Agreement; O: Percentage of Observed Agreement; E: Percentage of Expected Agreement; 95% CI: 95% confidence interval for Cohen's k ; --: statistic not computed; Mdn: median value.
** p < .05; † p < .001.*

convergent validity coefficients that were usually reported for *DSM-IV* axis II PD diagnoses [27 28].

Of course, our findings should not be considered as evidence for the validity of the categorical PD diagnoses; we would like to stress that a number of taxometric studies consistently documented the dimensional nature of PDs [7] and the clinical usefulness of dimensional models of personality dysfunction has also been demonstrated [1 6 22 29]. Rather, our data seem to suggest that the SCID-5-AMPD-III may represent a reliable measure to help clinicians shifting from the typological model of PD assessment to the dimensional model included in the *DSM-5* AMPD, while providing a reliable alternative to the *DSM-5* Section II PD diagnoses in clinical decision making or in the forensic assessment.

Although the use of a joint-interview design might have spuriously increased our inter-rater reliability estimates [30], our data seemed to indicate that all SCID-5-AMPD-III PD diagnoses could be safely reproduced across independent raters. Moreover, the Cohen's *k* values indexing the inter-rater reliability of the SCID-5-AMPD-III PD diagnoses were roughly of the same size of those that were observed for the corresponding SCID-5-PD diagnoses. Interestingly, the chance-corrected reproducibility (i.e., Cohen's *k* value) of the Obsessive-Compulsive PD diagnosis was higher for the SCID-5-AMPD-III than for the SCID-5-PD. Even the SCID-5-AMPD-III Antisocial PD diagnosis was adequately reliable in terms of between-rater reproducibility, although its Cohen's *k* value was smaller than the value that was observed for the SCID-5-PD Antisocial PD diagnosis. In our opinion, this difference may simply reflect the reliance of the SCID-5-PD on deviant behavior for Antisocial PD diagnosis. Interestingly, the SCID-5-AMPD-III allowed clinicians to reliably evaluate both Criterion A (median Cohen's k = .70) and Criterion B (Cohen's k = .69) indicators of the individual *DSM-5* AMPD diagnoses. In our study, fair agreement (i.e., $.50 < k < .60$ [31 32]) was observed for two SCID-5-AMPD-III indicators, whereas good-to-excellent agreement (i.e., $.61 < k < 1.00$ [31 32]) was observed for 53 (94.6%) SCID-5-AMPD-III indicators. Consistent with Christiansen and colleagues' data, our findings suggested that the SCID-5-AMPD-III was likely to provide LPFS scores that were provided with substantial inter-rater reliability [31 32]; the importance of this finding should not be overlooked since the opportunity to obtain reliable PD severity measures is relevant for both treatment planning and forensic assessment.

Finally, it should be observed that in our study the SCID-5-AMPD average administration time seemed to be comparable to the average administration time (90 minutes) that was reported for the Italian version of the SCID-5-PD [24]. This finding seemed to stress that the SCID-5-AMPD-III may represent a viable alternative to the SCID-5-PD in routine clinical PD assessment.

When PD consensus diagnoses were taken into account, the SCID-5-AMPD-III seemed to provide internally consistent PD diagnoses; all Cronbach's α values for the SCID-5-AMPD-III PD diagnoses were > .70 and were not worse than those that were observed for the

corresponding SCID-5-PD diagnoses. Moreover, our data seemed to suggest that using the SCID-5-AMPD-III is unlikely to result in a significant increase of the overall rate of PD diagnoses when compared to using the SCID-5-PD in personality pathology assessment.

Based on our findings, the convergent validity between SCID-5-AMPD-III PD diagnoses and SCID-5-PD diagnoses was on average (median k = .54) moderate [31] with fair clinical significance [32]. Interestingly, Cohen's k values were > .20 and significant for all SCID-5-AMPD-III PD diagnoses.

Based on Landis and Koch's [31] and Cicchetti's [32] "benchmarks" for interpreting Cohen's k (and intraclass r) values, in our study substantial agreement [31] between SCID-5-AMPD-III and SCID-5-PD diagnoses with good clinical significance [32] was observed for Narcissistic PD, Borderline PD, any PD diagnosis, overall number of PD diagnoses, and presence of multiple PD diagnoses. Moreover, moderate agreement [31] between SCID-5-AMPD-III and SCID-5-PD diagnoses with fair clinical significance [32] was observed for Antisocial PD and Avoidant PD.

Finally, fair agreement [31] between the SCID-AMPD-III and SCID-5-PD diagnoses with poor clinical significance [32] was observed only for Obsessive-Compulsive and Schizotypal PDs. In the case of Schizotypal PD, the low frequency (n = 2) of the SCID-5-PD Schizotypal PD diagnosis may have negatively biased the corresponding convergent validity estimate. Similarly, the relatively small Cohen's k value that was observed for the Obsessive-Compulsive PD diagnosis may have been influenced by the limited internal consistency reliability (i.e., Cronbach's a value) of the corresponding SCID-5-PD scale.

Notwithstanding their psychometric appeal, our convergent validity data seemed to suggest that the SCID-5-AMPD-III PD diagnoses are not completely redundant with the SCID-5-PD diagnoses. This finding was not unexpected, but it may have relevant clinical implications. Indeed, different from the SCID-5-PD, the SCID-5-AMPD-III does not rely on the participant's self-description on the self-report screening questionnaire. Moreover, the SCID-5-AMPD-III ask participants to report their personality problems in terms of impairment in self- and interpersonal functioning, as well as in terms of dysfunctional domains and traits; rather, the SCID-5-PD assesses personality pathology in terms of symptom-like features, usually starting from the participant's self-report. These considerations may help clinicians to appreciate that SCID-5-AMPD-III PD diagnoses are not simply a translation of selected *DSM-5* Section II PD categories into a different language, as well as the *DSM-5* Section II PDs are unlikely to convey the same clinical information of their *DSM-5* AMPD counterparts.

Indeed, both approaches have strengths and weaknesses. On the one hand, using the SCID-5-AMPD-III might hypothetically help keeping the PD assessment phase in continuity with the following PD psychotherapy treatment, since it helps subjects to describe themselves in terms of self-other dynamics, representations, and interactions (i.e., Criterion A areas), as well as in terms of basic tendencies, motivational/affective traits, and regulatory dimensions (i.e., Criterion B traits), while relying on operational criteria. On the other hand, the *DSM-5* AMPD approach to PD diagnosis may sound too "psychologically-oriented" to some interviewers. At the opposite, the SCID-5-PD has the advantage of representing a easy-to-administer instruments; however, it should be bear in mind that it relies on diagnostic criteria that are deemed to lack validity [1 6]. Interestingly, neither the SCID-5-AMPD-III nor the SCID-5-PD requires specific interviewer characteristics.

We feel that the substantial agreement that was observed in our study between the SCID-5-AMPD-III and the SCID-5-PD on the frequency of multiple PD diagnoses deserves a comment. Indeed, this finding seemed to indicate that using the SCID-5-AMPD-III and the SCID-5-PD is likely to result in a similar number of multiple PD diagnoses. In other terms, relying on the *DSM-5* AMPD PD categories is likely to result in roughly the same number of multiple PD diagnoses that would be obtained using the *DSM-5* Section II PD criteria. In our study, non-negligible co-occurrence rates were observed for all SCID-5-AMPD-III PD diagnoses, and large and significant odds ratios were observed for selected SCID-5-AMPD categorically-diagnosed PDs. Our findings are consistent with previous results [6 20] which suggested that relying on the *DSM-5* AMPD categorical PD diagnoses was likely to result in high rates of diagnostic overlap and diagnostic confusion.

Consistent with previous data [6], our findings seemed to suggest that the problem of the overlap among PD diagnoses does not stem from relying on the *DSM-5* Section II PD criteria; rather, it seems to stem from relying on imposing arbitrary boundaries on continuous personality dimensions. Of course, adopting a dimensional perspective on PD assessment based on a single PD-TS diagnosis is likely to represent the best answer to this problem [6]; it should be observed that a similar approach to PD assessment has been adopted in the 11th edition of the International Classification of Diseases [33]. In any case, relying on the SCID-5-AMPD might help clinicians shifting to a dimensional perspective on PD assessment by relying on its Module I, and possibly Module II.

Of course, we feel that our findings should be considered in the light of several limitations. In the present study, we relied on a sample of participants who voluntarily asked for psychotherapy treatment; samples

with different clinical and demographic characteristics may yield different results. Moreover, we relied on adult clinical participants; this limits the generalizability of our findings on the interrater reliability of the Italian translation of the SCID-5-AMPD to clinical adolescent populations, as well as to elderly and forensic populations. Pairwise interview designs are known to yield excessively optimistic estimates of the actual measurement reliability [30]; however, it should be observed that pairwise interview designs represent the most commonly used approach to inter-rater reliability assessment because of their simplicity and ecological validity (they are closely akin to the typical training to clinical diagnosis). In the light of these considerations, further studies on SCID-5-AMPD-III test-retest reliability are demanded. Although previous data on the psychometric properties of the SCID-5-AMPD Module I are already available [18], in our study we administered only the SCID-5-AMPD-III; future study on the psychometric properties of the SCID-5-AMPD Module I and Module II may provide useful information on their inter-rater reliability and validity. Even keeping these limitations in mind, we feel that our data support the hypothesis that the SCID-5-AMPD-III PD diagnoses are provided with adequate inter-rater reliability and convergent validity with SCID-5-PD diagnoses, at least among clinical adult participants who voluntarily asked for psychotherapy treatment.

Conflict of interest

The Authors declare to have no conflict of interest.

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Original article

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Psychotic-like experiences interaction with common risk factors for suicidal ideation

Summary

Suicide is a significant global health issue. A number of risk and protective factors have been associated with suicidal ideation, including resilience, social connectedness, adverse childhood experiences and psychotic-like experiences (PLEs).

In this study we aimed at measuring the impact of PLEs on suicidality and at exploring how the presence of PLEs moderates the effect of resilience, social connectedness and adverse childhood experiences on suicidal ideation in a sample of 500 undergraduate students using an on-line survey.

PLEs were strong predictors of suicidality in the whole sample (OR= 5.45, 95%CI [2.62, 11.30]). The effect of resilience, social connectedness and adverse childhood experiences on suicidality was assessed separately for individuals with and without psychotic experience. In individuals without PLEs adverse childhood experiences, poor social connectedness and poor resilience were strongly associated with suicide (OR = 1.87 [1.25, 2.80], OR = 3.68 [2.18, 6.21] and OR = 4.06 [2.37, 6.94] respectively). These associations were weaker in subjects with PLEs (OR = 1.28 [0.76, 2.06], OR = 2.12 [1.13, 3.99] and OR = 2.50 [1.26, 4.94] respectively).

The effect of interpersonal and environmental risk factors for suicide was hampered in presence of PLEs. Psychological implications are discussed.

Key words

Psychotic experiences • Resilience • Suicide • Social connectedness • Adverse childhood experiences

Introduction

Suicide is a significant social and public health problem. According the World Health Organization (WHO), about 800,000 persons die from suicide every year. Deaths from suicide are the highest between 15 and 29 years of age, and suicide is the third most common cause of death, up to the age of 34 years thereafter [1].

The study of risk factors for suicide is a central topic in current mental health research, with the aim of improving the accuracy of the existing predictive models of suicide. Suicidal ideation and suicidal behaviors result from the interplay of distal or predisposing factors (i.e. childhood trauma, genetic factors), developmental or intermediate factors (i.e. coping skills, cognitive biases, subclinical psychopathology, social isolation) and proximal or precipitating risk factors (subclinical psychopathology, full-blown mental illness) [2]. However, no universal model has reached satisfactory predictive power, leaving the question unresolved. A reason for this could be that different risk factors could act through different pathways in different sub-populations.

Mental Illness accounts for the vast majority of suicides and suicide attempts, with approximately 90% of individuals who die by suicide having an identifiable psychiatric disorder prior to death [3]. Psychotic disorders account for a consistent proportion of suicide attempts and deaths by suicide. Schizophrenia is the second most frequent diagnosis preceding inpatient suicide (20%), with a rate twice as high in comparison to outpa-

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tients [4]. Adults with schizophrenia and other psychotic disorders are at heightened risk of suicide. The estimated prevalence of suicides in schizophrenia is 5-14% [5 6], with suicide attempts occurring during the first years of illness in about 10% of patients [7]. The main clinical predictors of suicide include depressive and hallucinatory symptoms [8 9], male sex, high premorbid IQ, feelings of guilt or anxiety, substance abuse, duration of untreated psychosis, number of psychiatric admissions, history of suicide attempts or non-suicidal self-harm [10-13].

Suicidality extends to those with subclinical phenotypes as well, including Psychotic-like Experiences (PLE).

PLEs are hallucinations and delusional ideas associated with a minor interference with global functioning and are most frequently associated with partially intact reality testing. PLEs are relatively common in the general population, with a prevalence of around 7% [14-17], and were initially thought as a specific risk factor for transitioning to a full-blown psychotic disorder. However, in recent years it has become clearer that PLEs represent a risk factor for a wide range of mental disorders and poor mental health outcomes beyond psychotic disorders [18 19]. The early idea that PLEs could be specific risk factors for subsequent psychotic disorders was supported by the communality of genetic [20 21], environmental and also cognitive [22-24] risk factors observed for PLEs and psychotic disorders. Not just psychotic disorders, but also highly prevalent PLEs are strong predictors of suicidality: recent meta-analytic evidence have estimated a pooled OR of 2.4 for suicidal ideation, 3.15 for subsequent suicide attempt and 4.4 for death by suicide [25]. The impact of PLEs on suicidality is robust to adjustment for general psychopathology [26 27], suggesting that PLEs convey a specific risk on suicide, possibly independent of other common risk factors for suicide, such early childhood adversity and poor social connectedness.

Among others, stressful life events and social connectedness are often called into question as potent risk factors for suicide.

The association between suicidality and stressful life events, especially when occurring early in life, has been well established [28]. Certain types of early adversity, including sexual abuse, physical abuse, harsh domestic environment, have been shown to directly increase the risk of suicide attempts for both men and women [29].

Research has also identified loneliness and lack of social connectedness [30 31] as key predictors of suicide. Social connectedness is often included as a sub-construct of the widely-defined "resilience" construct. It is debated if social connectedness is related to the objective features of one's social network readily available in case of need, or rather to one's abilities to mobilize those social resources.

Social Connectedness is included in the wider construct of resilience [32]. As a whole, resilience has been shown to be a very strong protective factor against suicidal ideation [33].

The aim of the present study is to evaluate the association between PLEs as assessed by a self-report instrument and suicidal ideation. Furthermore, the effect that PLEs have in shaping the response to common risk factors for suicidal ideation will be taken into account.

Methods

Sample

For this study, a sample of 500 university students from central Italy was recruited. Students were contacted via e-mail and invited to participate to an online questionnaire. Two-thousand-six-hundred sixty-nine students visited the survey website. Data collection was automatically closed when 500 subjects had completed the questionnaire.

Measures

Prodromal Questionnaire-16, Italian version

The Italian version of the Prodromal Questionnaire-16 (iPQ-16) [34] was used to assess the presence of PLEs. iPQ-16 is a 16-itmes self-report instrument that explores the presence/absence of 16 PLEs, including perceptual aberrations/hallucinations, unusual thought content/delusions, and two negative symptoms, and their associated psychological distress score on a 4-point Likert scale ranging from 0 to 48. Although the iPQ-16 was originally designed as a screening tool for individuals at ultra-high risk (UHR) for psychosis in help-seeking populations, several studies have used this instrument in the general population as a measure of PLEs [35-38]. We used the distress scale as recommended for non-help-seeking populations by Savill et al. [39], using a cut-off of ≥ 11 as recommended by Pelizza et al. [40] according to the Italian field test.

Social Connectedness Scale – revised

Social connectedness was assessed using the Italian version of the Social Connectedness Scale – revised (SCS-R) [41]. The SCS-R is a 20-item questionnaire on a 6-point Likert scale (1 = strongly disagree to 6 = strongly agree) assessing experiences of closeness in interpersonal contexts, as well as problems establishing and maintaining a sense of closeness. Sample items include "I don't feel I participate with anyone or any group" and "I am in tune with the world." Authors consider a mean item score equal or greater than 3.5 (slightly agree to strongly agree) as indicating a greater tendency to feel socially connected. SCS-R has good psychometric properties, with average interitem correlation of 0.66 and alpha = 0.92 in our sample.

Risky Family Questionnaire

Childhood Adversity was assessed using the Risky Family Questionnaire (RFQ), a 13-items retrospective self-report questionnaire on a 5-point Likert scale derived from the Adverse Childhood Experiences questionnaire (ACE-q) by Felitti et al. [28]. RFQ investigates the exposure to harsh parenting during childhood. RFQ shows an average interitem correlation of 0,39 and an alpha = 0.88 in our sample. For simplicity of exposure, RFQ scores were standardized in the following analysis.

Suicidal ideation

Suicidal ideation was assessed using the four items relative to suicide included in the Clinical Outcomes in Routine Evaluation-Outcome Measure, Italian version (CORE-OM) [42]. The CORE-OM in its original formulation included 6 risk items, of which two items refer to risk of violence and aggression and four items refer to suicidal ideation, on a 6-point Likert scale. For this study, we averaged the score on the 4 suicide items. Suicidal ideation was coded as present in a binary variable if mean score of CORE-OM suicide items was ≥ 1.

Potential confounders

Confounders included in the analysis were gender, age, self-report substance use, self-report socio-economic status, family history of mental illness.

Analysis

The association between PLEs and Suicidal ideation was assessed using a logistic regression model in two steps: first, the unadjusted Odd Ratios (ORs) between the presence of PLEs and suicidal ideation were estimated, using both the endorsed and the distress scores modeled as continues standardized variable and a categorical variable based on the distress score with cut-off ≥ 11. In a second model, adjustment for selected potential confounders was introduced.

The association of RFQ and SCS-R with suicidal ideation was assessed using logistic regression. In a first wave of analysis, separate regression models were performed separately for RFQ and SCS-R, introducing in a second model the potential confounders. In a second wave on analysis, the regression models were repeated separately for individuals with and without PLEs.

Results

Descriptives

Characteristics of the sample are reported in Table I. Of the total sample, 6 participants were excluded from the analysis because of missing data on one of the variables of interest. Of the 494 individuals included in subsequent analysis, 352 (71.26%) were female. Mean age was 25.52 years (SD = 4.86). Twenty-four participants (4.86%) disclosed alcohol or substance abuse, 143 (28.74%), 343 (68.42%) and 14 (2.83%) participants disclosed respectively low, mid and high family income. Seventy-five (15.18%) participants reported family history of mental disorders.

TABLE I. *Characteristics of the sample.*

Variable	Total sample N (%) / mean (SD)
N	494
Gender	
Female	352 (71.26%)
Male	142 (28.74%)
Age	25.52 (5.85)
Alcohol/drug abuse	24 (4.86%)
Income	
Low	143 (28.60)
Mid	343 (68.60)
High	14 (2.80)
Family history of mental illness	75 (15.18%)
iPQ-16	
Mean Endorsed Score	4.02 (3.06)
Mean Distress Score	5.01 (5.24)
N ≥ 11 Distress Score	73 (14.78%)

iPQ-16: Prodromal questionnaire, Italian version.

Association between PLEs and suicidal ideation

Results from logisitc regression of different PQ scores on Suicidal Ideation are reported in Table II. In our sample, all of the three different PQ scores were strongly associated with suicidal ideation, with the Endorsed standardized score having OR = 1.92 [1.41, 2.60], Distress standardized score OR = 2.10 [1.59, 2.77] and Categorical score OR = 5.45 [2.62, 11.30]. Adjustment for selected confounders did not alter these results substantially, with Endorsed standardized, Distress Standardized and categorical score having respectively OR = 2.02 [1.45, 2.82], OR =2.29 [1.69, 3.12] and OR = 5.95 [2.68, 13.22].

Association between risk factors and suicidal ideation

Results from the second wave of analysis are reported in Table III and in Figure 1. RFQ, SCS-R and RSA displayed moderate to strong association with suicidal ideation in the total sample, respectively OR = 1.84 [1.37,2.47], OR = 3.41, [2.30,5.04] and OR = 3.83 [2.54, 5.78]. These association did not vary substantially after adjusting for potential confounders. In the subsample without PLEs (n = 426), association of RFQ, SCS-R

TABLE II. *Logistic regression results for different PQ scores on suicidal ideation.*

	Unadjusted (n = 500) OR [95% CI]	Adjusted [a] (n = 498) OR [95% CI]
PQ16-symptom	1.92*** [1.41, 2.60]	2.02*** [1.45, 2.82]
PQ16-distress	2.10*** [1.59, 2.77]	2.29*** [1.69, 3.12]
PQ16 distress ≥ 11	5.45*** [2.62, 11.30]	5.95*** [2.68, 13.22]

*[a] Adjusted by age, gender drug abuse family history of mental illness, familial income. PQ: Prodromal Questionnaire; OR: Odd Ratio; 95% CI: 95% Confidence Interval. *p < 0.05; **p < 0.005; ***p < 0.001.*

TABLE III. *Results from Logistic Regression of RFQ, SCS-R and RSA on suicidal ideation. Values indicate Odd Ratios with 95% confidence intervals.*

	Total sample (n = 498)		PQ16-symptom < 11 (n = 426)		PQ16-symptom ≥ 11 (n = 74)	
	Unadjusted	Adjusted [a]	Unadjusted	Adjusted [a]	Unadjusted	Adjusted [a]
RFQ	1.84*** [1.37,2.47]	1.94*** [1.40, 2.68]	1.87*** [1.25, 2.80]	1.96*** [1.25, 3.08]	1.28 [0.76, 2.06]	1.40 [0.84, 2,36]
SCS-R	3.41*** [2.30,5.04]	3.37*** [2.25, 5.04]	3.68*** [2.18, 6.21]	3.40*** [2.01, 5.76]	2.12* [1.13, 3.99]	2.42* [1.16, 5.11]
RSA	3.83*** [2.54, 5.78]	4.37*** [2.79, 6.85]	4.06*** [2.37, 6.94]	4.42*** [2.48, 7.89]	2.50** [1.26, 4.94]	3.28** [1.43, 7.51]

*[a] Adjusted by age, gender drug abuse family history of mental illness, familial income. PQ: Prodromal Questionnaire; RFQ: Risky Family Questionnaire; SCS-R Social connectedness scale revised; RSA: Resilience Scale for Adults. RFQ score is standardized; RSA and SCS-R scores are standardized and reversed. *p < 0.05; **p < 0.005; ***p < 0.001.*

and RSA with suicidal ideation did not vary significantly compared to the total sample, with unadjusted OR respectively 1.87 [1.25, 2.80] and 3.68 [2.18, 6.21]. In the subsample displaying PLEs (n = 74) no significant association was detected between RFQ and suicidal ideation (OR = 1,25, [0.76, 2.06]), while SCS-R effect on suicidality was conserved (OR=2.12 [1.13, 3.99]).

Discussion

In this paper we assess the relationship between self-reported PLEs and suicidal ideation in a relatively large sample of university students. Furthermore, we assessed the role of resilience, social connectedness and early life adversities on suicidal ideation separately for individuals with and without PLEs.

The main finding is that PLEs (as assessed using both symptom and distress score of the PQ-16, as well as using a categorical classification based on the symptom score with a cut-off of ≥ 11) are strong predictors of suicidal ideation. This result is in line with a large body of evidence on the role of PLEs in predicting suicidality in both clinical and non-clinical populations [25,26,43].

The second finding of this study is that, while a history of adverse childhood experiences displays a very strong risk effect on suicidal ideation in the subsample without PLEs, this effect is significantly reduced in individuals with PLEs. Similarly, although to a lesser extent, poor social connectedness and poor resilience display a smaller effect on suicidal ideation in individuals with PLEs compared to individuals without PLEs. As high resilience and social connectedness are frequently considered protective factors against suicide, our results need to be confirmed as resilience and social connectedness are less protective against suicidal ideation in individuals with PLEs.

Taken together, these results suggest that PLEs represent a strong risk factor for suicidal ideation in a non-help-seeking population. Furthermore, the presence of PLEs hampers the effects psychological and environmental risk and protective factors for suicide. In other words, PLEs moderate the effect of resilience, social connectedness and early life adversity on suicidal ideation. This could sound counterintuitive, considering previous reports of a strong association for example of resilience with depression in patients with schizophrenia [44]. However, further studies are needed in order to assess social anhedonia in individuals with and without PLEs and its relationship with resilience.

The moderation of PLEs on early life adversities in conveying risk for suicidal ideation could be explained in the light of the vulnerability-stress model. This model assumes that the presence of PLEs represents the behavioral manifestation of a genetic and/or environmental liability to psychosis [45]. The progression through the psychotic continuum is promoted by stress exposure striking an already genetically vulnerable individual. It

could be speculated that individuals with PLEs in our sample have a higher vulnerability that would account for a minor intensity of stressful events required to activate suicidal ideation.

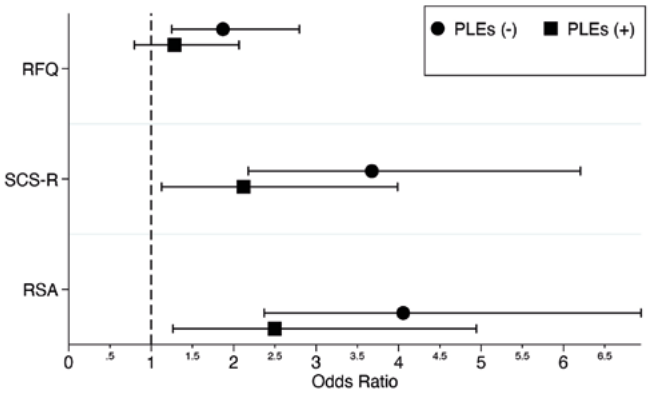
Concerning protective factors, both resilience and social connectedness are considered strong protective factors for suicidal ideation [30 31 33 46]. Although the mechanisms by which resilience and social connectedness would protect against suicidal ideation are still debated, a buffering-hypothesis is the most credited in the literature so far [46].

In our study, we observed an attenuation of the protective effect against suicidal ideation of resilience and social connectedness in individuals with PLEs. Both Social connectedness and resilience encompass an interpersonal dimension. The reduction of their protective effect may be due to a reduced sensitivity to social and interpersonal cues in individuals with PLEs. One reason for this could be Schizoid and Schizotypal traits, common in individuals with PLEs [47 48]. Schizotypy is typically associated with deficits in interpersonal functioning, and with a certain degree of indifference towards interpersonal cues, as captured by constructs like Asociality and Social Anhedonia. Asociality and Social Anhedonia are two constructs that belong to the negative symptoms of psychoses [49], although they are more often considered transdiagnostic features [50] and common traits in the general population. Social anhedonia has been associated with theory of mind and social functioning deficits in individuals with schizophrenia [51].

Under this perspective, we could speculate that for individuals along the psychotic spectrum, putatively showing a diminished interest in socially salient stimuli, the presence of social protective factors could play a limited role in defending from the effects of stressful events on suicidal ideation.

Limitations

This study presents some limitations. Firstly, all psychometric measures were self-report questionnaires, conveying a risk of overestimation of both early life adversities and PLEs. In fact, the prevalence of individuals displaying PLEs in our sample is considerably larger than expected. Secondly, an on-line data collection on a voluntary basis may involve self-selection bias. Thirdly, the present study has been carried out of a student population, that could hamper the generalizability of the results.



Relative Odd Ratios (with 95% Confidence Intervals) of common risk factors for Suicidal Ideation separately for individuals without (round markers) and with (square markers) PLEs, respectively "PLEs (-)" and "PLEs (+)". PLEs: Psychotic Like Experiences; RFQ: Risky Family Questionnaire; SCS-R: Social Connectedness Scale – Revised; RSA: Resilience scale for Adults. RFQ score is standardized; RSA and SCS-R scores are standardized and reversed.

FIGURE 1. *Odd Ratios with 95% confidence intervals for suicidal ideation.*

Conclusions

Individuals experiencing PLEs are at heightened risk for suicide. Our results suggest, however, that common risk factors for suicide, such as poor social connectedness, lower resilience and childhood adversities, have a weaker association with suicidality in individuals with PLEs compared to individuals without PLEs.

Conflicts of interest

The Authors declare to have no conflict of interest.

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Original article

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Dissociative symptoms in complex post-traumatic stress disorder and in post-traumatic stress disorder

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Abstract

Since it is possible to find the definition of complex post-traumatic stress disorder (cPTSD) only in International Classification of Diseases (ICD-11), several studies have used different definitions of "complex PTSD", consequently very few studies examine the correlation between dissociative symptoms and cPTSD according to the ICD-11definition.

The primary objective of this study was to explore differences in dissociative experiences (measured with Dissociative Experience Scale, DES) between PTSD and cPTSD according to ICD-11 criteria. Furthermore, we examined relations between total and subscales of dissociation (amnesia, absorption, derealization/ depersonalization) and clinical symptomatological variables of PTSD and cPTSD patients. Results showed that 30 subjects affected by cPTSD had significantly higher DES scores than those 20 affected by PTSD, with large effect sizes. Only DES Amnesia subscale is positively correlated with total Clinician-Administered PTSD Scale (CAPS) score, with Hamilton Depression Rating Scale (HAM-D) total score, with Impact of Event Scale-Revised (IES-R) Re-Experience subscale and IES-R total score in PTSD sample, while only Beck Depression Inventory (BDI) somatic subscale is related with DES Amnesia subscale and DES Absorption subscale in cPTSD sample. The findings from this study sustain cPTSD as a severe clinical syndrome with higher dissociative symptoms respect to PTSD.

Key words

Complex Post-Traumatic Stress Disorder • Post-Traumatic Stress Disorder • Dissociation • Dissociative Symptoms

Introduction

Post-traumatic stress disorder (PTSD) is a psychiatric illness caused by psychological traumatic events, where the fear memories are aberrantly consolidated, and the fear extinction fails to function [1]. In their lifetime 60.7% of men and 51.2% of women may be exposed to traumatic events that have the potential to trigger the development of PTSD [2 3]. Lifetime prevalence of PTSD is estimated between 2.3% [4] and 6.1% [5 6] in civilians and 30% in veterans[4]. The difference between the prevalence of traumatic events and the prevalence of stress-related disorders could be due to protective factors such as resilience [7]. Not only resilience protects the individual from developing a stress-related psychopathology, but it could also mitigate the severity of a full-blown disorder [8].

The 11th revision to the International Classification of Diseases (ICD-11), released in the 2018 by the World Health Organization (WHO) [9], separates two distinct post-traumatic stress syndromes: PTSD and complex PTSD (cPTSD). PTSD is comprised of three symptom clusters: re-experiencing of the trauma in the here and now, avoidance of traumatic reminders and a persistent sense of current threat that is manifested by exaggerated startle and hypervigilance. cPTSD, generated by interpersonal traumatic experiences perpetuated in the time from which victims have limited or no possibilities to avoid, includes all PTSD clusters and three additional

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clusters that reflect 'disturbances in self-organisation' (DSO): affect dysregulation, negative self-concept and disturbances in relationships [10].

Despite dissociation does not appear in diagnostic criteria for PTSD/cPTSD it has a relevant role in post-traumatic phenomenological clinical picture, sometimes determining a clinical subtype with specific features [11-16]. Moreover, dissociative symptoms are central in trauma-related disorders and their clinical management because of their association with self-harm and suicidal behaviour [17 18]. Since it is possible to find the definition of cPTSD only in ICD-11, several studies have used different definitions of "complex PTSD" [19], consequently very few studies examine the relations between dissociative symptoms and cPTSD according to the definition of ICD-11. Results indicate that dissociative experiences are particularly relevant for patients with cPTSD [19].

The primary objective of this study was to explore the presence and the severity of dissociative experiences in PTSD and cPTSD according to ICD-11 criteria. We examined also the association between some clinical dimensions of dissociation (amnesia, absorption, derealization / depersonalization) and other post-traumatic symptomatological variables, separately in PTSD patients and cPTSD patients. We hypothesized that dissociation may be a relevant clinical feature in differentiating PTSD and cPTSD.

Methods

Participants

The sample consisted in subjects affected by PTSD/cPTSD on the basis of ICD-11 criteria, evaluated in the period between February 2018 and October 2019 by two independent psychiatrists (LL and GDL) at the Psychiatry and Clinical Psychology Unit, in the Fondazione Policlinico Tor Vergata, the Hospital of University of Rome Tor Vergata.

These subjects met also the following inclusion criteria for the study: an age between 16 and 60; being able to take part in the interview for clinical evaluation; acceptance of informed consent. Exclusion criteria were: the presence of mental retardation (IQ < 70); delirium; neurodegenerative disorders; all other factors affecting the psychiatrist's ability to complete a complete assessment.

A total of 50 PTSD patients were included in the final sample: 30 patients (60%) met the criteria for PTSD, 20 patients (40%) for cPTSD.

Measures

The Clinician-Administered PTSD Scale (CAPS) measures frequency and intensity of PTSD symptoms rated for the last-week period [20].

The Hamilton Depression Scale (HAM-D), due to its good psychometric properties, is one of the most frequently used tools of depressive symptoms [21].

The Impact of Event Scale-Revised (IES-R) is self-report questionnaire used to assess post-traumatic symptoms [22]. The three subscales of the IES-R reflect the three clusters of symptoms presented in Post-Traumatic Stress Disorder: intrusion, avoidance, hyper-arousal.

The Symptom Checklist-90-Revised (SCL-90-R) is a 90-item self-report that measures a broad range of psychological symptoms [23]. The SCL-90-R categorizes symptoms into nine clinical sub-scales (Somatization, Obsessive-Compulsivity, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation, and Psychoticism) and three global indices including Global Severity Index (GSI), Positive Symptom Distress Index (PSDI) and Positive Symptom Total (PST). For the purposes of the current study, and in accord with previous reports [24 25], we used PSDI.

The Beck Depression Inventory (BDI) is a 21-item self-report inventory that evaluates cognitive and somatic symptoms of depression (range 0-63) [26].

The Dissociative Experience Scale (DES) is a self-rating instrument comprising 28 items that build on the assumption of a "dissociative continuum" ranging from mild normative to severe pathological dissociation. Subjects are asked to make slashes on 100-mm lines to indicate where they fall on a continuum for questions on experiences of amnesia, absorption, depersonalization, and derealization [27].

The Beck Hopelessness Scale (BHS) is a self-report scale developed by Beck et al. [28] to measure three major aspects of hopelessness, associated to suicidal ideation and behaviour: feelings about the future, loss of motivation, and expectations.

The Childhood Trauma Questionnaire (CTQ) is a retrospective self-completed questionnaire covering the following five domains of childhood trauma: sexual abuse, physical abuse, emotional abuse, physical neglect, emotional neglect and minimization [29].

Statistical analysis

In order to compare clinical and demographic features of PTSD and cPTSD patients, Pearson Chi-squared tests and t-test were used, as appropriate. Correlation analysis was performed with Spearman's rho. Statistical significance was set at $p < 0.05$.

Results

The two samples were primarily composed by women (66.67% of PTSD group, 80% of cPTSD group, p = .353) with a mean age of 34.933 (SD = 12.457) for PTSD and 35.150 (SD = 9.172) for cPTSD group (p = 0.944, d = 0.020) (see Table I). Patients with PTSD had a slight-

TABLE I. *Statistics of sociodemographic and clinical characteristics of sample.*

	PTSD	cPTSD	P_2-tailed	Cohen's d
Gender (w/m)	20/10	16/4	0.353	
Age (years)	34.933 (12.457)	35.150 (9.172)	0.944	0.020
Education (years)	15.333 (3.633)	14.050 (2.645)	0.155	0.404
Employed (yes/no)	28/2	15/5	0.100	
Stable relationship (yes/no)	10/20	6/14	1.000	
CTQ-Emotional abuse	7.207 (3.342)	10.294 (4.043)	**0.013**	0.832
CTQ-Physical abuse	5.414 (1.181)	8.176 (3.432)	**0.005**	1.076
CTQ-Sexual abuse	5.103 (0.409)	7.765 (4.777)	**0.036**	0.785
CTQ-Emotional neglect	9.241 (3.632)	15.118 (6.051)	**0.001**	1.178
CTQ-Physical neglect	6.241 (1.864)	9.471 (5.444)	**0.029**	0.794
CTQ-Minimization	10.207 (2.782)	6.941 (3.132)	**0.001**	1.102
Psychiatric comorbidity (yes/no)	19/11	18/2	**0.050**	
Psychotropic drug (yes/no)	12/18	17/3	**0.003**	

Note: CTQ: Childhood Trauma Questionnaire

ly higher education respect to the patients with cPTSD. The 93.33% of PTSD patients and 75% of cPTSD was employed. Only the 33.33% (10) of PTSD and 30% (6) of cPTSD patients was in stable relationship (see Table I). It is important to note that 3 of the 20 patients with PTSD diagnosis without stable relationship were widowers.

The two groups are statistical different respect to the presence of childhood trauma. In particular patients with cPTSD reported a major presence in all subscale of Childhood Trauma Questionnaire (see Table I): Emotional Abuse (d = 0.832), Physical Abuse (d = 1.076), Sexual Abuse (d = 0.785), Emotional Neglect (d = 1.178), Physical Neglect (d = 0.794) were significantly higher in cPTSD whereas Minimization (d = 1.102) was significantly lower in cPTSD.

Furthermore, 63.33% (19) of PTSD sample and 90% (18) of cPTSD sample had a psychiatric comorbidity (p = .050); only 40% (12) of patients with PTSD take psychotropic drugs respect to 85% (17) of patients with cPTSD (p=.003, see Table I).

The descriptive statistics for all symptomatological variables (included total and subscale scores of DES) are presented in Table II.

cPTSD group had significant higher scores of traumatic symptomatology in total and subscale score of CAPS (administered by the clinician) and IES-R (completed by the patients) (see Table II). In particular, cPTSD sample showed higher scores respect PTSD sample in CAPS-Re-Experience subscale (d = 1.1070), in CAPS-Avoidance-Numbing (d = 1.146), CAPS-Hyper-arousal (d = 1.015), CAPS-Associative Features (d = 1.014) and in CAPS total score (d = 1.561; Fig. 1).

At the same time, PTSD group showed higher score in IES-Re-Experience subscale (d = 0.896), IES-Avoidance subscale (d = 0.894), IES-Hyper-arousal subscale (d = 0.956) and in IES total score (d = 1.033; Fig. 1).

Also regard depressive symptoms, the groups had significant different scores in HAM-D (administered by clinicians): cPTSD showed higher scores (21.900, SD = 5.418 respect PTSD group (d = 2.276; Fig. 1). This difference was observed also in BDI total score (d = 0.831; Fig. 1), in BDI-Cognitive (d = 0.791) but not in BDI-Somatic subscale (p = 0.624, d = 0.145).

The two groups were also different in PSDI index of SCL-90-R (d = 0.834; Fig. 1).

Respect the dissociative symptoms, patients with cPTSD showed significant differences respect to patients with PTSD (see Table II). In particular, cPTSD sample had higher scores respect PTSD sample in DES-Amnesia subscale (7.321, SD: 7.002 vs 3.476, SD: 3.293 respectively, p = 0.031, d = 0.703), in DES-Absorption subscale (d = 1.309; Fig. 1), in DES-Derealization-Depersonalization subscale (d = 0.934; Fig. 1) and in DES-Total Score (d = 1.174; Fig. 1).

Statistical differences were present also in BHS-Feelings subscale (d = 0.714), BHS-Loss of motivation subscale (d = 0.996), BHS Total score (d = 1.094; Fig. 1) but not in BHS-Future Expectations subscale (p = 0.059, d = 0.528).

Results of correlations analyses for symptomatological and dissociative symptoms are shown in Table 3. No significant correlation was found between DES total score and all symptomatological variables explored. DES-Amnesia subscale showed positive correlations

TABLE II. *Statistics of symptomatological variables of sample.*

	PTSD	cPTSD	P_2-tailed	Cohen's d
CAPS-Re-experience	17.533 (6.606)	23.800 (4.526)	< 0.0001	1.107
CAPS-Avoidance-numbing	20.133 (6.415)	26.700 (4.953)	0.000	1.146
CAPS- Hyper-arousal	16.500 (6.241)	22.400 (5.345)	0.001	1.015
CAPS-Associative features	10.333 (6.483)	17.200 (7.046)	0.001	1.014
CAPS-Total	76.400 (20.498)	104.400 (14.936)	0.000	1.561
IES-Re-experience	16.633 (8.282)	22.900 (5.399)	0.002	0.896
IES-Avoidance	14.667 (6.890)	20.100 (5.139)	0.003	0.894
IES-Hyper-arousal	12.267 (5.650)	17.050 (4.261)	0.001	0.956
IES-R-Total	43.567 (18.878)	60.050 (12.382)	0.001	1.033
HAM-D	11.300 (3.743)	21.900 (5.418)	0.000	2.276
BDI-Cognitive	10.367 (6.305)	15.600 (6.916)	0.010	0.791
BDI-Somatic	7.333 (3.546)	7.900 (4.229)	0.624	0.145
BDI-Total	17.467 (8.136)	24.200 (8.069)	0.006	0.831
SCL-90-R-PSDI	1.716 (0.421)	2.143 (0.589)	0.009	0.834
DES-Amnesia	3.476 (3.293)	7.321 (7.002)	0.031	0.703
DES-Absorption	9.964 (4.709)	19.911 (9.656)	0.000	1.309
DES-Derealization-depersonalization	1.488 (1.785)	5.018 (5.038)	0.006	0.934
DES-Score	14.464 (7.669)	30.964 (18.344)	0.001	1.174
BHS-Feelings	2.133 (1.074)	2.800 (0.768)	0.014	0.714
BHS-Loss of motivation	2.700 (1.685)	4.400 (1.729)	0.001	0.996
BHS- Future expectations	2.933 (1.680)	3.650 (0.933)	0.059	0.528
BHS-Total	9.167 (3.333)	12.350 (2.412)	0.000	1.094

Note: CAPS: Clinician-Administered PTSD Scale; IES-R: Impact of Event Scale-Revised; HAM-D: Hamilton Depression Rating Scale; BDI: Beck Depression Inventory; SCL-90-R: Symptoms CheckList-90-Revised, DES: Dissociative Experiences Scale; BHS: Beck Hopelessness Scale.

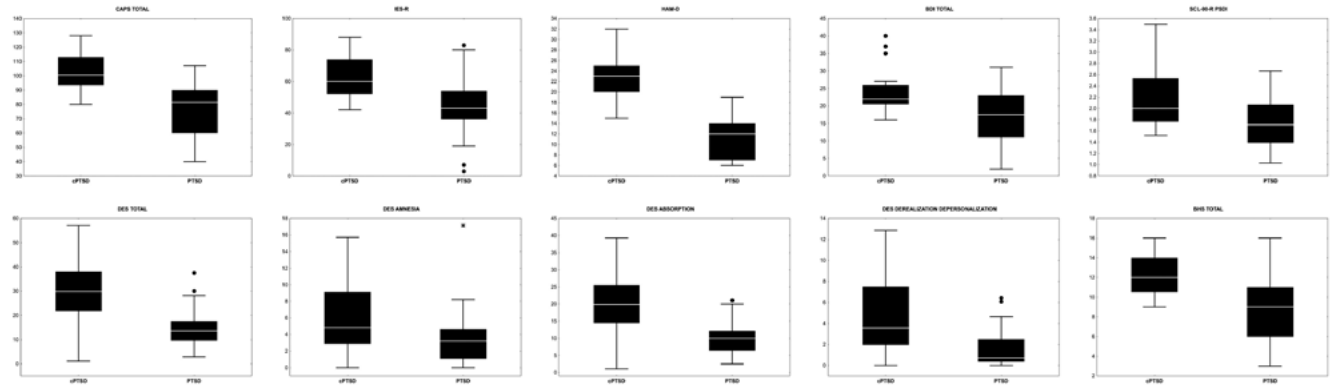

FIGURE 1. *Boxplots of CAPS total score, IES-R total score, HAM-D total score, BDI total score, SCL-90-R PSDI, DES total score, DES amnesia, DES absorption, DES derealization – depersonalization, and BHS total score in cPTSD and PTSD.*

TABLE III. *Statistics of Spearman's rho correlations between symptomatological variables and dissociative symptoms. Significant correlations are indicated in bold.*

	DES-Tot. score		DES-amnesia		DES-absorption		DES-Dep-Der	
	PTSD	cPTSD	PTSD	cPTSD	PTSD	cPTSD	PTSD	cPTSD
CAPS-Re-experience	0.168	-0.211	0.355	-0.236	0.107	-0.111	0.083	-0.145
CAPS-Avo-numbling	-0.049	-0.050	0.011	0.216	-0.050	0.041	-0.180	-0.249
CAPS-H-arousal	0.086	0.036	0.305	0.017	-0.031	0.146	-0.191	0.185
CAPS-Assoc. F.	0.071	0.095	0.105	0.146	0.149	0.144	0.251	0.035
CAPS-Total	0.180	-0.018	**0.367**	0.065	0.123	0.099	0.012	-0.028
IES-R-Re-experience	0.274	0.181	**0.451**	0.208	0.192	0.090	0.001	0.227
IES-R-avoidance	0.062	-0.107	0.185	-0.020	0.012	-0.193	-0.125	-0.166
IES-R-H-arousal	0.228	0.271	0.265	0.321	0.176	0.212	0.076	0.070
IES-R-total	0.223	0.149	**0.387**	0.154	0.148	0.074	-0.042	0.092
HAM-D	0.328	0.093	**0.499**	0.186	0.239	0.143	0.001	0.013
BDI-Cognitive	0.066	0.110	0.080	0.156	0.019	0.216	0.173	0.102
BDI-Somatic	-0.089	0.418	0.196	**0.526**	-0.138	**0.455**	-0.132	0.144
BDI-Total	0.053	0.202	0.139	0.265	0.001	0.287	0.142	0.110
SCL-90-R-PSDI	0.213	0.298	0.154	0.355	0.188	0.330	-0.007	0.309
BHS-Feelings	-0.126	0.085	-0.312	-0.082	-0.001	0.131	0.292	0.335
BHS-Loss of mot	0.181	-0.078	0.162	0.141	0.215	0.042	0.163	-0.091
BHS-Future exp	-0.123	-0.099	-0.281	-0.291	-0.045	-0.004	0.120	-0.054
BHS-Total	0.024	-0.133	-0.189	-0.149	0.119	-0.047	0.128	-0.221

Note: CAPS: Clinician-Administered PTSD Scale; IES-R: Impact of Event Scale-Revised; HAM-D: Hamilton Depression Rating Scale; BDI: Beck Depression Inventory; SCL-90-R: Symptoms CheckList-90-Revised, DES: Dissociative Experiences Scale; BHS: Beck Hopelessness Scale.

with CAPS total score (r = 0.367), IES-R-Re-experience subscale (r = 0.451), IES-R total score (r = 0.387) and HAM-D total score (0.449) in PTSD sample but not in cPTSD sample (respectively: r = 0.065; r = 0.208; r = 0.154; r = 0.186). In contrast, DES-Amnesia subscale showed a statistical correlation with BDI-Somatic subscale in cPTSD group (r = 0.526; Fig. 2) but not in PTSD group (r = 0.196). DES-Absorption subscale not show significant correlation with all symptomatological variables explored except for BDI-Somatic subscale in cPTSD patients (r = 0.455; Fig. 2). No correlation was found between depersonalization-derealization subscale of DES and any variable explored.

Discussion

The primary objective of this study was to explore the associations between dissociative experiences and PTSD/cPTSD according to ICD-11 criteria. We found significant differences in dissociative experiences scores between PTSD and cPTSD. Patients with cPTSD showed significantly higher scores respect to those patients with PTSD in Amnesia subscale (d = 0.703), in Absorption subscale (d = 1.309), in Derealization-Depersonalization subscale (d = 0.934) and in DES Total Score (d = 1.174) (see Table II and Fig. 1). Consequently, our hypothesis that dissociation may be a relevant clinical feature in differentiating PTSD and cPTSD was confirmed. These findings are in line also with those results published before [30] and after [19] the ICD-11 formulation of cPTSD.

The presence of more severe symptoms in dissociative domains of patients with cPTSD is also a confirmation of Van der Hart's structural theory of dissociation [31 32] in according to which individuals who have complex trauma reactions experience a division of their personality resulting in multiple dysfunctional outcomes such as fixation and avoidance [33]. Consequently, the severity of dissociation would be expected to increase from PTSD to cPTSD. However, according with dissociative subtype of PTSD in DSM-5 [13], previous studies suggested that dissociation reflects a unique cluster of PTSD symptoms [11 12]. A recent study [16] showed that patients with dissociative PTSD had more severe symptomatology in all CAPS clusters except avoidance, while another study showed that patients with dissociative PTSD had

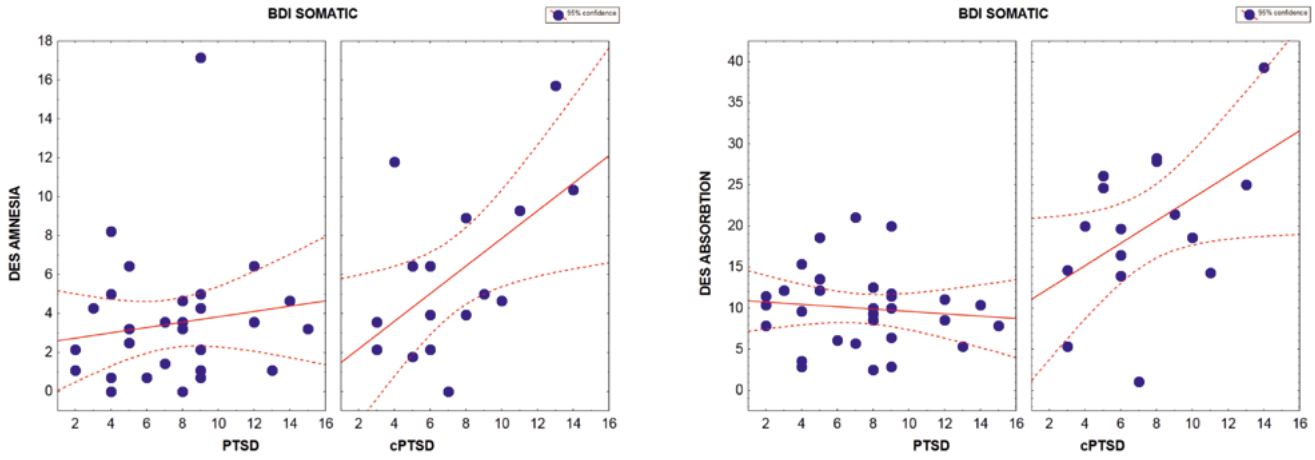

FIGURE 2. *Scatterplots of DES amnesia and DES absortpion vs BDI somatic in cPTSD and PTSD.*

high levels both all PTSD symptoms and dissociative symptoms [14]. In contrast, in our study only amnesia subscale of dissociative symptoms is related with total CAPS score (r = 0.367), with IES-R Re-Experience subscale (r = 0.451) and IES-R total score (r = 0.387) in PTSD sample.

In cPTSD sample only BDI somatic-subscale is related with DES-Amnesia subscale (r = 0.526) and DES-Absorption subscale (r = 0.455). A previous study, before the ICD-11 edition, show that at hierarchical regression analyses only dissociative and depression symptoms were significant predictors of somatic symptoms in PTSD [34]. We can hypothesize that somatic depression symptoms in cPTSD patients may be a form of somatoform dissociation.

Somatoform dissociation is concept describing specific forms of dissociative symptoms experienced as somatic disturbances due to alterations of normal integrative functions of consciousness, memory or identity related to stressful experiences [35-37].

Similar to previous studies [19 38-40], our study supports the diagnostic differences between the two constructs of PTSD and cPTSD of ICD-11. Early life events (as measured by CTQ), post-traumatic psychopathology (CAPS and IES-R), depressive symptoms (HAM-D and BDI), hopelessness (BHS) and general psychopathology (SCL-90-R PSDI) were significantly higher in cPTSD respect to PTSD, with large effect sizes.

Literature shows that individuals with cPTSD are more likely to be unemployed, less likely to be married and more likely to live alone [41] compared to individuals with PTSD. At the same way, cPTSD diagnosis has been associated with lower social status education [42]. Conversely, our study not show differences between PTSD and cPTSD sample in employment status, stable relationship and in educational level.

Our study has several limitations. Firstly, the study was based on a small, predominately women, clinical sample. Secondly, current research was an observational study with cross-sectional data, therefore no follow-up analysis of symptomatological variables could be made. Thirdly, our study was conducted in a single geographic area. Fourthly, one of the clinical instruments we utilized was the CAPS, a semi-structured interview that assesses PTSD symptomatology on the basis of DSM criteria.

In conclusion, current study confirmed that cPTSD clinical picture is characterized by a more severe post-traumatic psychopathology respect to PTSD. Subjects affected by cPTSD had more dissociative experiences than those affected by PTSD. Dissociative dimensions were weakly related to other psychopathological dimensions of trauma-related disorders, differently in PTSD and cPTSD. Further studies are required to better understand the relation between dissociation and other symptoms in cPTSD. Moreover, more in general, PTSD and cPTSD need to be better investigated, not only at clinical level but looking also to biological level [4 15 24 25 43-45], searching for features might possibly explain their psychopathological differences.

Conflict of interest

The Authors declare to have no conflict of interest.

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Examining subjective experience of social cognition in early psychosis: validation of the Italian version of the GEOPTE scale in an adolescent and young adult clinical sample

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Summary

Objective

Social cognition is a set of cognitive processes that underlie social interactions. Prior research found that social cognitive impairment is an important determinant of functional outcome in early psychosis. Aim of this study was to assess reliability and validity of the Italian version of GEOPTE scale (i-GEOPTE) of social cognition for psychosis in a clinical sample of adolescent and young adult community help-seekers.

Methods

The i-GEOPTE scale was completed by 325 individuals (aged 13-35 years) entered the "Reggio Emilia At-Risk Mental States" (ReARMS) program. Reliability was evaluated examining internal consistency (using Cronbach(s alpha) and calculating short-term (2-week) coefficient of stability. Concordant validity was established with CAARMS ("Comprehensive Assessment of At-Risk Mental States") subscale scores using Spearman(s correlation coefficients. A confirmatory factor analysis was also carried out.

Results

The i-GEOPTE showed good to excellent short-term test-retest reliability (coefficient of stability = 0.813 for i-GEOPTE total score) and internal consistency (Cronbach(alpha = 0.90). Moreover, i-GEOPTE total scores had significant positive correlations with CAARMS subscale and item scores measuring subjective change of soco-cognitive functions.

Conclusions

The i-GEOPTE showed satisfactory psychometric properties. Thus, it appears to be a suitable instrument for assessing subjective experience of social cognition in Italian mental health care services, also in order to evaluate functional outcomes of intervention.

Key words

Social cognition • Emotion recognition • Theory of mind • High risk mental states • First episode psychosis • Prodrome

Introduction

Social cognition has been defined as a set of cognitive functions that underline social interactions [1]. These mental operations involve the perception, processing, and interpretation of social information in order to generate a response to the intention and behaviors of others [2]. In this sense, social cognition is crucial for daily functioning. Indeed, as suggested by Raballo (2017) [3], "our everyday, pragmatic immersion in the social world strongly relies on a series of face-to-face encounters with others, whose mental states are seamlessly disclosed to us in the immediacy of such interaction".

A growing body of evidence indicate that relevant impairments in social cognition are a common feature in patient with schizophrenia-spectrum disorders [4]. Indeed, these social cognitive deficits are present not only in

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advanced phases of schizophrenia, but are manifested in early phases as well: for example, at the time of the First Episode of Psychosis (FEP) [5 6], in which anomalies of social cognition seem to be significant determinants of bad functional outcome and poor psychosocial adjustment [7 8]. Impaired social cognition has also been found in individuals at Ultra-High Risk (UHR) for psychosis [4 9], in which is considered to result in worse social functioning, a well-established risk factor for psychosis transition [10].

Expert surveys identified four core domain of social cognition in schizophrenia and psychosis research: (1) emotion processing (i.e. the ability in perceiving and displaying emotions, in recognizing different emotional states through facial expressions or voice intonations, and in managing emotions in oneself and in relation to others), (2) theory of mind (i.e. the capacity to represent the mental states of others, intentions, dispositions, or beliefs), (3) social perception (i.e. the ability in decoding and interpreting social cues in others and in identifying social roles and rules, as well as social context), and (4) attributional style (i.e. the way in which individuals explain the cause, or make sense, of social events or interactions to the self, others or the environment) [11]. However, most of the neuropsychological tests used to assess social cognition in schizophrenia research require a long time to be administered and therefore few clinicians use such scales in their daily practice [12]. According to Sanjuan et al. (2003) [13], the great distance between research and clinical practice and the modest utilization of scales by the physician is not primarily a problem of poor praxis, rather it is probably because their use does not seem to substantially improve the therapeutic approach. As an attempt to decrease such gap between research and clinical practice within the field of diagnosis and treatment of psychosis, the Spanish Group for the Optimization and Treatment of Schizophrenia (GEOPTE) developed a new scale for assessing social cognition in psychotic disorders [13]. The GEOPTE scale is a quick and easy (15-item) self-report questionnaire aimed to be able to relate basic cognitive deficits (or more specifically their subjective perception) with the subjective experience of social cognition.

To the best of our knowledge, no study using the GEOPTE scale in an Italian clinical sample has been reported in the literature to date. Thus, in the current research we want to test the reliability and the validity of the Italian version of the GEOPTE scale (i-GEOPTE) (Appendix I) in examining the subjective experience of social cognition in a population of adolescent and young adult help-seekers with FEP or at UHR for psychosis. Moreover, a Confirmatory Factorial Analysis (CFA) was conducted to evaluate the adequacy of the theoretical model proposed in the original validation study of the Spanish version of the GEOPTE scale [13] (Appendix I).

Materials and methods

Setting

As detailed in Raballo et al. (2014) [14], the "Reggio Emilia At-Risk Mental States" (ReARMS) protocol is an early detection and intervention infrastructure implemented in the Reggio Emilia Department of Mental Health (i.e. a semirural catchment area of approximately 550.000 inhabitants, in the Northern Italy) since September 2012. The ReARMS program purposes (a) to detect individuals with FEP and at clinical high risk of psychosis according to defined FEP/UHR diagnostic criteria [15] among young adult and adolescent help-seekers (aged 13-35 years), and (b) to offer evidence-based interventions that are shown to be effective in FEP/UHR subjects (i.e. individual cognitive-behavioral therapy, psychoeducational sessions for family members, intensive case management, and pharmacotherapy [as appropriated]) [16 17].

Participants

Psychometric properties of the GEOPTE scale were tested in a sample of help-seeking (i.e. voluntarily sought treatment) adolescents and young adults, aged 13-35 years, consecutively attending to one of all child/adolescent and adult mental health care services of the Reggio Emilia Department of Mental Health between September 2012 and December 2018. Referrals were mainly performed by General Practitioners, emergency room and general hospital, family members, school, social services, or they were self-referred [18 19].

For the specific aim of the study (i.e. testing psychometric properties of the Italian version of the GEOPTE scale), ReARMS inclusion criteria were: (a) specialist help-seeking; (b) age between 13 and 35 years; (c) presence of UHR criteria as defined by the Comprehensive Assessment of At-Risk Mental States (CAARMS) [15] or (d) a Duration of Untreated Psychosis (DUP) < 2 years in case FEP is detected at baseline assessment. Specifically, in the context of the clinical staging model of psychosis [20], three different subgroups of UHR mental states was identified: (a) Genetic Risk and Functioning Deterioration Syndrome (GRFD), a trait/state risk condition in which the individual has a family history of psychosis (in first-degree relatives) or manifests schizotypal personality disorder along with low functioning maintained for ≤ 1 month; (b) Brief Limited Intermittent Psychotic Symptoms (BLIPS), i.e. transient positive symptoms that spontaneously disappear within 1 week; and (c) Attenuated Psychotic Symptoms (APS), i.e. sub-threshold positive psychotic symptoms [15]. Moreover, according to the CAARMS criteria, FEP threshold is defined by operationalized clear-cut levels of full-blown positive symptoms occurring for the first time for > 1 week, either daily or > 3 time a week with each symptom continuing for > 1 hour on each occasion [15]. Young help-seekers who

were below the UHR/FEP threshold were considered as CAARMS negative cases (i.e. CAARMS-) [21 22].
Exclusion criteria were: (a) previous full-blown psychotic episodes, either schizophrenic and affective, as defined in the Diagnostic and Statistical Manual of Mental Disorders, IV Edition, Text Revised (DSM-IV-TR) [23]; (b) history of previous exposure to antipsychotics; (c) current substance dependence, (d) known mental retardation (IQ < 70), (e) neurological disorders (such as temporal lobe epilepsy), head injury or any other medical condition associated with psychiatric symptoms; and (f) insufficient fluency in the Italian language. Specifically, in the ReARMS protocol, we considered previous exposure to antipsychotic (i.e. before ReARMS enrollment) as an equivalent of past psychotic episode. Indeed, according to the psychosis criteria defined by Yung et al. (2015) [15] in the CAARMS, the threshold of FEP is essentially that at which antipsychotic medication would probably have started in common clinical practice.
All help-seekers entering the ReARMS protocol and their parents (if minors) agreed to participate to the research and gave their informed consent to the psychopathological assessment, composed – among others (for details, see also Raballo et al., 2014) [14] – by the CAARMS (approved Italian version [CAARMS-ITA]) [24] and the GEOPTE scale of social cognition for psychosis (approved Italian translation [i-GEOPTE]) [25]. Relevant local ethical approvals were sought for the study. The current research has been carried-out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experimental protocols including humans.

Instruments and measures

The *CAARMS* is a semi-structured clinical interview specifically developed to examine different aspects of attenuated psychopathology as well as functioning (via the integrated SOFAS ["Social and Occupational Functioning Assessment Scale"] module) [15]. It takes approximately 1-1.5 hours to be administered and consists of 27 items (each one rated in terms of intensity [0-6] and frequency/duration [0-6]), which can be clustered in seven subscales: (a) "Positive Symptoms"; (b) "Cognitive Change, Attention and Concentration"; (c) "Emotional Disturbance"; (d) "Negative Symptoms"; (e) "Behavioral Change"; (f) "Motor/Physical Changes"; and (g) "General Psychopathology". The CAARMS "Positive Symptoms" subscale, which covers delusions, hallucinations and thought disorder, is used to determine both the UHR criteria and the threshold for psychosis. CAARMS interviews are conducted by specialized clinical psychologists and psychiatrists, trained by the main author of the approved Italian translation (CAARMS-ITA) [20], who was trained at Orygen, The National Centre of Youth Mental Health in Melbourne, Australia. Regular CAARMS supervision sessions and scoring workshops ensured the inter-rater reliability of these assessments. Specifically, the CAARMS-ITA showed good to excellent inter-rater reliability [26 27].
The *GEOPTE* scale [13] is a self-report questionnaire specifically aimed, with its simplicity of design, to be of easy and quick use in the clinical practice for measuring social cognition in psychosis. It consists of 15 items, each one rated on a 5-point Likert scale (from 1 = "no" to 5 "a lot"). A total score was obtained by summing all item subscores. The original Spanish version of the GEOPTE scale showed excellent internal consistency and good construct validity in a clinical sample of 87 adult patients with psychosis [13]. An Exploratory Factor Analysis (EFA) identified 2 factors that explained a total variance of 39%. The first factor is composed by the first 7 items, specifically related with basic cognitive functions (i.e. attention, understanding, speech, learning, memory, concentration, and abstraction), and by items 11 and 12, involving tasks (i.e. ability to resolve problems and self-care capacity) that require the application of the basic cognitive functions for their achievement (for details, see Appendix I). The remaining items are related with factor 2, which refers to the four main aspects of social cognition (i.e. recognition of emotions, interpretation of social signals, sensitivity to social signals, activity planning, ability in relationships, and sexual satisfaction) [13]. However, in the original validation study of the GEOPTE scale, extraction of a single factor in the EFA was also satisfactory, explaining 33% of total variance. Therefore, as communality range of all items verified that an underlying common attribute existed, a single score is fully justified[13]. In the current study, we investigated the psychometric properties of the authorized Italian translation of the GEOPTE scale (i-GEOPTE) [21], adapted from the original Spanish version (Appendix I).

Procedures and statistical analysis

All the participants underwent an extensive diagnostic assessment (for details, see also Raballo et al., 2014) [14]. The axis-I diagnosis was made according to DSM-IV-TR criteria [23] by two trained ReARMS team members, using the Structured Clinical Interview for DSM-IV-TR Axis I Disorders [28]. After CAARMS interviews, adolescents were divided into three groups according to UHR/psychosis criteria: (a) UHR+ group (i.e. APS, BLIPS and GRFD), (b) FEP group, and (c) CAARMS- group (i.e. those individuals under the threshold of the CAARMS inclusion criteria) [15 19].
All the UHR/FEP help-seekers referred to the ReARMS protocol were assigned to a multi-professional team including a child/adolescent neuropsychiatrist, a clinical psychologist and a case-manager for early rehabilitation, generally within 2-3 weeks. According to their symptoms, UHR/FEP individuals were then provided

with a comprehensive two-year intervention package including (a) a multi-element psychosocial intervention (combining individual cognitive-behavioral therapy [CBT], psychoeducational sessions for family members, and a recovery-oriented case management) as first step and (b) a pharmacological treatment as second step, according to current guidelines [16 17]. The prescription of antipsychotics was avoided unless UHR individuals (a) had an imminent risk of suicide or severe violence, (b) were overwhelmed by abruptly worsening full-blown psychotic symptoms, (c) were rapidly deteriorating in daily functioning, or (d) did not respond to any other treatment [21]. Low-dose atypical antipsychotics were used. Selective serotonin reuptake inhibitor or benzodiazepines were used to treat depressive symptoms, anxiety, and insomnia [22].

The overall validation procedure of the i-GEOPTE was modeled on the methodological procedure adopted by Sanjuan et al. (2003) [13] to validate the original version of the GEOPTE scale. Data were analyzed using the "Statistical Package for Social Science" (SPSS) 15.0 for Windows [29] and R version 3.5.3 [30] with "Psych" and "Lavaan" software packages [31 32]. All tests were two-tailed, with $\alpha = 0.05$. Non-parametric statistics were used, due to non-normality (Kolmogorov-Smirnov test with Lilliefors significance correction: $p < 0.05$) in all explorations. In inter-group comparisons, categorical data were analyzed with Chi-square or Fisher(s exact test, as appropriate (i.e. when any expected frequency was < 1 or 20% of expected frequency was ≤ 5). The Kruskal-Wallis and the Mann-Whitney U test (as post-hoc procedure with Holm-Bonferroni correction for multiple comparisons) [33] were used to compare ordinal variables.

In the present research, we measured short-term test-retest reliability of the i-GEOPTE over two weeks calculating the coefficient of stability [34] on a subsample of 25 consecutive FEP participants. Specifically, as stability coefficients require three time points to estimate reliability, the i-GEOPTE scale was completed after 7 and 15 days from baseline assessment. This rather short-time interval was chosen to limit the possible impact of both symptomatic changes and memory effects [35]. According to Heise (1969) [36], we interpreted test-retest reliability coefficients as follows: ≥ 0.90 excellent reliability, 0.81-0.90 good reliability, 0.71-0.80 acceptable reliability, 0.61-0.70 questionable reliability, 0.51-0.60 poor reliability, and ≤ 0.50 unacceptable reliability.

As reliability measure, internal consistency of the i-GEOPTE was examined using Cronbach(s alpha within the total sample. A score above 0.70 was considered sufficient internal consistency [36]. In addition, we examined how each i-GEOPTE item correlated with the total score. Correlations less than r = 0.30 indicated that the item might need to be removed from the questionnaire to make it more reliable [36]. Finally, we were interested in Cronbach(s alpha value if each iGEOPTE item was deleted. If this value went up after item deletion, removal should be considered to ameliorate the reliability of the instrument [36].

As measure of concurrent validity, correlation analyses between iGEOPTE total scores and CAARMS subscores measuring impairments in basic cognitive functions and social cognition (i.e. subjective cognitive change, observed cognitive change, subjective experience of disorganized speech, avolition/apathy, anhedonia, and social isolation) were performed using Spearman(s correlation coefficient with Holm-Bonferroni correction to revise p-value for multiple comparisons [33]. Furthermore, we examined any relevant association of i-GEOPTE total scores with sociodemographic variables (i.e. gender, age, and years of education) and Duration of Untreated Illness (DUI, defined as the time interval [in weeks] between the onset of a prominent psychiatric symptom and the administration of the first pharmacological/psychological treatment) [37], using Chi-square test or Spearman(s correlation coefficient (as appropriate).

Finally, CFA was carried out to evaluate the adequacy of the 2-factor structure proposed in the validation study of the original Spanish version of the GEOPTE scale [13], using the robust weighted least squares (WLSMV) estimator. Indeed, the WLSMV estimator handles ordinal data well for moderately large samples [38]. The criterion of Brown (2006) [39] was used to assess the results. This criterion recommends using four common fit indices to evaluate fit of the overall model and to calculate both the satisfactory global functioning and model adjustment: Comparative Fit Index (CFI), Tucker-Lewis Index (TLI), Root Mean Square Error of Approximation (RMSEA), and Standardized Root Mean Square Residual (SRMR). According to Hu and Bentler (1999) [40], the following general rules of thumb were used in the present research: TLI/CFI > 0.95 (good fit), 0.90 to 0.95 (borderline fit), and < 0.90 (poor fit); RMSEA < 0.06 (good fit), 0.06 to 0.08 (fair fit), 0.08 to 0.10 (borderline fit), and > 0.10 (poor fit); SRMS < 0.08 (good fit).

Results

Sample characteristics and i-GEOPTE scores

Over the course of the study, 325 individuals (180 males, 55.4%) consecutively attended an intake interview within the ReARMS protocol. Age ranged from 13 to 35 years (mean age = 21.23 ± 5.85 years), level of education from 7 to 18 years (mean level of education = 11.65 ± 2.41 years), and the DUI from 4 to 208 weeks (mean DUI = 76.81 ± 60.89 weeks). In the total sample, the distribution of age, level of education (in years), and DUI (in weeks) was skewed towards the left (respectively, skewness =

TABLE I. *i-GEOPTE total scores, sociodemographic and clinical characteristics of the total sample and the three subgroups.*

Variable	Total sample (n = 325)	CAARMS- (n = 97)	UHR (n = 92)	FEP (n = 136)	χ^2	Post hoc test
Gender (males)	180 (55.4%)	47 (48.5%)	34 (47.8%)	89 (65.4%)	9.58†	FEP > UHR=CAARMS-††
Ethnic group (Caucasian)	284 (87.4%)	83 (85.6%)	84 (91.3%)	117 (86.0%)	1.78	-
Mother tongue (Italian)	295 (90.8%)	91 (93.8%)	85 (92.4%)	119 (87.5%)	3.10	-
Age	21.23 ± 5.85	21.01 ± 6.32	18.78 ± 4.32	23.04 ± 5.80	30.56*	FEP > CAARMS->UHR**,††,‡‡
Education (in years)	11.65 ± 2.41	11.59 ± 2.47	11.48 ± 2.30	11.80 ± 2.46	1.22	-
DUI (in weeks)	76.81 ± 60.89	65.25 ± 53.21	63.28 ± 46.75	96.45 ± 71.06	9.24‡	FEP > UHR=CAARMS-‡‡
i-GEOPTE						
Total score	35.19 ± 11.90	29.57 ± 11.42	38.32 ± 11.02	36.88 ± 11.76	34.91*	UHR = FEP > CAARMS-**
"Basic Cognitive Functions" subscore	19.96 ± 7.40	16.85 ± 7.30	21.50 ± 7.04	21.23 ± 7.08	31.91*	UHR = FEP > CAARMS-**
"Social Cognition" subscore	16.87 ± 5.87	114.29 ± 5.32	18.49 ± 5.37	17.61 ± 6.00	31.84*	UHR = FEP > CAARMS-**

Note. Frequencies (percentages), mean ± standard deviation, Kruskal-Wallis and Chi-squared test (χ^2) values are reported. Post-hoc analyses were performed using Mann-Whitney U test. °p < 0.001; †p < 0.01; ‡p < 0.05; °°Holm-Bonferroni corrected p-value < 0.001; ††Holm-Bonferroni corrected p-value<0.01; ‡‡Holm-Bonferroni corrected p-value < 0.05. i-GEOPTE = Italian version of the GEOPTE Scale of social cognition for psychosis; GEOPTE = "Grupo Espanol para la Optimización y Tratamiento de la Esquizofrenia" (Spanish Group for the Optimization and Treatment of Schizophrenia); DUI = Duration of Untreated Illness; CAARMS = Comprehensive Assessment of At-Risk Mental States; FEP = First Episode Psychosis; UHR = participants who met CAARMS Ultra-High Risk (UHR) criteria; CAARMS- = participants who were below CAARMS-defined UHR/FEP criteria.

0.660, 0.187, and 0.918; Kolmogorov-Smirnov test with Lilliefors significance correction: p < 0.001).

Table I shows i-GEOPTE total scores, demographic and clinical characteristics of the total sample and the three subgroups, i.e. FEP (n = 136; 41.8% of the total sample), UHR (n = 92; 28.4%), and CAARMS- (n = 97; 29.8%).

Among the UHR group, 83 met APS criteria (90.2% of UHR individuals), 5 met BLIPS criteria, and 4 met GRFD criteria.

The FEP group consisted of patients with DSM-IV-TR schizophrenia (n = 63; 46.3% of FEP individuals), affective (bipolar or major depressive) psychosis (n = 31), psychotic disorder not otherwise specified (n = 28), substance-induced psychotic disorder (n = 8), and brief psychotic disorder (n = 6).

The remaining participants were below the CAARMS-defined FEP/UHR criteria and composed the CAARMS- group. They were diagnosed with DSM-IV-TR non-schizotypal personality disorder (n = 37; 38.1% of CAARMS- individuals), depressive disorders (n = 29; 29.9%), anxiety disorders (n= 26; 26.8%), and eating disorders (n = 5).

In comparison with UHR and CAARMS-, FEP patients showed a significantly higher age at ReARMS enrollment, a greater percentage of males, and a longer DUI (Tab. I). Moreover, at baseline assessment UHR individuals had a younger age than CAARMS- participants. No inter-group difference in terms of ethnic group, mother tongue, and years of education was found.

In comparison with CAARMS-, both UHR and FEP subjects showed significantly higher i-GEOPTE total score, as well as "Basic Cognitive Functions" and "Social Cognition" subscale scores (Tab. I).

Reliability

The i-GEOPTE was re-administered to 25 consecutive FEP participants within 2 weeks (i.e. on the 7th and 15th day) from the baseline assessment in order to calculate short-term test-retest reliability. Their sociodemographic characteristics were comparable to those of the total sample, with a mean age of 20.26 ± 1.02 years and a mean level of education of 12.22 ± 1.93 years. Fourteen (56%) out of these 25 FEP participants were males.

The coefficient of stability was 0.813 for i-GEOPTE total score, 0.824 for "Basic Cognitive Functions" subscore, and 0.807 for "Social Cognition" subscore.

Within the total sample, i-GEOPTE total score showed a Cronbach(s alpha of 0.90 (95% confidence intervals = 0.88-0.92). All item-total correlations were higher than 0.30 (Tab. II). Thus, all i-GEOPTE items appeared to be worthy of retention, resulting in a decrease in the alpha coefficient if deleted.

Concurrent validity

All i-GEOPTE total scores showed significant positive correlations with DUI and with CAARMS "Subjective Cognitive Change" and "Objective Cognitive Change" subscale scores, as well as with CAARMS "Disorganized speech – Subjective change", "Concentration/

TABLE II. *Internal consistency of the i-GEOPTE scale (n = 325).*

i-GEOPTE items	Item-total correlation	Cronbach(s alpha if item deleted
It is difficult for you to pay attention?	.587	.894
It is difficult for you to follow a conversation in which several people are participating?	.693	.890
It is hard for you to learn new things?	.724	.889
Do you forget to do things asked of you, tasks, or errands?	.524	.896
When you have to speak to someone, do you have problems in expressing yourself?	.692	.890
Do you have problems understanding what a picture is about?	.413	.900
Is it difficult for you to understand the meaning of a conversation?	.678	.892
Is it hard for you to recognize the emotions of others (for example, sadness, happiness, rage)?	.454	.899
When you are in a group, do they usually tell you that you have misunderstood the attitudes, looks, or expressions of the others?	.517	.897
Do you feel very sensitive to looks, words, or expressions of others?	.556	.896
If you are alone at home and some problem arises (for example, an appliance breaks down), is it difficult for you to look for a solution?	.603	.893
Do you find it hard to maintain personal hygiene (to be clean and washed)?	.541	.896
Do you find it hard to make plans for the weekend?	.665	.891
Is it hard for you to make plans with friends?	.580	.895
Are you generally unsatisfied with your sexual life?	.525	.897

Note. i-GEOPTE = Italian version of the GEOPTE Scale of social cognition for psychosis; GEOPTE = "Grupo Espanol para la Optimización y Tratamiento de la Esquizofrenia" (Spanish Group for the Optimization and Treatment of Schizophrenia). Correlation r coefficients and Cronbach(s alpha values are reported.

Attention subjective disorders", "Selective Attention subjective disorders", "Formal Thinking subjective disorders", "subjective Difficulty in Understanding", "Memory subjective problems", "Observed Inattention during the interview", "Observed Inattention during Mental Status Testing", "Avolition/Apathy", "Anhedonia", and "Social Isolation" item subscores (Tab. III).

Furthermore, i-GEOPTE total scores had significant negative correlations with age. Specifically, younger participants (aged ≤ 21 years) showed significantly higher i-GEOPTE total scores than older individuals (aged > 21 years) (Tab. IV). Finally, no significant associations of i-GEOPTE total scores with gender and years of education were found (Tabs. III-IV).

Confirmatory factor analysis

The indices CFI, TLI, RMSEA and SRMR were analyzed to assess the adjustment of the original 2-factor GEOPTE model of 15 items in our sample (Tab. V). All these fit indices remained adequate, maintaining acceptable values (0.957, 0.950, 0.079, and 0.062, respectively). Factor loadings of the i-GEOPTE items are reported in the Tab. V.

Discussion

To the best of our knowledge, no study to validate the Italian version of the GEOPTE scale of social cognition for psychosis in a clinical sample of adolescent and young adult help-seekers has been performed to date.

In comparison with CAARMS-, both UHR and FEP participants had significantly higher i-GEOPTE total scores, indicating a broader impairment. Overall, these results show that the Italian version of the GEOPTE scale has good construct validity and substantially confirm findings of other comparable studies reporting relevant impairments of social cognition both in FEP and UHR individuals [5 6 9]. According to Raballo (2017) [3], this evidence highlights a clinical feature which is rather familiar to any professionals dealing with the field of early detection in psychosis: i.e. UHR and FEP subjects spend considerably more time (i.e. almost twice as much) on emotional recognition (allegedly a core component of social cognition) than healthy controls [41]. This is generally interpreted as the effect of compensatory mechanisms buffering the (more or less mutually reinforcing) decline in neurocognitive and socio-cognitive proficiencies.

However, in the current research no difference in terms of iGEOPTE total scores was found between UHR and FEP individuals. This result is not in line with other studies reporting that performance in social cognitive domains in UHR subjects was generally intermediate between FEP and healthy control groups [5 41].

Reliability

In the current research, the Italian version of the GEOPTE scale showed good short-term (2 week) test-retest reliability (coefficient of stability = 0.813 for the total score, 0.824 for "Basic Cognitive Functions" subscore, and 0.807 for "Social Cognition" subscore).

TABLE III. *Spearman's correlations among GEOPTE scores, age, and CAARMS subscale scores.*

Variables	GEOPTE total score (ρ)	GEOPTE "Basic Cognitive Functions" subscore (ρ)	GEOPTE "Social Cognition" subscore (ρ)
CAARMS			
Disorganized speech – subjective change	.334*	.361*	.257*
Subjective Cognitive Change	.322*	.346*	.258*
Concentration and attention disorders	.302*	.318*	.239*
Selective attention disorders	.358*	.356*	.314*
Formal thinking disorders	.308*	.339*	.248*
Difficulty in understanding	.329*	.370*	.237*
Memory problems	.203*	.242*	.126‡
Objective Cognitive Change	.238*	.267*	.173†
Observed inattention during the interview	.245*	.282*	.174†
Observed inattention during Mental Status Testing	.158†	.177†	.115‡
Avolition/apathy	.361*	.348*	.342*
Anhedonia	.382*	.373*	.357*
Social isolation	.341*	.371*	.324*
Age	-.159†	-.187†	-.112‡
Years of education	-.018	-.031	-.002
DUI (in weeks)	.160‡	.183†	.134‡

*Note. GEOPTE = "Grupo Espanol para la Optimización y Tratamiento de la Esquizofrenia" (Spanish Group for the Optimization and Treatment of Schizophrenia), CAARMS = Comprehensive Assessment of At-Risk Mental States; SOFAS = Social and Occupational Functioning Assessment Scale; DUI = Duration of Untreated Psychosis; *Holm-Bonferroni corrected p-value < 0.001; †Holm-Bonferroni corrected p-value < 0.01; ‡Holm-Bonferroni corrected p-value <0.05. Spearman(s rank correlation coefficient (ρ) values are reported.*

Moreover, we found good to excellent reliability of the iGEOPTE scale with regard internal consistency (i.e. Cronbach(s alpha = 0.90 for the total score). Moreover, all item-total correlations were higher than 0.30. Thus, all i-GEOPTE items appeared to be worthy of retention, resulting in a decrease in the alpha coefficient if deleted. Similarly, in the validation study of the Spanish original version of the GEOPTE scale Sanjuan et al. (2003) [13] found a Cronbach(s alpha of 0.86, with corrected item-total correlations exceeding the 0.30 value for all the items. Therefore, the GEOPTE scale of social cognition for psychosis appears to be reliably good in different samples and cultures.

Concurrent validity

As expected, iGEOPTE total scores showed significant positive correlations with CAARMS subscale and item subscores measuring impairments in basic cognitive functions and social cognition (e.g. subjective cognitive change, observed cognitive change, subjective experience of disorganized speech, avolition/apathy, anhedonia, and social isolation). These findings suggest good concurrent validity of the Italian version of the GEOPTE scale and are a further confirmation of the construct validity of the instrument, also reported in the original validation study by Sanjuan et al. (2003) [13]. Moreover, our CFA findings suggest that the 2-factor model of the original Spanish version of the GEOPTE scale fitted our data reasonably well, and that these two subscales (i.e. "Basic Cognitive Functions" and "Social Cognition") measure discrete constructs, although related to each other.

In the present study, significant negative correlations between age and iGEOPTE total scores were also found. Specifically, younger individuals (aged ≤ 21 years) had significantly higher levels of subjective experience of impaired basic cognitive functions and social cognition than older participants. Differently, in a meta-analysis on social cognition in individuals in the early stage of psychosis, van Donkersgoed et al. (2015) [10] found no moderator effects for age. However, our findings could first be interpreted in the light of a greater awareness of subjective deficits in social cognition in adolescents than in young adults. Indeed, in the developmental age social cognition is crucial for an adequate psychosocial adjustment and to be accepted in the peer group. Therefore, subjective experience of impaired social functioning may slow or stop the basic developmental stage that leads adolescent to a pragmatic immersion in the social world, so inducing a higher psychological distress. Otherwise, in the current research older participants were more frequently diagnosed with FEP and consequently

TABLE IV. *Association of i-GEOPTE total scores with age and gender (n = 325).*

Variable	Total sample (n = 325)	Age group I < 15 years (n = 52)	Age group II 15-18 years (n = 92)	Age group III 18-21 years (n = 56)	Age group IV > 21 years (n = 134)	χ^2	Post hoc test
i-GEOPTE							
Total score	35.19 ± 11.90	37.50 ± 13.60	36.71 ± 11.62	36.96 ± 11.99	32.61 ± 10.95	11.10‡	I = III = II > IV‡‡
"Basic Cognitive Functions" subscore	19.96 ± 7.40	22.37 ± 9.39	21.14 ± 7.34	20.56 ± 7.30	18.61 ± 6.87	11.76†	I = II = III > IV‡‡
"Social Cognition" subscore	16.87 ± 5.87	16.30 ± 6.97	17.76 ± 5.82	17.71 ± 6.27	16.12 ± 5.44	8.02‡	II = III = I > IV‡‡

Variable	Total sample (n = 325)	Age group I < 21years (n = 191)	Age group II > 21 years (n = 134)	Z
i-GEOPTE				
Total score	35.19 ± 11.90	37.00 ± 12.23	32.61 ± 10.95	-3.33††
"Basic Cognitive Functions" subscore	19.96 ± 7.40	21.13 ± 7.65	18.61 ± 6.87	-3.05††
"Social Cognition" subscore	16.87 ± 5.87	17.52 ± 6.16	16.12 ± 5.44	-2.10‡‡

Variable	Males (n = 180)	Females (n = 145)	Z
i-GEOPTE			
Total score	34.08 ± 11.35	36.57 ± 12.45	-1.71
"Basic Cognitive Funtions" subscore	19.54 ± 7.13	20.48 ± 7.71	-0.94
"Social Cognition" subscore	16.29 ± 5.62	17.58 ± 6.10	-1.83

*Note: i-GEOPTE = Italian version of the GEOPTE scale of social cognition for psychosis; GEOPTE = "Grupo Espanol para la Optimización y Tratamiento de la Esquizofrenia" (Spanish Group fo the Optimization and Treatment of Schizophrenia). Frequencies (percentages), mean ± standard deviation, Kruskal-Wallis test (χ2) and Mann-Whitney U test (Z) values are reported. Post-hoc analyses were performed using Mann-Whitney U test. *p < 0.001; †p < 0.01; ‡p < 0.05; **Holm-Bonferroni corrected p-value < 0.001; ††Holm-Bonferroni corrected p-value < 0.01; ‡‡Holm-Bonferroni corrected p-value < 0.05.*

could have a lower insight on their subjective experience of attenuated psychopathology and psychosocial functioning. Consistently with this hypothesis, there is also evidence of positive correlation between i-GEOPTE total scores and a longer DUI, which has been widely reported to be related with lower insight and poor daily functioning both in UHR than FEP individuals [37].

Finally, in the present study no significant correlations of i-GEOPTE total scores with gender and years of education were found. Likewise, a meta-analysis on social cognition in UHR individuals reported no significant moderator effect for gender and level of education [10].

Limitations

In the current research, there are some methodological limitations to be acknowledged. First, a possible weakness is that the GEOPTE scale was specifically developed to measure subjective experience of social cognition and related basic cognitive functions. This does not allow a direct comparison with results of previous studies on social cognition using specific neuro-socio-cognitive tasks for emotional recognizing, theory of mind, social perception, and attributional style. Indeed, main aim of the GEOPTE scale was to be a quick and easy self-report questionnaire contributing to decrease the gap between research and clinical practice within the field of diagnosis and treatment of early psychosis [13].

Secondly, another weakness of this study is that findings on iGEOPTE total scores were not checked for IQ and antipsychotic dosage. Thus, further research involving specific measures on intelligence quotient and use of antipsychotics are needed.

Conclusions

Findings of this research indicate that the Italian version of the GEOPTE scale of social cognition for psychosis is reliable and valid, showing satisfactory psychometric

TABLE V. *Indices of adjustment and item factor loadings obtained in the Confirmatory Factor Analysis (CFA) using the original Spanish version of the GEOPTE scale of social cognition for psychosis (Sanjuan et al., 2003)* [13].

Indice of adjustment	GEOPTE scale (15 items)	Accepted values
CFI	0.957	≥ 0.90
TLI	0.950	≥ 0.90
RMSEA	0.079	≤ 0.06-0.08
SRMR	0.062	≤ 0.08
Item	Factor 1 Basic cognitive functions	Factor 2 Social cognition
Geopte1	0.678	-
Geopte2	0.801	-
Geopte3	0.825	-
Geopte4	0.575	-
Geopte5	0.775	-
Geopte6	0.549	-
Geopte7	0.820	-
Geopte11	0.703	-
Geopte12	0.646	-
Geopte8	-	0.579
Geopte9	-	0.593
Geopte10	-	0.644
Geopte13	-	0.795
Geopte14	-	0.697
Geopte15	-	0.611

Note. GEOPTE = "Grupo Espanol para la Optimización y Tratamiento de la Esquizofrenia" (Spanish Group for the Optimization and Treatment of Schizophrenia)CFI = Comparative Fit Index; TLI = Tucker-Lewis Index; RMSEA = Root Mean Square Error of Approximation; SRMR = Standardized Root Mean Square Residual.

properties in assessing subjective experience of socio-cognitive functions in adolescent and young adult community help-seekers. Hence, the iGEOPTE appears to be a suitable self-report instrument for routine use in mental health care services, also in order to evaluate functional outcomes of our intervention. Indeed, it is becoming clearer that to assess if psychopharmacological and/or cognitive-behavioral treatments (as well as cognitive rehabilitation programs) have a repercussion in daily life and improve the individual(s prognosis, we should measure the change in social functioning and not simply the variations in the neurocognitive tests [13]. Furthermore, as psychotic experiences during adolescence index increased risk for psychotic disorders in adult life and are commonly correlated to specific neurocognitive anomalies (such as working memory deficits), the routine use of instruments assessing subjectively experienced socio-cognitive functions may also be useful to provide prompt and targeted intervention counteracting the possible early cognitive functioning decline in psychotic disorders [42].

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Conflict of interest

The Authors declare to have no conflict of interest.

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APPENDIX I. *The Italian version of the GEOPTE Scale of social cognition for psychosis (Raballo, 2005)* [21].

Cognome ……..Nome……Data……

Di seguito sono elencate alcune situazioni, sensazioni, emozioni che potrebbero esserti capitate o che potresti avere provato. Segna con una crocetta il numero corrispondente alla frequenza con cui sono/sono state presenti.

		No/per nulla	Poco	Medio	Abbastanza	Molto
1	Fai fatica a stare attento?	1	2	3	4	5
2	Trovi difficile seguire una conversazione in cui partecipano molte persone?	1	2	3	4	5
3	Ti risulta faticoso apprendere cose nuove?	1	2	3	4	5
4	Ti dimentichi di fare cose che ti vengono chieste, compiti, commissioni?	1	2	3	4	5
5	Quando devi parlare con qualcuno, hai dei problemi a esprimerti/farti capire?	1	2	3	4	5
6	Fai fatica a comprendere il soggetto di un quadro?	1	2	3	4	5
7	È difficile per te comprendere il significato di una conversazione?	1	2	3	4	5
8	Ti è difficile riconoscere le emozioni degli altri (per esempio: tristezza, allegria, collera)?	1	2	3	4	5
9	Quando sei in gruppo, ti viene detto spesso che hai frainteso gli atteggiamenti, gli sguardi o le espressioni degli altri?	1	2	3	4	5
10	Ti senti particolarmente sensibile agli sguardi, parole o espressioni degli altri?	1	2	3	4	5
11	Se ti trovi da solo in casa e subentra qualche problema (per esempio si rompe un apparecchio domestico), fai fatica a trovare una soluzione?	1	2	3	4	5
12	Fatichi a badare alla tua igiene personale (essere pulito, lavato)?	1	2	3	4	5
13	Trovi difficile fare piani per il fine settimana?	1	2	3	4	5
14	Ti risulta difficile fare amicizia?	1	2	3	4	5
15	Sei globalmente insoddisfatto della tua vita sessuale?	1	2	3	4	5

Note. GEOPTE = "Grupo Espanol para la Optimización y Tratamiento de la Esquizofrenia" (Spanish Group fo the Optimization and Treatment of Schizophrenia).

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Acute cognitive and psychomotor impairment in a patient taking forty different herbal products and dietary supplements: a case report

Summary

The use of dietary supplements and herbal medicines is spreading across many developed countries. Although patients without specific problems can administer most, relevant toxicities might occur with a reckless use of dietary supplements, especially when psychiatric or medical comorbidities are present. Limited research is available on these compounds. We describe the case of a suspected intoxication due to a reckless use of a number of dietary supplements and herbal medicines (forty different compounds) in a patient with a history of recurrent depression and gromerulonephritis, hospitalized for acute cognitive and psychomotor impairments.

Key words

Nutritional supplements • Herbal • Cholinergic syndrome

Introduction

The World Health Organization (WHO) and the United States (US) Dietary Supplements Health and Education Act, in the early '90, defined dietary supplements as a product (other than tobacco) that is meant to supplement the diet [1]. Both organizations include vitamins, minerals, herbs, botanical products, amino acids, or dietary substances in their definitions [2]. Since then, dietary supplements and herbal medicines are playing a growing role in health care. Vitamins and minerals are necessary for enzymatic reactions and bodily functions. It is well known that the lack of these compounds can lead to deficiency-related diseases [2]. However, by the arbitrary classification in *herbals'* and *other medicinal* products as *dietary supplements*, DSHEA obscured the fundamental differences between the two classes of products [3], even if there is no scientific basis for calling the *herbals supplements*. Authentic *supplements*, are multivitamins or calcium: they have nutritional value and are safe when used in recommended doses.

According to the 2006 American Association of Poison Control Center (AAPCC), there were a total of 972,073 significant adverse events due to the exposure to pharmaceutical products, with 6,809 major outcomes, 507 of whom resulting in deaths [4]. Of the above-mentioned adverse events, 76,364 (7.9%) were in some way related to the use of dietary supplements and vitamins, with 42 major outcomes (0.6%) and 3 deaths (0.6% of all deaths). Thus, despite the impressive widespread of these products, the adverse outcomes and deaths are reported as exceptional. Dietary supplements and herbal medicines seem to be relatively harmless when appropriately used, even if there is growing concern on both the interactions with concurrent drugs and the potential adulteration of such compounds. The Food and Drug Administration (FDA) had issued

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warnings about 300 tainted products that can cause serious adverse events, including stroke, organ failure and death [5]. Nonetheless, some adulterated products remain in the marketplace even after recalls [6].

Reports suggesting a relationship between an improper or a reckless use of these products and the onset of clinically relevant side effects are still under-estimated for a number of reasons, namely: a common perception in the patients' population that these products are inherently safe; the lack of information amongst medical professionals on their potential toxicity; the lack of systematic studies on such compounds when concurrent chronic medical diseases are present; the underestimation of their chronic abuse; the underestimation of the interactions between different herbals.

In this case report, we hypothesize that the use of a uncommon number of dietary supplements (forty different compounds at the same time) in a patient with a chronic kidney disease and a history of recurrent depression could be related to the onset of acute psychomotor and cognitive impairments. The presentation of this case report followed the CARE Guidelines [7] (2013). The patient signed an informed consent encompassing the data collection and presentation both for research and clinical purposes. However, even if the patient signed the above-mentioned consent form, all the information reported in this case report was anonymous.

Case presentation

A 38-year-old Caucasian male patient suffered from a recurrent major depressive disorder, with two major depressive episodes of moderate severity up to the present that remitted spontaneously. The family anamnesis regarding mental disorders was negative, and the patient did not use any psychotropic agents such as alcohol, nicotine or any illicit drugs. The patient lived in

TABLE I. *Timeline description of the case report.*

Psychopathological dimensions	2 weeks before hospitalization	On admission	During hospitalization before discontinuation of dietary supplements	1-week after discontinuation of dietary supplements	At discharge
Cognition	No signs or symptoms	Severe speech impairment; thoughts contents not described	Unable to provide useful information oh his cognitive state or performances (catatonia?)	Recovery with description of thoughts contents and mood states	Recovery with description of thoughts contents and mood states
Mood	Depressive mood Inner tension Emotional instability and liability	Unable to perform an evaluation or to describe his mood.	Unable to provide useful information oh his cognitive state or performances (catatonia?)	Patient able to perform a clinical interview. He described a subjective elevated mood, with decreased inner sense of tension	Euthymic
Circadian Rhythms	Severe insomnia	Severe insomnia	Severe insomnia	Improved sleep quality	Improved sleep quality. No insomnia
Psychomotor signs and symptoms	Widespread tremor Psychomotor retardation Rigidity	Severe psychomotor retardation Catatonia-like syndrome Rigidity Tremor Impaired gait	Severe psychomotor retardation Catatonia-like syndrome Rigidity Tremor Impaired gait	Improvement of psychomotor functions, with recovery	No evident or subjectively perceived psychomotor impairment
Other signs/ symptoms	Hyperhidrosis Bronchorrea	Sialorrhea, Hyperhidrosis	Sialorrhea, Hyperhidrosis	No hyperhidrosis No sialorrhea.	No thought abnormality

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a stable partnership (married 15 years before) without children and he was an employee, at the time of hospitalization. There was a relevant somatic comorbidity for hypertension and idiopathic glomerulonephritis. Before present hospitalization he was treated with ramipril (10 mg/day), bisoprolol (5 mg/day), doxazosin (8 mg/day), and amlodipin (5 mg/day). He reported also a period of treatment with corticosteroids due to the glomerulonephritis, few months before, but he was unable to describe more in detail dosage and treatment duration.

During the last two weeks before hospitalization, the patient had problems to fall asleep, with pronounced inner tension, depressive mood, emotional instability, dyspnoea, bronchorrea, and hyperhidrosis. These symptoms remarkably increased in the following days resulting in retardation, rigidity, widespread tremor, and mutism. Thus, the patient's wife contacted a psychiatrist. Psychosocial stress factors or any other circumstances that might have been plausibly involved in the causation of the described syndrome were ruled out. The psychiatrist diagnosed a catatonia with psychomotor retardation, and prescribed lorazepam (up to 15 mg/day), with no significant improvement. Then the patient was hospitalized (Tab. I).

On admission, the patient was drowsy, with a severe psychomotor retardation, oriented as to time and places but unable to give more detailed information on his mental state. He presented hypomimia, drooling, bradykinesia, impaired oculomotor movements (upward gaze and convergence), festinating gait, moderate intermittent tremor (both at rest and in motion), trunk and limbs rigidity, and oculo-cephalic reflex with optokinetic nystagmus. A specialist in internal medicine and a neurologist evaluated the patient. No acute medical condition was considered as related to clinical picture. The neurological signs and symptoms lead to a number of clin-

ical hypotheses: Posterior Reversible Encephalopathy Syndrome, limbic Encephalitis, Parkinsonism, Cortical Atrophy, Lewy-Body Dementia. A Magnetic Resonance Imaging (MRI) was performed. No abnormalities were found. Electroencephalography (EEG) showed mild generalized background slowing of cerebral electrical activity, probably due to the administration of lorazepam before hospitalization. SPECT DAT-SCAN was negative for nigro-striatal degeneration. PET scan identified a generalized reduction of cortical glucose metabolism in the occipital area on both hemispheres. Uptake of sub-cortical regions, thalamic regions, striatum and cerebellum was normal. Even a lumbar puncture was performed with negative results. According to the neurologist, there was no explanation for the described symptomatology.

Metabolic abnormalities were ruled out considering the normal ranges of complete blood count, serum glucose and electrolytes. Levels of vitamin B12 and folates were also within normal range. Blood culture urine cultures were negative, as well as neuro-degenerative proteins, (namely, neuro-oncogens, Ab Anti Hu, Ab Anti Yo, Ab Anti Ri, Ab Anti Anfifisin, Ab anti GAD, Ab Anti NMDA and Ab Anti VGKC). Negative blood tests and imaging led the clinicians to consider a Parkinsonism, even if the patient was not taking psychotropic medications. The patient was, then, empirically treated with levodopa and carbidopa, but no improvement was observed. During hospitalization, the patient had a gradual improvement only when a number of dietary supplements and herbal medicines he was taking at home and he was autonomously managing, were progressively discontinued, and when trihexyphenidyl was added for rigidity. The patient reported that, during the last 6 months, he added to ramipril, bisoprolol, doxazosin, and amlodipin a number of *natural* compounds that he was still taking during hospitalization, namely: syiybum marianum, curcuma longa, taurine, pneumus boldus, glutathione, phyllantus amarus, taraxacum officinal, crataegus oxycantha, allium sativum, leonurus cardiaca, betual verrucosa, fumaria officinalis, passiflora, actium lappa, betula alba, cynara scolimus, berberis vulgaris, cynodon dactylon, spirulina maxima, mellitus officinalis, ribes nigrus, marrubium vulgare, ruscus aculeatus, cupressus serpenvirens, proantocianidine, boswella serrata, elastine, dioscorea opposita, diosgenina, glucosamine, thea sinensis, epigallocatechine, cochiearia armoracia, glucorafanine, sulforafane, soja, genisteine, magnesium, zinc, selenium.

According to the patient, all these compounds were prescribed 6 months before by a *phyto-therapist*, as add-on to the usual treatments for gromerulonephritis and hypertension.

The discontinuation of these compounds during hospitalization was concomitant with a gradual improvement. Thus, the patient recovered regarding his mimic and speech ability; rigidity faded with a normal posture and motion. Mood was euthymic and no thought abnormality or residual cognitive impairment was found. The patient was then discharged.

Discussion

It's virtually impossible to affirm with certainty that psychomotor and cognitive impairments that lead to patient's hospitalization could have been directly provoked and sustained by the protracted use of the impressive number of dietary supplements and herbal medicines that the patient was taking during the last 6 months. However, no other possible explanations were found, and the discontinuation of such compound was concomitant with clinical remission.

Our hypothesis is that the protracted use of such compounds produced a clinical syndrome of cholinergic overstimulation, with bronchorrhea, respiratory muscle weakness and delayed neurotoxic effects with prevalent extra-pyramidal symptoms mimicking catatonia. Resolution after the discontinuation of herbal/nutritional supplements and with the administration of trihexyphenidyl is suggestive of such explanation.

To our knowledge, no studies have been conducted on the cholinergic effects of herbal supplements. However, It is well documented that patients with chronic illnesses (such as, in our case, a glomerulonephritis) are most likely to consume dietary supplements or herbal medications, with a significant risk of interactions [8]. A problem is also the contamination of herbals with microorganisms, fungal toxins such as aflatoxin, with pesticides and heavy metals that might be related with a cholinergic over-stimulation [9]. For patients taking multiple medications and dietary supplements or herbal medicines, physicians should look out for herb-drug interactions. However, It is impossible to check the interactions between forty different compounds (as in the described case) or to have reliable information on their purity. This case report, in our opinion, is raising questions on the importance of a more aware use of herbals, and on the importance of a more effective communication between health professionals and patients on the potential risks of products whose benefits, side effects, and reciprocal interactions are still largely unknown. Further research is necessary to investigate individual risk factors and preparation-specific characteristics that might predispose to the development of side effects, especially when herbal compounds are taken for a long time. Experience from our clinical unit suggests that most patients may use herbal products that are absent from the substances whose interaction risks are described in a systematic manner. Physicians might warn their patients on the potential risk linked to *herbal extracts,*

but in most cases without soundly based evidence from literature. We believe that promoting an active vigilance strategy for herbal compounds may help to generate better evidence, together with the promotion of specific education tools about the potential interactions of such compounds. The development of *integrative medicine centers* promoting interdisciplinary collaboration between patients, physicians, psychiatrists, and researchers formed in this field could be a possible future target.

Contributors

Marco Maiello, M.D. and Manuel Glauco Carbone written the case report; Liliana Dell'Osso M.D., and Marly Simoncini, M.D. were the case managers of the patient and contributed to describe the case report; Mario Miniati, M.D., revised the case report for intellectual content.

Conflict of interest.

The Authors declare to have no conflict of interest.

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