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JOURNAL OF PSYCHOPATHOLOGY

GIORNALE DI PSICOPATOLOGIA

Editor-in-chief: Alessandro Rossi

EDITORIAL



107 Suicide and autism spectrum disorder: the role of trauma

ORIGINAL ARTICLES



110 On the notion of psychosis: semantic and epistemic concerns

118 Quality of life and psychopathology of patients awaiting kidney/pancreas transplants

127 Empathic and cognitive processing in people with schizophrenia: a study on an Italian sample

135 Sleep disorders in adult ADHD: a key feature

141 Quality of life, alexithymia, and defence mechanisms in patients affected by breast cancer across different stages of illness

ASSESSMENT AND INSTRUMENTS IN PSYCHOPATHOLOGY



149 Development, cross-cultural adaptation process and preliminary validation of the Italian version of the Nepean Dysphoria Scale

157 Development and validation of an abridged version of the Social Provisions Scale (SPS-10) in Italian

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Editorial

Suicide and autism spectrum disorder: the role of trauma <i>L. Dell’Osso, C. Gesi, C. Carmassi</i>	107
---	-----

Original articles

On the notion of psychosis: semantic and epistemic concerns <i>J. Adan-Manes, P. Ramos-Gorostiza</i>	110
Quality of life and psychopathology of patients awaiting kidney/pancreas transplants <i>M. Mauri, A. Calderone, P.F. Calabrò, S. Augusto, G. Ceccarini, P. Piaggi, P. Vitti, F. Santini, U. Boggi</i>	118
Empathic and cognitive processing in people with schizophrenia: a study on an Italian sample <i>I. Riccardi, A. Carcione, M. D’Arcangelo, R. Rossi, G. Dimaggio, P.H. Lysaker, P. Stratta</i>	127
Sleep disorders in adult ADHD: a key feature <i>L. Salerno, N. Makris, S. Pallanti</i>	135
Quality of life, alexithymia, and defence mechanisms in patients affected by breast cancer across different stages of illness <i>G. Marrazzo, L. Sideli, R. Rizzo, A.M. Marinaro, A. Mulè, A. Marrazzo, C. La Cascia, D. La Barbera</i>	141

Assessment and instruments in psychopathology

Development, cross-cultural adaptation process and preliminary validation of the Italian version of the Nepean Dysphoria Scale <i>A. D’Agostino, E. Manganelli, A. Aportone, M. Rossi Monti, V. Starcevic</i>	149
Development and validation of an abridged version of the Social Provisions Scale (SPS-10) in Italian <i>E. Iapichino, P. Rucci, I.E. Corbani, G. Apter, M. Quartieri Bollani, G. Cauli, C. Gala, M. Bassi</i>	157

Suicide and autism spectrum disorder: the role of trauma

Mental disorders are considered among the leading risk factors for suicide. According to the World Health Organization, more than 90% of people committing suicide suffer from a mental disorder. For this reason, suicide prevention needs to devote great importance to grow the awareness of the mental conditions that are most likely to raise the risk of suicidal behaviors. Several psychiatric disorders are classically linked to suicide. The lifetime risk of suicide is estimated to be 4% in patients with mood disorders¹, 8% in people with bipolar disorder^{2,3}, 5% in people with schizophrenia⁴, and 7% in people with alcohol dependence⁵. Post-traumatic stress disorder (PTSD) as well is frequently associated with suicidal ideation and suicide attempts⁶. Suicide, in fact, has been reported as one of the most important causes of death among veterans, with the risk for intentional death continuing to be high many years after service^{7,8}, but remarkable rates have also been reported in general populations exposed to natural disasters worldwide⁹⁻¹².

Neurodevelopmental disorders are usually overlooked in statistics of mental conditions enhancing the risk of suicide. Notwithstanding, a recent systematic review of studies involving subjects with Autism Spectrum Disorder (ASD) found percentages of suicidality ranging from 10.9 to 50% and pointed out that individuals with ASD might comprise 7.3 to 15% of suicidal populations¹³. This seems to suggest that neurodevelopmental disorders could play a role as important as other mental disorders in suicide risk.

For decades, ASD prevalence estimates have ranged from 0.2 to 0.9 %, far below the prevalence of depression (around 16%)¹⁴, alcohol dependence (around 5.4%)¹⁵, bipolar disorders (about 2.1%)¹⁶. This may be one of the reasons why research about suicide risk in ASD subjects has been scant and ASD is not included among mental disorders at high risk for suicide. But what should we expect now that most recent data on ASD prevalence highlight rates up to 1.4% and growing data have shown that this prevalence might still be on the rise? Whatever such growth in prevalence is due to an increased incidence or it is likely due to a greater recognition of ASD, together with the growing attention devoted to partial and sub-threshold cases¹⁷, autism related conditions might be expected to climb the rankings of suicide risk factors in the close future.

Recent evidence indicates that ASD subjects may present with a very broad range of manifestations of suicidality, including completed suicide, attempted suicide, and sui-

cidal ideation, with this latter being the most common¹⁸⁻²². Few data also indicate that ASD subjects who attempt suicide tend to engage in more lethal methods²². Moreover, adolescence appears to be the highest-risk period, and high functioning ASD individuals at higher risk than low functioning ones^{13,18-22}.

Despite additional research is necessary to better understand how this unique population expresses suicidal tendencies¹³, extant literature highlights the role of stressful life events (e.g. bullying, relationship difficulties) as triggers for suicidal attempts. It has been shown that important adverse life events, such as bereavement or exposure to natural disaster, may be particularly disruptive for subjects suffering from ASD^{23,24}. Nonetheless, their limited cognitive flexibility, their rigid attitudes, their executive functioning and problem-solving difficulties make ASD subjects less likely to adjust even to minor stressors, such as small changes in daily life or failures in work or private relationships, even in those cases diagnosed with subthreshold autism conditions¹⁷. Besides anecdotal reports of suicidal behaviors following the difficulty of ASD patients to cope with life stressors^{25,26}, Kato and colleagues²² recently examined 587 suicidal patients hospitalized for inpatients treatment, reporting that the 43 with ASD were more likely to have attempted suicide in the framework of an adjustment disorder compared to non-ASD patients, who in turn were more likely to present a mood disorder. Across the different developmental stages, a range of situations may be difficult to deal with for subjects with ASD: inclusion in the group of peers, school performance, intimate relationships. Even in those cases with normal or above normal intellectual abilities, the difficulties in expression, empathy and understanding of shared codes of communication easily lead to chronic traumatization and to social exclusion across the entire life^{27,28}. Given their difficulties in mentalizing emotionally charged situations, what is usually considered a stressful life situation may come to ASD patients as a true traumatic event, while suicide may represent the only extreme way to express inner feelings and to cope with conflicts.

Further data suggest a link between suicidality and trauma and stress-related conditions among ASD subjects. In fact, despite only a few studies explored PTSD prevalence rates among ASD patients, and those who did it reported only low rates^{23,29,30}, Storch and colleagues³¹ recently found that comorbidity with depression or PTSD is associated with increased risk for suicidal thoughts and behaviors in youth with ASD and speculated about a potential link

between ruminative thoughts associated with depression and PTSD that may increase suicide risk.

It is surprising that a population characterized by a significant vulnerability lying on the severe impairment in interpersonal relationships and the inability to cope with conflicts or deep affective involvements show low prevalence of PTSD. One possible explanation might be that the characteristic difficulties in understanding, mentalizing and expressing relationship may also latch onto the capability of understanding and expressing a traumatic event, especially in subjects with intellectual or language disability. On the other hand, another important issue to be considered is the commonly used definition of *trauma*. Our unpublished data showed that individuals with mild autistic traits and no intellectual impairment are prone to develop a full PTSD-like syndrome following "minor traumas", such as peer victimization, unsuccessful social exposures, being accused of a theft. Such stressful events do not endorse the definition of trauma of DSM-5, allowing, at the best, the diagnosis of Adjustment disorder. However, it is possible that such "adjustment disorders" underlie a more complex post traumatic stress symptomatology, also including the high risk of suicidal behavior recently shown in PTSD patients⁸⁻¹².

A further perspective arising from recent studies is worth being considered about the relationship among autism, suicide and trauma. While the few data available show only low rates of PTSD in ASD samples, several authors agree about ASD patients being at high risk of traumatic events, particularly because of their chronic interpersonal traumatization^{27,28}. In attempting to explain the inconsistency between the high rates of traumas and the low prevalence of PTSD among ASD patients, King²⁷ pointed out that the typical impairments of ASD may also impact individual's capability of understanding, mentalizing and referring events as traumatic, limiting the chance that a post traumatic stress symptomatology would be recognized as such. In addition, a few authors hypothesized that ASD patients are likely to show a particular form of PTSD, arising from multiple traumas, named Complex PTSD²⁷²⁸. Complex PTSD symptomatology is often chronic and more severe than typical PTSD symptoms, including deficits in emotional regulation, negative self-perception, interpersonal problems and dissociative symptoms^{27,32,33}. It has been observed that the symptoms of Complex PTSD, prolonged across time, lead to long-term instability in interpersonal relationships, emotional lability, unstable self-perception, as well as to maladaptive behaviors, such as a broad range of suicidal behaviors and substance abuse, so that these subjects might even be labeled as having a Borderline personality disorder (BPD)²⁷. From such a perspective, trauma and stress-related disorders might be the link between autistic dimension and suicidality not only among subjects with a known ASD, either

subthreshold or full-blown, but also among those with a borderline phenotype covering an autistic constellation of symptoms, or in ASD subjects in which a diagnosis of comorbid BPD has been made. Somehow in agreement with this hypothesis, a small study conducted on 41 BPD patients found that those with comorbid ASD show grater suicidality than those with BPD alone³⁴.

While further experimental data are needed to test this latter hypothesis, we think that ASD will be gaining greater importance among risk factor for suicidality in the near future and that research into this field would benefit from focusing not only on severe autism spectrum conditions, but also on subthreshold and partial forms. The role of traumatic life events as triggers of suicide attempts among ASD subjects will also require investigation. Conversely, a more comprehensive investigations of autistic traits among PTSD patients showing suicidal tendencies should be a priority for future research.

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On the notion of psychosis: semantic and epistemic concerns

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Summary

In spite of its frequent and apparently unproblematic use, the meaning of the term “psychosis” remains largely unclear. Throughout this paper we will analyse some of the reasons underlying psychiatry’s failure to define the notion of psychosis in a clear and unambiguous fashion, highlighting the inadequacy of a natural-scientific framework (inherited by psychiatry through its development as a medical discipline) when dealing with subjective experience. Following a longstanding trend in

psychopathology, we will argue for the need to follow a hermeneutical approach, which is both perspectival and theory-laden. In order to prevent arbitrariness or a crude relativism, we will describe the notion of “hermeneutic objectivity” as an epistemic construct aimed at legitimising psychiatric judgement and its pretension of truth.

Key word

Psychosis • Psychopathology • Hermeneutics

Introduction

As psychiatrists, we are expected to identify individuals who are experiencing a psychosis and clearly differentiate them from those who are not. This is no trivial task, since identifying someone as psychotic might have extremely serious consequences:

- a. clinical: those who are included under the category “psychosis” will often be prescribed antipsychotic medication and will hence be at risk of experiencing significant side-effects, just like failing to identify a patient as psychotic might prevent him from receiving more adequate treatment. A clear and precise differentiation between psychosis vs no-psychosis has become particularly relevant in early intervention services working with individuals who are at high risk of transition to psychosis;
- b. legal: the identification of an individual as psychotic at the time that he committed an offence could act as an exculpatory circumstance. Also, labelling someone as psychotic can legitimise having him sectioned in an inpatient unit;
- c. social: the stigma and the risk of social exclusion and discrimination linked to the notion of psychosis demands that this diagnosis is not established arbitrarily. Moreover, labelling someone as psychotic might have a negative impact on self-image and lead to disempowerment¹.

In consequence, labelling a patient as psychotic should

not be done arbitrarily but with a high degree of certainty. In the modern era, it is scientific knowledge that has achieved the status of *knowledge proper* and as such it represents the path towards truth and certainty. In fact, it is psychiatry’s adoption of a natural-scientific methodology, inherited through its development as a medical discipline, that legitimises the practice of treating millions of kids with amphetamines worldwide, depriving patients from their freedom or deciding that an individual was unaware of what he was doing when he committed an offence. As such, psychiatry aims towards a pretension of truth that is characteristic of the natural sciences, a deterministic and law-abiding truth that is universally accepted.

So that the term “psychosis” is applied rigorously in clinical practice, two different though interrelated questions should be answered. There is a *semantic* question – *how can I define the term psychosis in clear and unambiguous terms?* and an *epistemic* question – *how can I rightly include a particular individual under the kind psychosis?* Throughout the next paragraphs we will attempt to understand how psychiatry has approached these questions from within the framework of medical semiology. We will then proceed to exemplify the failure of psychiatry’s attempt to define one of its core notions, that of psychosis, in clear and unambiguous terms. In a next step we will argue for the reasons underlying this failure (namely the illegitimacy of some of psychiatry’s epistemic assump-

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tions), and we will conclude by offering an alternative approach for psychiatry's quest for knowledge.

How does psychiatry traditionally address the semantic and epistemic questions?

Before addressing these questions, we must consider where psychiatry, taken as a medical/natural-scientific discipline, stands.

In the first place, psychiatry inherited a set of ontological assumptions and a specific epistemological framework through its development as a medical discipline ^{2 3}. In short, this framework (namely, medical semiology) states that a specific set of symptoms represents an unseen internal lesion (i.e. aetiology), whether structural or functional ^a, with which it is linked through a causal and deterministic relation (this causal relation can be traced back through biochemical, anatomical, physiological, microbiological, or genetic processes ^b). Since this specific set of symptoms univocally represents (i.e. stands in the place of) its unseen internal lesion, they may both be equated. Hence, disease X may be defined either by the specific set of observable and objective symptoms (a descriptive definition) or by its aetiology (an essential definition).

By adopting this epistemological framework, psychiatry assumed that mental symptoms were causally linked to their unseen internal cause ⁴ (i.e. a putative neurological dysfunction, whether anatomical, physiological or functional) ^c. Since this relation was deemed to be causal and deterministic, an objective nature was necessarily assumed for mental symptoms, for deterministic relations exist only in the realm of space-time objectivity.

Further, it is commonly accepted that mental disorders have come to be defined according to descriptive criteria such as those found in the DSM and the ICD. These classificatory systems rely on the idea (borrowed from Logical Positivism) ⁵ that mental disorders should be described according to a purely descriptive and theory-free approach. This widely accepted idea reinforces the above-mentioned assumption that mental symptoms are objective entities, for if they are to be defined by means

of atheoretical and purely descriptive terms they must be apprehended through observation (i.e. in an object-like fashion).

So, turning back to the semantic question, what is psychiatry's answer? As we have already mentioned, psychiatry's answer (taken as a medical discipline and hence deploying medical semiology as its epistemological framework) is that psychosis should be defined through the description of a set of objective features that are causally linked to a yet unknown internal lesion and that can be identified as being either present or absent. For over a hundred years the term "psychosis" has been linked to the notions of irrationality, incomprehensibility ⁶ or loss of touch with reality. Since these notions lack the kind of objectivity expected from descriptive definitions and are very likely to be either theory or value-laden, psychosis eventually came to be defined by those allegedly objective features that typically occurred in patients considered as irrational, as incomprehensible or as having lost touch with reality: delusions, hallucinations, disorganised speech, or catatonic behaviour ^d (i.e. psychotic symptoms). Following this line of argument, the term "psychosis" will refer to a yet unknown neurological dysfunction that is common to all psychotic symptoms.

Let's move on to the epistemic question (how can I rightly include a particular individual under the kind "psychosis"?). Clinical judgement has been argued to follow an abductive logic ¹⁰ (in short, it follows a "known-effect-to-putative-cause" reasoning direction, with different possibilities of interpretation of the empirical fact). In this sense, clinical judgement always implies a sign-token (any particular item that belongs to a specific type) and a sign-type (a universal or category, whether a symptom or a disease, which is synonymous with the descriptive definition of a sign) under which the token must be included. Following the principles of medical semiology, the descriptive definition for a sign-type includes all the necessary and sufficient features required for the complete characterisation of sign-token. Hence, the identification of the allegedly objective features that characterise psychosis (i.e. the descriptive criteria characterising delusions, hallucinations, disorganised speech, or cata-

^a The multiple realisability of psychological kinds implies a one-to-many relation between psychological kinds and neural kinds. These different neural kinds would lead to a common functional or computational state common to all tokens of a particular kind ⁷.

^b In the case of psychiatry, functional, cognitive, or computational processes have also been proposed, all of which retain an allegedly causal and deterministic character.

^c The assumed existence of this putative internal lesion characteristic of psychosis is clearly exemplified by empirical research ^{8,9}.

^d The assumption of the allegedly objective nature of these phenomena is clearly instantiated by current empirical research (i.e. identification of neurobiological correlates that are causally related to delusions and hallucinations) and theoretical research (i.e. development of theoretical models that assume the existence of more or less opaque causal relations between symptoms and their unseen internal cause).

tonic behaviour) allows for the immediate inclusion of the individual under the kind “psychosis”, which in turn refers to the existence of an underlying (yet unknown) neurological dysfunction that is common to all psychotic symptoms.

Some problems related to the concept of psychosis

Unfortunately, and in spite of psychiatry’s natural-scientific aspirations, both the meaning of the term “psychosis” and the path for its indubitable application in clinical practice are far from clear. Let’s have a quick look at some of the problems that the notion of psychosis faces:

- a. the notion of psychosis is very often equated or reduced to schizophrenia. In this sense, a vast amount of papers that include the term “psychosis” in their title actually focus on schizophrenia. Whereas this condition represents a paradigmatic type of psychotic disorder, the term “psychosis” seems to be equally applicable to a wide range of non-schizophrenic disorders (e.g. chronic delusional disorder, acute psychotic episode, affective psychoses etc.);
- b. a direct consequence of defining psychosis by the presence of delusions, hallucinations, disorganised speech, or catatonic behaviour is the fact that non-productive psychoses become highly problematic or even contradictory (in this sense, what is psychotic about Simple Schizophrenia?)^{11 12}. In a similar fashion, the ascertainment of attenuated or transient delusions and hallucinations (as the Comprehensive Assessment of At-Risk Mental States does) often fails to identify the prodromal phases of schizophrenia, where such symptoms are most often not even present. Further, equating psychosis to the presence of delusions or hallucinations neglects a longstanding psychopathological tradition according to which these symptoms are secondary or even contingent¹³⁻¹⁶;
- c. a widely heterogeneous clinical sample might report phenomena that satisfy the commonly accepted descriptive criteria for delusions (i.e. high subjective evidence and incorrigibility). These could allegedly include paranoid delusions in schizophrenic patients, delusions in the context of affective disorders, overvalued ideas, fanatic religious beliefs, obsessive-like phenomena, rigid cognitive patterns found in autistic spectrum disorders or an exaggerated mistrust found in paranoid personality disorders. In spite of their complying with superficial descriptive criteria, their deep structure and the relation they hold with co-presenting phenomena varies to such a degree that assuming the existence of a common (anatomical, psychological, functional, computational, or neurocognitive) path or

an identical psychological structure would lead to a rough conflation and a complete lack of specificity, eventually rendering the concept of psychosis meaningless. In a similar fashion, labelling as psychotic all patients who satisfy the descriptive criteria for auditory hallucinations (these have been described in a wide variety of disorders, ranging from schizophrenia to affective disorders, personality disorders¹⁷, conversive disorders¹⁸, sensory deprivation¹⁹, or anxiety disorders²⁰) would arguably render the extension of the term “psychosis” extremely heterogeneous and hence of little use for both research and clinical practice;

- d. a descriptive definition of psychosis doesn’t really say much about what psychosis actually is (all it offers are the descriptive features that an individual must allegedly satisfy in order to be identified under the kind “psychosis”). So, what is it that psychotic symptoms have in common? In short, most mental health professionals would answer to this question by saying that they all somehow imply losing touch with reality or, more technically speaking, a failure in reality testing or reality monitoring. However, no matter how often we talk about reality, little thought is actually given to what reality actually is or to how we get to know things about the world. In fact, a number of tacit and unacknowledged ontological and epistemological assumptions are held, most of which are still subject to vivid debates (e.g. ontological realism, a correspondence theory of truth, a representational theory of mind, an ontic independence between man and world, the existence of a clear and unambiguous matching between world and language etc.);
- e. there is little agreement as to whether this term should be applied in certain cases (e.g. emotionally unstable patients who report hearing voices that encourage them to self-harm, anxiety-related overvalued paranoid thoughts, mood-congruent ideas in affective disorders, body-image distortion in anorexia nervosa etc.) and clinicians often disagree as to whether a particular token represents an instance of a specific kind of psychotic symptom. These facts point toward the idea that the allegedly descriptive features that characterise psychosis are not as objective as we wish they were. Probably the simplest illustration of this idea is the fact that a patient presenting with all the allegedly objective and descriptive features for any psychotic symptom might be after all malingering...

What’s the reason underlying these problems?

In our view, the main reasons underlying psychiatry’s failure to achieve the conceptual and epistemic consistency it aims for (clearly exemplified by the history of psychosis)

is the fact that psychopathological phenomena are not objective entities, they do not stand in causal relations with regards to co-existing objects, their eliciting requires the use of non-representational information and, most important, utterances and behaviour, understood as psychopathological phenomena, only acquire meaning when interpreted from within their horizon of meaning (i.e. the individual understood as a meaning-bestowing totality).

Psychopathological phenomena are not mere objects standing in the realm of space and time. They are not directly apprehended, but are the product of an interpretative endeavour: no one can actually see a delusion or a hallucination. An utterance only acquires meaning when analysed within its specific context, i.e. the individual understood as a horizon of meaning²¹. Only then, when we take into account the patient's biography, his personality traits, his hopes for the future, his fears, his traumas, his world etc., can we really understand the meaning of an utterance and hence label it as a delusion with a certain degree of certainty. Depending on this horizon, the interpretation of the utterance will have one meaning or another: he might be malingering, his paranoid traits might be due to past traumatic events, his high degree of conviction might be due to rigid cognitive patterns, the incorrigibility might be due to his reluctance to accept evidence that would shatter his world, etc. Similarly, no fragment of behaviour carries meaning in itself. It is only when we reach an understanding of the individual that we can ascribe meaning to his behaviour. Since psychotic symptoms are always identified as such through an interpretative process that requires taking into account the individual's idiosyncrasy, they may never be directly apprehended as physical *things* (i.e. in an object-like fashion). Furthermore, since the individual (understood as the horizon of meaning upon which interpretations take place) can never be fully or exhaustively apprehended, the result of the reconstructive process will remain inevitably open and unfinished (new information can always be obtained that might lead to an alternative reconstruction). Trying to establish a deterministic (fixed, causal and law-abiding) relation between psychotic symptoms (the reconstruction of which is always open, as the result of an interpretative process) and a specific internal lesion (anatomical, functional, physiological etc.), the meaning of which is closed or fixed, therefore seems rather illegitimate.

We will probably all agree that there are certain clinical cases where we all believe a patient to be psychotic (let's say, the very typical schizophrenic patient who experiences paranoid delusions, passivity phenomena and commenting auditory hallucinations, a severely depressed patient who assures that he's already dead, a jealous husband who *knows* that his wife is cheating on him without any evidence etc.). This intersubjective consensus might lead us into believing that there is something characteristic and specific about psychosis that we are all apprehending and that this feature could also be objectively identified in all other psychotic patients (after all, it might make sense to believe that we're apprehending an objective, descriptive and representational feature of psychosis if we're all agreeing on the conclusion). However, the fact remains (as the history of psychiatry has shown) that the meaning of psychosis cannot be codified in analytical terms and there is no set of specific features that are identified in all psychotic patients. One of the main reasons for this has been argued to lie in the role of present, although *non-representational* information that modulates the meaning of apprehended phenomena (following Rejon's example, the difference between schizophrenic and melancholic delusions may be observed and pointed out^e – it may receive an ostensive definition – but it cannot be found in the descriptive definition of delusion¹⁰). This is clearly seen in clinical practice, where we continuously face atypical cases (that don't comply with commonly accepted descriptive features) in which diagnostic dissensus is the rule. It is in this sense that the role of non-representational information (how it is articulated, taken into account or simply neglected) helps in understanding some of the reasons why some psychiatrists might conclude that a particular patient is psychotic whereas others won't^f.

Introducing an alternative approach

According to the previous line of argument, we conclude that the natural-scientific pretension of truth that psychiatry aims for (i.e. based on certainty and law-abiding determinism) rests on illegitimate assumptions (based on the naturalisation or objectification of psychopathological phenomena). In spite of this, we are still committed to a pretension of truth that allows for valid and reliable

^e This non-representational information plays a major role in the way we learn to identify psychosis through ostensive definitions during our training period¹⁰.

^f Though being non-representational, this information still holds semantic and interpretative value. It is arguably the role of non-representational information that led Minkowski to say that metaphors seemed more adequate than definitions when trying to grasp the meaning of the notion of "vital contact with reality"²⁶, whose distortion played a major role in his understanding of schizophrenia.

judgements that underpin and justify our clinical decisions. However, the pretension of truth we aim for is different from that of the natural sciences. Whereas these aim at establishing apodictic knowledge about the physical world by means of its subsumption under deterministic causal laws, psychopathology (taken as an alternative epistemic framework for psychiatry that aims at creating intelligibility) stabilises the meaning of clinical data through a hermeneutical procedure²²⁻²⁴ that allows for the systematic and theory-guided articulation of raw data (including utterances, fragments of behaviour, non-representational information and contextual information). However, the open texture implied in all interpretative endeavours precludes reaching a “one and only” valid conclusion (after all, as Jaspers wrote, in the realm of hermeneutics “... a final ‘terra firma’ is never reached”²⁵). Hence, the pretension of truth that hermeneutics aims for has a different value than the one aimed at by the natural sciences. There is no Truth, just like there is no definitive diagnosis (according to the hermeneutical method, further information added to the global picture or a different guiding theoretical approach might allow for the different reconstruction of a particular case, leading to a different diagnostic conclusion), but only a multiplicity of perspectivist truths. However, not all interpretations are equal.

Hermeneutic objectivity: psychopathology's quest for certainty

Hermeneutic reconstructions must respect certain constraints in order to avoid spurious interpretations and arbitrariness. In order for a community of psychiatrists to be able to make sense of the notion of psychosis (i.e. share a common understanding regarding its meaning and the way it is applied in clinical practice), they must be able to share a set of theoretical⁸, pragmatic and common sense assumptions that might guide the reconstructive process through a common path, allowing for a common diagnostic conclusion (or at least for the establishment of a dialogical interaction focused on the interpretative process leading to a diagnostic rationale). In this sense, the result of an interpretative activity (such as psychiatric diagnosis) might achieve a varying degree of *hermeneutic objectivity*, the value of which will depend on features such as its

plausibility, its global coherence, its capacity to articulate contextual and non-representational information, its capacity to justify the relation between symptoms present and absent, its acknowledgement of underlying theoretical implications, its predictive power or its capacity to offer effective paths for intervention.

As an oxymoron, the notion of “hermeneutic objectivity” must be understood in a metaphorical sense. As we already mentioned, hermeneutical endeavours never disclose natural objects that could ultimately be subsumed under universal laws (as a natural-scientific approach would pretend). This metaphorical notion of objectivity makes reference to *fallible constructs* that can *never* fully account for the totality of the reconstructed individual. Further, such constructs can never be directly grasped or intuited, but only apprehended through a narrative (reconstructive) and intellectual effort. However, the better a reconstruction complies with the abovementioned features (those that determine the value of “hermeneutic objectivity”) the more it will *resemble* an ideal of objectivity (i.e. in the sense of achieving a greater level of intersubjective validity, global coherence and plausibility)^h.

In essence, the semantic and epistemic value of psychopathological terms (i.e. the way they are defined and how they are applied in clinical practice) does not rely on objective measures, nor does it abide by deterministic laws. On the contrary, this value relies on the strength of the context-dependent and theory-laden reconstructive consensus reached by the community of those who struggle to make sense of altered subjective experience through clinical practice.

How, then, can we define the term “psychosis” and apply it in clinical practice?ⁱ

The first point we need to make clear is that psychosis is not a thing, a definite and objective entity that can be fully defined in descriptive terms. We can argue that there is something that most patients who have been labelled as psychotic throughout the last century seem to share. In this sense, Heinimaa finds in the notion of “un-understandability” the core semantic trend followed by the notion of psychosis throughout the 20th century (following Bleuler, Jaspers, Schneider, Spitzer and eventually the DSM)⁶. In our opinion, un-under-

⁸ Most important, these theoretical assumptions must include an understanding regarding the nature of subjectivity and reality (after all, psychosis is understood as a disorder of subjective experience or as a disturbance in the way in through which individuals apprehend reality).

^h Consensual Qualitative Research, a methodological approach for subjective experience deployed in phenomenological investigations, represents a practical endeavour that is based on a very similar line of thought²⁷.

ⁱ It must be kept in mind that this paper has merely semantic and epistemic purposes. We are hence trying to understand the conditions of possibility for defining psychosis and not trying to achieve such a definition.

standability could be argued to represent a disadjustment between man and world^j that is experienced by an observer as an irreducible estrangement. However, not all forms of un-understandability can be considered as abnormal, pathological, or psychotic (see for example the eccentric or the genius who is ahead of his time). In this sense, we must keep in mind that what we aim at understanding is a fellow human being in his relation towards the world (it is a person that we fail to understand, and hence a person who is psychotic – not a symptom). We therefore identify a need to articulate the relationship between man and world, between subjectivity and reality, so that we may determine which forms of incomprehensibility should count as psychotic (hence psychosis becomes a theoretical construct that tries to account for certain forms of incomprehensibility). Unfortunately, an understanding of the relationship between man and world is the very task that philosophy has struggled with for over 2500 years and no definitive answers have become available. Hence, a theoretical commitment with the most appealing theoretical assumption regarding the nature of the relationship between man and world (or subjectivity and reality)^k seems to represent an indispensable requirement in order to reach a definition for the term “psychosis”. Once the structure of this relationship has been disclosed, an account of how it might break down will come to define the deep structure of psychosis (or several accounts might come to define different possible ways of becoming psychotic). In this sense, we identify a trend (focused mainly on schizophrenia) that expanded throughout the 20th century and that realised that reconstructing an individual for diagnostic purposes demands the previous articulation of the relationship between man and world^l (Minkowski’s loss of vital contact with reality¹⁵, Binswanger’s Transcendence²⁸, Blankenburg’s loss of natural self-evidence¹⁴, Stanghellini’s loss of common sense²⁹, Sass and Parnas’ ipseity disturbances³⁰ etc.). In fact, the notion of incomprehensibility as a core element pertaining to the notion of psychosis seems to have drawn back in the last dec-

ades^m, allowing for a growing focus on the ontological status of man and on the idea of a disadjustment between man and world²⁹⁻³².

However, these ideas imply a risk that should not be neglected. The underlying theoretical assumptions implied in the notion of psychosis cannot say in definitive terms what man or world are, for they only represent one approach among many (the history of philosophy is clear proof of this point). This should preclude descriptive definitions aimed at saying what psychosis *is*, for 1) they falsely imply *knowing* what man and world *are*, and 2) they neglect the fact that psychosis is a theoretical construct (whose meaning is also modulated by legal and social dimensions) and the product of a hermeneutic reconstruction. In spite of its perspectivist flavour, a definition of the kind “taking into account this theory about man, world and reality, the term psychosis could be understood as...” would seem, in our opinion, more epistemologically sound.

As we already mentioned, not all definitions (understood as theoretical constructs) should be granted the same value. The better a definition complies with the values ascribed to hermeneutic objectivity (in the sense of plausibility, global coherence, appropriation of theoretical assumptions, articulation of contextual information etc.) the better it will be, the closer it will stand with regards to our aspired value of truth and the more it will resemble an ideal of objectivity.

According to the proposed view, the methodological framework that underlies the use of the term psychosis in clinical practice is a theory-guided hermeneutical process. The fact is then that a single patient might be interpreted or reconstructed according to different alternative theories or perspectives that offer different value to contextual and non-representational information. His utterances, his behaviour, other accompanying phenomena, his expression, his biography, his personality traits, his hopes and desires, his life-world as a meaning-bestowing totality, they all have semantic value, the relevance of which will be determined by different factors³³ (one of

^j This notion of world should not be understood as the totality of objects, as a world-in-itself, but as an intersubjectively constituted horizon of meaning that allows for the object’s appearance.

^k Ontological realism, nominalism, transcendental idealism, a representational theory of mind, a correspondence theory of truth, a coherence theory of truth etc.

^l Interestingly, these accounts tend to consider delusions or hallucinations as contingent phenomena and, most important, allow for an understanding of the internal structure that interweaves the different clinical manifestations (namely what Minkowski called *trouble générateur*¹⁵).

^m In fact, the notion of incomprehensibility as a core feature of psychosis has been repeatedly contested throughout the last decades: a) a lack of understanding might be due to my own incapacity to understand a patient, b) the act of understanding is context-dependent (someone might be considered as incomprehensible in a particular context and understandable in a different setting), c) a particular theory regarding a breakdown in the relationship between man and world might render certain phenomena (previously considered as incomprehensible) understandable...

which, as we have already mentioned, is the theoretical model in place). Hence, a patient can be considered both as psychotic and as non-psychotic at the same time (it is not at all strange that we find this happening in clinical practice). There is thus no certainty, at least not in the causal-deterministic terms implied by the pretension of truth of the natural sciences. Once again, however, not all interpretations should be granted the same value. The greater the value of hermeneutic objectivity, the better the individual reconstruction will be and hence the more the clinical judgement will approach a value of truth.

A final remark regarding psychotic symptoms. Although these can no longer be considered to bear the meaning of the term psychosis, they still play a central role in clinical practice. They represent the most frequent and characteristic forms through which an observer may conceptualise or categorise the experience of estrangement that interaction with a fellow human being might arouse. The fact that we might be able to reconstruct an utterance or a fragment of behaviour as a psychotic symptom does not allow for identifying the individual under the kind "psychosis". However, the initial identification of an utterance or a fragment of behaviour as an instance that satisfies the descriptive features of a specific type of psychotic symptom can be taken to represent an initial (and essential) step that catalyses the interpretative diagnostic process^{33 34}.

Conclusions

A pretension of truth based on causal relations and deterministic laws requires an epistemic framework that does not legitimately apply to psychiatry, for psychopathological symptoms are not directly apprehended as spatio-temporal physical objects nor do they stand in causal relations with surrounding objects. Given the nature of psychiatry's object of study (i.e. subjective experience), psychopathological raw data (i.e. uninterpreted utterances and behaviour) must be rendered meaningful through an interpretative process. The hermeneutic nature of this endeavour precludes both a single and universally accepted definition for psychosis and a uniquely valid diagnostic conclusion for any particular individual. It is hence due to the very nature of psychopathological phenomena as belonging to the realm of subjective experience that the semantic and epistemic questions defy an answer in the kind of terms expected by the natural sciences. However, neither all definitions nor all individual diagnostic reconstructions can be granted the same value. According to the above-mentioned view, the better they comply with certain features (such as global coherence, plausibility, acknowledgement of theoretical and philosophical assumptions, the capacity to articulate contextual informa-

tion, predictive power or the capacity to open paths for intervention), the better the interpretation will be and the more it will resemble an ideal of objectivity.

Finally, we observe that the notion of incomprehensibility, a core element in the history of the notion of psychosis, seems to have drawn back in the last decades allowing for a growing focus on the ontological status of man and on the idea of a disadjustment between man and world²⁹⁻³². In this sense, we believe that further theoretical and philosophical input on the relational structure between man and world will allow for better and more solid conceptualisations of psychosis.

Conflicts of Interest

None.

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Quality of life and psychopathology of patients awaiting kidney/pancreas transplants

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Summary

Objective

Patients awaiting kidney/pancreas transplants are suffering from ESRD or severe IDDM, which may contribute to renal insufficiency with or without other medical complications such as diabetic neuropathy. Such patients may experience psychopathological distress that can impair their daily lives. The aim of this study was to assess the QOL, lifetime and current DSM-IV Axis-I and II disorders, sub-threshold mood and panic/agoraphobic phenomenology in a large sample of ESRD and IDDM patients waiting kidney-pancreas transplants.

Methods

Consecutive transplant candidates of both genders aged between 18 and 65 years were enrolled ($n = 227$). Axis-I and -II diagnoses were determined by experienced clinicians using SCID-I and II. Patients were also administered MOODS-SR (self-report) and PAS-SR questionnaires to assess mood and panic-

agoraphobic spectrum, and the Q-LES-Q questionnaire to assess QOL, enjoyment and satisfaction.

Results

The prevalence of current Axis-I disorders was 13.2%. The most common current axis-I disorders were agoraphobia (4.8%) and major depressive episode (4.0%). No difference in the distribution of Axis I disorders between the two groups (ESRD and IDDM) was found. QOL among the sample study was overall poorer than that of a healthy adult control population.

Conclusions

The prevalence of current mental disorders was approximately three times higher compared to the general Italian population, emphasising that the need for transplantation plays an important role in patients' psychopathology and underlines the importance of careful evaluation of sub-syndromal symptoms.

Key words

Transplants • Spectrum symptoms • Quality of life

Introduction

Chronic physical illnesses represent an increasingly major public health concern. Elevated levels of stress inevitably affect chronically-ill individuals as they deal with physical pain, difficult diagnostic procedures, treatment side-effects and hospital admissions which have a strong impact on the quality of life; these patients show an increased risk of psychological distress compared to the general population¹. Moreover, the relationship between psychological status and clinical outcomes after organ transplant has long been matter of debate².

Patients awaiting kidney/pancreas transplants are suffering from end-stage renal disease (ESRD) or severe insulin dependent diabetes mellitus (IDDM), which may contribute to renal insufficiency with or without other medical complications such as diabetic neuropathy. Such patients may experience psychopathological distress that can impair their daily lives.

Impairment of daily well-being and quality of life may be remarkably affected by dietary restrictions, intensive insulin therapy and monitoring³. In the advanced phases of ESRD and IDDM, the impact of the illness on quality of life perceived by the patient can be relevant. Health-related quality of life (HRQL) is currently used as an important outcome parameter to assess. The level of subjective well-being is determined by several dimensions such as physical status of the patient, state of mind, functional competence in everyday life and impact on interpersonal relationships⁴. HRQL represents the patient's assessment of the impact of a disease and its treatment on daily life, well-being and functioning. HRQL is considered by some researchers essential for understanding the impact of the disease and its treatment on health outcomes. Scientific evidence has demonstrated the utility of self-reported outcomes in evaluating a broad range of health care interventions².

Most of the literature on quality of life (QOL) of patients

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awaiting transplants focuses on the substantial decrements in QOL experienced during end-stage chronic diseases, including impairments in both physical and mental health domains⁵⁻¹¹. In recent years, increasing attention has been given to the individual characteristics of patients affected by chronic disease, concentrating emphasis on social situations, socioeconomic status, perceptions and responses to the illness, to physicians/healthcare providers, spouses and families and the effects they may have on the transplant outcome¹². Anxiety and depression may be induced by chronic illness, obviously contributing to the perception of QOL in psychological and social domains as well as the physical domain¹³. Indeed, during hospitalisation for ESRD and IDDM, affective disorders have been described as the most common psychiatric disorders¹⁴⁻¹⁶. Lee et al. theorised that depression possibly affects medical outcomes in ESRD patients through modification of immunologic and stress responses, impact on nutritional status and/or reduction of compliance with, or access to, prescribed dialysis and medical regimens¹⁶. In the majority of transplant programs, a psychiatrist evaluates potential candidates for psychosocial aptness to transplantation. Actually, although psychiatric and psychological screenings for disease are standardised, the psychosocial criteria for transplantation are not. There are only few studies on the prevalence, diagnosis and treatment of depression in this population using accurate, well-defined diagnostic criteria and appropriate epidemiologic methods^{13 17-21}. Although a depressive mood or depressive symptomatology may be expected in some transplant candidates, there are few systematic clinical reviews using well-defined diagnostic criteria and appropriate epidemiological methods to assess the psychopathology of waiting list patients^{13 17-21}.

The aim of this study was to assess lifetime and current DSM-IV (Diagnostic and Statistical Manual of Psychiatric Disorders, 4th Edition) Axis-I and II disorders, quality of life and sub-threshold mood and panic-agoraphobic phenomenology in a large sample of ESRD and IDDM patients awaiting kidney-pancreas transplants.

Materials and methods

Study sample

The study sample included consecutive transplant candidates of both genders, aged between 18 and 65 years, seeking treatment at the Outpatient Division of General and Transplantation Surgery of the University Hospital of Pisa, between March 2003 and October 2008.

Exclusion criteria were mental retardation, illiteracy or poor knowledge of the Italian language.

The diagnostic assessment was conducted by psychiatrists trained and certified to the use of the interviews us-

ing the SCID-I (Structured Clinical Interview for DSM-IV Axis-I) for DSM-IV diagnoses²² and the SCID-II (Structured Clinical Interview for DSM-IV Axis-II) for personality disorders²³.

The Ethics Committee at the Azienda Ospedaliera Universitaria Pisana reviewed and approved all study procedures, and all participants gave written informed consent after receiving a complete description of the study and having the opportunity to ask questions.

The work described in the present article was carried out in accordance with the Code of Ethics of the World Medical Association for experiments involving humans.

Instruments

The MOODS-SR (Mood Spectrum Instrument-Self-Report)²⁴ is a self-report instrument derived from the corresponding structured interview²⁵ that explores features associated with mood disorders. It consists of 161 items coded as present or absent for one or more periods of at least 3-5 days over a lifetime. For some questions exploring temperamental features or the occurrence of specific events the duration is not specified because it would not be applicable. Items are organised into 3 manic-hypomanic and 3 depressive domains exploring mood, energy and cognition, plus a domain that explores disturbances in rhythmicity (i.e. changes in mood, energy and physical well-being according to the weather, the season and phase of menstrual cycle) and in vegetative functions, including sleep, appetite and sexual activity. The sum of the scores of the three manic-hypomanic domains constitutes the manic-hypomanic component and that of the three depressive domains "the depressive component". Both the interview and self-report have been shown to be valid, reliable and suitable for administration to patients and normal controls²⁴⁻²⁶.

Factor analysis is a statistical method used to describe variability among observed, correlated variables in terms of a potentially lower number of unobserved variables called factors.

Two factor analyses of the depressive and manic components of MOODS-SR spectrum identified 6 depressive factors and 9 manic-hypomanic factors^{25 26}: "Depressive mood", "Psychomotor retardation", "Suicidality", "Drug/illness-related depression", "Psychotic features" and "Neurovegetative symptoms".

The factors of mania/hypomania are: "Psychomotor Activation", "Creativity", "Mixed Instability", "Sociability/Extraversion", "Spirituality/Mysticism/Psychoticism", "Mixed Irritability", "Inflated self-esteem", "Euphoria" and "Wastefulness/Recklessness".

The lifetime self-report panic/agoraphobic spectrum (PAS-SR) consists of 114 items coded as present or absent items for one or more periods of at least 3 to 5 days in the lifetime²⁷.

The factor analysis of the lifetime PAS-SR has identified 10 factors: “panic symptoms”, “agoraphobia”, “claustrophobia”, “separation anxiety”, “fear of losing control”, “drug sensitivity and phobia”, “medical reassurance”, “rescue object”, “loss sensitivity” and “reassurance from family members”²⁷.

The Q-LES-Q (Quality of Life Enjoyment and Satisfaction Questionnaire)^{28,29} is a self-report measure of quality of life, enjoyment and satisfaction. The 16-item version used in the present study includes 14 items exploring general activities as well as 2 items measuring overall satisfaction. Items are scored on a Likert scale (1 = very little to 5 = extremely). The 14 items evaluated each subject’s satisfaction with his or her physical health; social relations; ability to function in daily life; ability to get around physically; mood; family relations; sexual drive and interest; ability to work on hobbies, work, leisure time activities; economic status; household activities; living/housing situation; overall sense of well-being. There are two global items, number 15 and 16, that are not included in the Q-LES-Q total score: medication and life satisfaction and contentment over the last week. The total score is the sum of the first 14 items and is expressed as a percentage of the total score of 70.

Statistical analyses

Baseline demographic and clinical variables of patients with nephropathy were compared to patients with diabetes using a chi-square test or Fisher’s exact test (categorical variables), T-test (continuous variables with normal distribution), or Mann-Whitney Test (skewed variables),

as appropriate. A stepwise linear regression analysis was carried out to assess the relationship between quality of life and the lifetime MOODS-SR and PAS-SR factors in the total sample and in patients with nephropathy and diabetes, separately.

Analyses were conducted using SPSS, version 15 (SPSS Inc., Chicago, Ill). Data were presented as means and standard deviation ($\pm$ SD) or percentages.

Results

Characteristics of the sample

Of the 227 patients waiting for a kidney and/or pancreas transplant, 130 (57.3%) were males and 97 (42.7%) females; 58.9% of subjects were married, 38.7% had a high school diploma and 61.5% were employed (Table I). The primary illness responsible for the transplant was: complicated type I diabetes mellitus in 177 patients (78%) and nephropathy in 50 patients (22%). The onset of type I diabetes was on average at 16 years, significantly earlier than the onset of nephropathy (Table I).

Axis I and II disorders

Table II presents current and lifetime prevalence of Axis I Psychiatric Disorders in the overall sample, and in patients with nephropathy and diabetes. The prevalence of lifetime Axis I Psychiatric Disorders in the overall sample was 15.9%.

The most common lifetime Axis-I disorders were Major Depressive Episode (9.7%), Panic Disorder (3.5%) and

TABLE I.
Demographic and clinical characteristics of the transplant candidates.

	All subjects (N = 227)	Nephropathy (N = 50)	Diabetes (N = 177)	Test and p (= value)
Age, mean (SD)	41.6 (9.7)	42.8 (11.9)	41.4 (8.9)	t = 0.73, p = 0.466
Gender F (%)	98 (42.6)	18 (36.0)	79 (44.6)	$\chi^2 = 1.19$, p = 0.276
Educational level (%)				$\chi^2 = 0.88$, p = 0.927
Elementary school	15 (6.7)	3 (6.0)	12 (6.8)	
Junior high school	77 (34.2)	16 (32.0)	61 (34.5)	
Training course	20 (8.9)	3 (6.0)	16 (9.0)	
Senior high school	87 (38.7)	19 (38.0)	67 (37.9)	
Degree	26 (11.6)	7 (14.0)	19 (10.7)	
Married or living with partner (%)	135 (58.9)	35 (70.0)	100 (56.5)	$\chi^2 = 2.95$, p = 0.086
Working status (%)				$\chi^2 = 3.40$, p = 0.334
Employed	124 (61.4)	31 (70.5)	92 (59.0)	
Unemployed	25 (12.4)	3 (6.8)	22 (14.1)	
Retired	39 (19.3)	6 (13.6)	32 (20.5)	
Other	14 (6.9)	4 (9.1)	10 (6.4)	
Mean age at onset	18.8 (11.1)	28.0 (11.2)	16.4 (9.7)	t = 5.83; p < 0.001

TABLE II.
Lifetime and current Axis I disorders in the transplant candidates.

		Type of disease		
		All subjects (N = 227)	Nephropathy (N = 50)	Diabetes (N = 177)
Lifetime Axis I disorder				
Major depressive episode	22 (9.7)	3 (6.0)	19 (10.7)	p = 0.423
Bipolar II disorder	7 (3.1)	1 (2.0)	6 (3.4)	p = 1.000
Panic disorder	8 (3.5)	1 (2.0)	7 (4.0)	p = 0.689
Panic disorder – paucisymptomatic	1 (0.4)	0	1 (0.6)	p = 1.000
Substance use disorder	3 (1.3)	0	3 (1.7)	p = 1.000
Any Axis I disorder	36 (15.9)	5 (10.0)	31 (17.5)	p = 0.199
Current Axis I Disorder				
Major depressive episode	9 (4.0)	1 (2.0)	8 (4.5)	p = 0.688
Panic disorder	3 (1.3)	1 (2.0)	2 (1.1)	p = 0.528
Agoraphobia	11 (4.8)	3 (6.0)	8 (4.5)	p = 0.710
Panic disorder with agoraphobia	3 (1.3)	0	3 (1.7)	p = 1.000
PTSD	2 (0.9)	0	2 (1.1)	p = 1.000
Social phobia	1 (0.4)	0	1 (0.6)	p = 1.000
Generalised anxiety disorder	4 (1.8)	3 (6.0)	1 (0.6)	p = 0.034
Anorexia Nervosa	1 (0.4)	0	1 (0.6)	p = 0.594
Any Axis I disorder	30 (13.2)	7 (14.0)	23 (13.0)	p = 0.853

Table III.
Axis II disorders in the transplant candidates.

	All subjects (N = 227)	Type of disease		
		Nephropathy (N = 50)	Diabetes (N = 177)	p (= value)
Avoidant	3 (1.3)	2 (4.0)	1 (0.6)	p = 0.123
Obsessive-compulsive	46 (20.3)	14 (28.0)	32 (18.1)	p = 0.123
Oppositional	7 (3.1)	1 (2.0)	6 (3.4)	p = 1.000
Depressive	4 (1.8)	1 (2.0)	3 (1.7)	p = 1.000
Paranoid	11 (4.8)	1 (2.0)	10 (5.6)	p = 0.463
Histrionic	4 (1.8)	0	4 (2.3)	p = 0.578
Narcissistic	2 (0.9)	1 (2.0)	1 (0.6)	p = 0.393
Borderline	3 (1.3)	0	3 (1.7)	p = 1.000
Any Axis II disorder	64 (28.2)	16 (32.0)	48 (27.1)	p = 0.498

Bipolar II Disorder (3.1%). Of the 36 subjects with at least one disorder, 5 (2.2%) met criteria for two diagnoses. Female patients showed a higher frequency of lifetime depression than male patients (N = 17, 17.5% vs N = 5, 3.8%, respectively, $\chi^2 = 11.88$, $p = 0.001$), but no differences were found for the other Axis I disorders.

Psychiatric disorders

The prevalence of current Axis-I disorders was 13.2%. The most common current Axis-I disorders were Agoraphobia (4.8%) and Major Depressive Episode (4.0%) (Table II). In the overall sample, 64 (28.2%) subjects met criteria for Axis-II disorders (Table III); of those, 13 (5.7%) met

TABLE IV.Total scores (mean $\pm$ SD) of lifetime MOODS-SR and PAS-SR and in Q-LES-Q.

	All subjects (N = 227)	Nephropathy (N = 50)	Diabetes (N=177)	Mann-Whitney test and p
MOOD-SR-LT	32.7 (21.4)	30.9 (22.1)	33.0 (21.1)	Z = -0.72 p = 0.470
PAS-SR-LT	18.4 (18.2)	18.1 (17.7)	18.5 (15.6)	Z = -0.46 p = 0.643
Q-LES-Q	54.6 (15.1)	58.3 (15.1)	53.5 (15.1)	Z = -2.56 p = 0.010

criteria for two disorders and 1 (0.4%) subject met criteria for four disorders. The most common Personality Disorder was Obsessive-Compulsive Disorder (20.3%), followed by Paranoid Disorder (4.8%) and Oppositional Disorder (3.1%). Of the 50 patients with nephropathy, 5 (10%) had a lifetime Axis-I disorder, 7 (14.0%) a current Axis-I disorder and 16 (32.0%) a Personality Disorder. Of the 177 patients with diabetes, 31 (17.5%) had a lifetime axis-I disorder, 23 (13.0%) a current Axis-I disorder and 48 (27.1%) a personality disorder. No significant differences were found in the diagnostic distribution between patients with diabetes and those with nephropathy.

Mood spectrum and panic-agoraphobic spectrum phenomenology

Mood and panic-agoraphobic spectrum scores were examined in 226 subjects out of 227, because one patient failed to complete the assessment. Table IV shows mean scores on the MOODS-SR and the PAS-SR total scores, in patients with nephropathy and diabetes. Mood and panic-agoraphobic spectrum total scores did not differ between patients with type I diabetes mellitus and with nephropathy. When analysing factor scores of the MOODS-SR and PAS-SR spectra, we found that only the rescue object factor of the lifetime PAS-SR was significantly higher in patients with diabetes compared to those with nephropathy (0.9 ± 1.0 vs 0.5 ± 0.9 , respectively $Z = -2.57$, $p = 0.010$). Lifetime MOODS-SR factors were not significantly different among the two diseases (all $p > 0.05$).

Quality of life

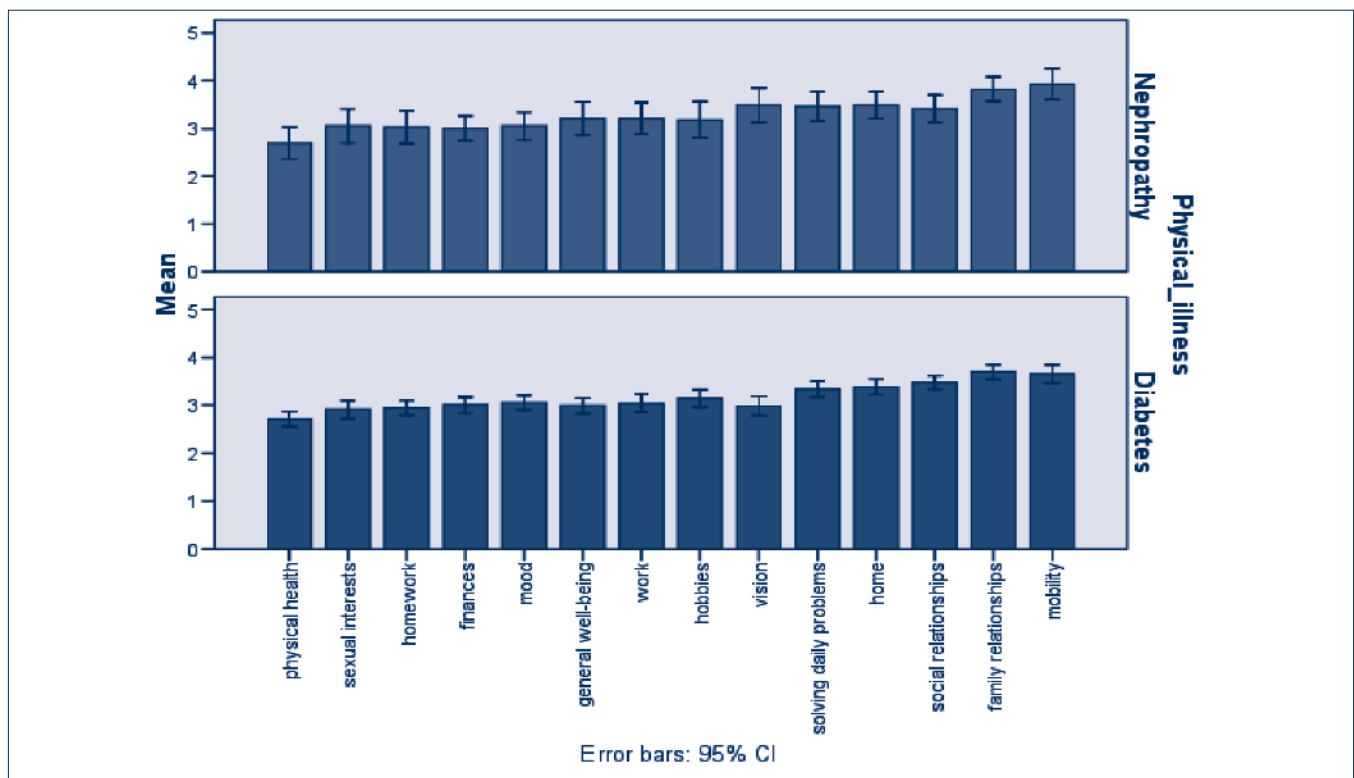
The mean Q-LES-Q score was lower in patients with type I diabetes than in patients with nephropathy (Table IV). Areas of higher dissatisfaction were physical health, sexual interests and homework with no differences between the two diseases (Figure 1).

Using a stepwise linear regression model, we found that, in the overall sample, Q-LES-Q total score was negatively associated with depressive mood factor ($\hat{\alpha} = -0.40$,

$t = -6.23$, $p < 0.001$) of the depressive component of the MOODS-SR, with mixed irritability ($\hat{\alpha} = -0.24$, $t = -3.18$, $p = 0.002$), inflated self-esteem ($\hat{\alpha} = -0.21$, $t = -2.73$, $p = 0.007$) factors of the manic/hypomanic component of the MOODS-SR and with separation anxiety factor ($\hat{\alpha} = -0.27$, $t = -4.01$, $p < 0.001$) of the PAS-SR. Moreover, the quality of life was positively associated with sociability/extraversion factor ($\hat{\alpha} = 0.19$, $t = 2.64$, $p = 0.009$) of the manic/hypomanic component of the MOODS-SR. Significant associations between quality of life and MOODS-SR and PAS-SR factors in patients with diabetes and in patients with nephropathy are shown in Table V. In patients with nephropathy, the quality of life was negatively associated only with psychotic features of the depressive component of the MOODS-SR. In patients with diabetes, the quality of life was positively associated with creativity factor of the manic/hypomanic component of the MOODS-SR and negatively with depressive mood factor of the depressive component of the MOODS-SR, mixed irritability and inflated self-esteem factors of the manic/hypomanic component of the MOODS-SR and separation anxiety factor of the PASSR.

Discussion

In our study, lifetime depression was the disorder most represented both in the ESRD (6%) and IDDM (10.7%) subgroups. These results confirm and expand our preliminary data on this matter^{47 48}. These rates were consistent with the prevalence estimation reported in the general Italian population^{30 31}. In our sample, current Generalised Anxiety Disorder (GAD) was significantly more represented in ESRD (6%) than IDDM (0.6%). The reasons for this difference in the prevalence of GAD between the 2 groups is not known. We can speculate that chronic kidney disease remains asymptomatic and unrecognised for a long time. Therefore, the time elapsed between diagnosis and transplantation in ESRD patients is usually much shorter than in IDDM patients who are often aware

**FIGURE 1.**

Areas of dissatisfaction of quality of life. In both nephropathy and diabetes, the areas of higher dissatisfaction were physical health, sexual interest and homework.

TABLE V.

Relationship between mood and anxiety spectrum factors and quality of life score (Q-LES-Q).

Factors retained in stepwise linear regression models	Nephropathy (N = 50)			Diabetes (N = 177)		
	Standardised beta coefficients	T-test	p (value)	Standardised beta coefficients	T-test	p (value)
MOODS-SR depressive component						
Psychotic features	-0.33	-2.30	0.026			
Depressive mood				-0.44	-6.09	< 0.001
MOODS-SR manic/hypomanic component						
Mixed irritability				-0.27	-3.22	0.002
Creativity				0.21	2.61	0.010
Inflated self-esteem				-0.22	-2.59	0.011
PAS-SR						
Separation anxiety				-0.29	-3.81	< 0.001

of their disease since childhood, and are already accustomed to therapies and hospitalisation at the time that transplantation is proposed³².

However, in our sample, the prevalence of current mental disorders (13.2%) and major depression (4.0%) was around three times higher compared to the current preva-

lence in the general Italian population (3.2% and 1.4%, respectively)^{30,31}.

These data confirm epidemiological studies indicating that diabetic patients (both type I and type II) present depressive symptomatology³³⁻³⁵ and that depressive symptoms are common among ESRD patients, especially after

the initiation of renal replacement therapy. Furthermore, high rates of depression have been reported among patients on haemodialysis ^{36 37}.

The prospect of organ transplantation, not just the chronic disease, may play an important role in the development of current psychopathology; in particular, the awareness of an imminent major surgical procedure and its possible complications, or the awaiting of inevitable surgery from a cadaveric donor may contribute to the development of anxiety and depression ³⁸.

Psychiatric assessment is required to identify personality traits that can reduce the good outcome of transplant procedures. The process of transplant requires a series of adaptations to modify physical and social functioning. Severe personality disorder has been proposed as a potential absolute or relative contraindication for transplantation ³⁹. Our results show that Obsessive-Compulsive (O-C) disorder is the most prevalent personality disorder both in the overall sample and in the two sub-groups examined. Probably, the needful for dietary restrictions and attentive treatment compliance (e.g. insulin therapy) could affect the development of obsessive-compulsive behaviours. In our opinion, the need for structure and order of a typical obsessive-compulsive personality would be adaptive to the demands of transplantation before and after surgery. While it is known that there is a correlation between diabetes and anxiety symptoms, there are no recent studies that focus on the relationship between O-C symptoms and diabetes. However, one study showed an increase of O-C symptoms in children with diabetes compared to healthy controls, which was interpreted as psychological adjustment. Because type I diabetes usually onsets during childhood or adolescence, we can assume that these symptoms may represent the onset of an obsessive-compulsive personality disorder in adulthood ⁴⁰.

Among diabetic subjects, opportunistic, alienated and explosive personality traits were found to be associated with poor management of the disease ⁴¹; patients with Cluster B dependent profiles exhibited poorer metabolic control than other patient profiles; in diabetic patients, non-compliance is often associated with borderline personality disorder ⁴¹.

In the present report, the psychopathological sub-threshold features were assessed using validated spectrum instruments. Patients with diabetes showed higher levels of separation, anxiety and rescue object scores compared to patients with nephropathy. This factor includes items indicating the need to take objects such as an umbrella, a hat, a good luck charm or a bottle of water. In our context, this may be interpreted as a learned behaviour because patients with diabetes, since childhood, have associated the use of drugs and medical devices to safety. Furthermore, thirst is a common early symptom of diabetes or hyper-

glycaemia, which may justify the need for a water bottle everywhere. These results are in agreement with literature data showing that anxiety is an important comorbidity in patients with diabetes. Indeed, patients with diabetes and anxiety symptoms show increased diabetes symptoms burden, increased diabetes complication, increased pain, reduced QOL, increased depression and greater disability ⁴². In agreement with current literature data, the mean QOL among the overall sample was poorer than that of a healthy adult population ⁴³. In our overall sample the QOL was positively associated with sociability/extraversion factor of the manic/hypomanic component of the MOODS-SR. Patients presenting this component have maintained openness to social contacts, avoiding the isolation that the disease can facilitate, thereby having a better QOL.

The mean Q-LES-Q score was lower in patients with diabetes than in those with nephropathy confirming that diabetes may deeply affect several aspects of life. Despite the increasing interest in sub-threshold mood disorders and in QOL research, very little is known about the relationship between QOL and sub-threshold affective and anxiety symptoms in chronically-ill patients. We found significant negative associations between sub-threshold affective and anxiety symptomatology and QOL in both diabetic and nephropathic patients.

Our results underline that in patients with diabetes, sub-threshold depressive mood, irritability, inflated self-esteem and separation anxiety are linked to increased functional and physical disability, decreased energy and interest in leisure, lower motivation, and impairment with family and social relationships. In patients with nephropathy, low levels of QOL were associated with the presence of psychotic features. This factor includes paranoid thoughts and psychotic symptoms that are widely reported in patients with major depressive episodes. Patients with kidney disease have a better QOL because the disease involves fewer complications than diabetes. We can speculate that only the presence of severe psychiatric symptoms may lead to impaired quality of life in ESRD patients.

These data confirm previous observations concerning the relationship between syndromal and sub-syndromal depressive symptoms and quality of life or symptoms indirectly related to quality of life, such as psychosocial impairment and disability ⁴³. Sub-threshold symptoms of depression or anxiety, may further increase psychosocial dysfunction in patients waiting for organ transplant.

Conclusions

An organ transplant procedure is generally the last therapeutic option of a long-standing chronic disease. The pre-surgical iter induces a significant psychological stress

load, which can determine the onset of full-blown and/or sub-threshold mood or anxiety symptomatology and impairment of QOL.

Among subjects suffering from chronic physical illness, patients awaiting transplants represent a sub-group that deserves careful consideration.

Routine assessment of psychosocial data of transplantation candidates has led to the investigation of psychosocial vulnerability as a potential predictor of post-transplant outcome, with the aim to identify patients at risk. Previous prospective studies have demonstrated that psychosocial variables are capable of predicting both psychosocial and physical outcomes after transplantation; pre-transplant psychiatric disorders have been shown to be predictors of lack of psychosocial adjustment after the operation, i.e., high pre-transplant anxiety or neuroticism values predict low post-transplant QOL⁴⁴.

As such, professional assessment of QOL and psychosocial functioning at all the different stages of IDDM and chronic renal insufficiency (from early stages through to end-stages) can be extremely important for treatment outcome. In addition, appraisal of psychosocial variables such as cognitive beliefs, companionship and social networks that represent essential markers of psychosocial vulnerability may facilitate early identification of those patients at risk for psychosomatic and/or psychiatric symptoms after surgical intervention.

Numerous reports describing the relationship between depression and the outcome of the surgery in renal transplant recipients suggest the importance of establishing this diagnosis³³, and it has been amply demonstrated that a depressive disorder can increase the risk of non-compliance to therapy⁴⁵.

Emerging evidence shows that preoperatively assessed psychosocial variables can predict post transplantation psychopathological outcome among recipients of most organ types⁴⁶. Notwithstanding, little attention is dedicated to spectrum symptoms and their relationship to patient's QOL.

At present, there is a lack of studies describing the psychopathology in terms of sub-threshold symptomatology and Axis I and II disorders using standardised interviews. Our findings underline the importance of careful evaluation of anxiety and depression symptoms during kidney/pancreas pre-transplant and post-transplant phases that involve subsyndromal symptoms evaluation. A systematic screening for depressive symptoms by means of self-report instruments, such as panic-agoraphobic instruments during the pre- and post-transplant phases, is valuable with particular attention to diabetic patients.

Conflicts of Interest
None.

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Empathic and cognitive processing in people with schizophrenia: a study on an Italian sample

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Summary

The aim of this study was to explore the relationships among empathy processes in terms of self-report empathy evaluation and recognition of emotional cues and Theory of Mind components. We used the Empathy Quotient – short form (EQ-s), the Pictures of Facial Affect (POFA) system, a (ToM) Irony appreciation task and the Wisconsin Card Sorting Test (WCST), respectively. The Positive and Negative Symptoms Scale (PANSS) and Global Assessment of Functioning (GAF) were also used to investigate the relationship with symptomatology and functioning. The sample consisted of 30 participants with diagnosis of schizophrenia. Our results found no significant correlations between EQ-s and other cognitive or clinical variables. PoFA total score and recognition of fear correlated with time spent to give a correct response to the ToM irony comprehension. Time spent

to correctly respond to both ToM and physical vignettes correlated with negative symptoms. Positive, negative and cognitive clusters of the PANSS correlated with the GAF. The relationships we found among the considered constructs suggest that empathic processing acts on functionality improving the personal efficiency, in terms of readiness and rapidity, to cope with one's environment, in the multifaceted social setting. Given that emotion perception in particular has been connected to social competence, independent living and community functioning, it is conceivable that emotion processing may be a potential catalyst within the mindreading process, which can have an impact both on symptomatology and social functioning.

Key words

Theory of Mind • Irony • Pictures of Facial Affect • Social Functioning

Introduction

People interact in social settings ascribing mental states (such as beliefs, desires, intentions, emotions) to others, often with no significant mental effort, despite the complexity of the task. Nevertheless, a complex network of systems exists which allows humans to make inferences in social situations about the other mental states, i.e. have a Theory of Mind (ToM), as well as inferring emotions from nonverbal cues, such as prosody and facial expressions and eventually empathise with the person engaged in the interaction¹⁻³.

To explore this complex phenomenon in schizophrenia, the issues we considered are: i) the role played by ToM, Empathy and Emotion Recognition constructs in social understanding, reporting evidence and considerations on their interactions; ii) the role of these components in relation to the symptoms of schizophrenia and functioning. Previous studies on the relationships among these constructs have yielded inconsistent results. On one hand, they seem to work independently; indeed as Baron-Cohen⁴ hypothesised, both cognitive ToM and the ability to

correctly grasp emotions from persons' facial expressions are independent contributors to empathy. In addition, Benedetti et al.⁵, by using a task requiring individuals to empathise with the affective states of the characters of stories, reported empathy deficits in schizophrenia. On the other hand, it is possible to hypothesise a reciprocal influence between the constructs. As Derntl and colleagues⁶ found, patients reported difficulties with empathy which correlated with poor emotion recognition and perspective-taking, as well as poor affective responsiveness. Of note, while some have presented data suggesting that cognitive and affective components of ToM are dissociable (e.g. Shamay-Tsoory et al.⁷), other studies show how ToM and affective components can be reduced to a single factor^{8,9}.

Following this path, we can argue that the mental state of *reasoning*, which taps the cognitive aspect of ToM, and the mental state of *'emotional' decoding*, or the ability to automatically infer what the other is feeling based on nonverbal cues^{10,11}, may represent different, but reciprocally interacting, aspects of the mindreading process¹². Emotion recognition, contributing to the perception of a

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kind of 'first glance' empathy, is essential to infer with immediacy some mental states. Since this ability requires 'gut feelings' rather than effortful verbal processing, it may be more closely related to social perception and functioning¹¹⁻¹³. Moreover, irony is an ability well considered to be related both to ToM and empathy, with *reasoning* (i.e. cognitive) and *decoding* (i.e. emotional) components¹⁴⁻¹⁶. From this perspective, the reasoning component fits well with the social cognitive aspect of ToM¹⁷, while the *decoding* component fits well with the social perceptual aspect of ToM^{7,18}.

How do these variables interact? Specifically, it has been suggested that a poor understanding of others' minds can affect empathy. In fact, ToM appears to involve the capacity to reason about mental states and the ability in decoding mental states, that is, to form quick impression of what others think and feel. On the other hand, the opposite can be possible: to infer the others' states of mind, the person first needs to intuit what the others feel, think and wish, and then to put oneself in the others' shoes, seeing things from a different and decentred stance^{19,20}. Finally, burgeoning evidence suggests that impaired the cognitive and emotional aspects of ToM bear effects on symptoms and functioning^{3,8,21-24}. Intentions inferring deficits have been found to correlate with thought disorder and negative symptoms^{25,26}. Deficits in understanding others' intentions through indirect hints²⁷ and irony understanding²⁸ seem to be related to negative and behavioural signs of schizophrenia^{14,30}. Recent findings have also demonstrated relationships between ToM deficits and persecutory delusions²⁹.

Aim of the study

Supported by these observations and hypotheses derived from the literature, we speculated that multiple interacting abilities intervene to cope with one's environment. ToM, emotional inference from non verbal hints and empathy allow one to grasp cues that lead the person to be efficient i.e. efficacious and ready in social context. We aimed to explore the relationships among these processes as well as their associations with symptomatology and functional outcomes.

We hypothesised that empathy and emotional processing can be related to cognitive processing speed and the readiness that environmental functioning requires.

Methods

Subjects

A total of 30 consecutive outpatients diagnosed with DSM-IV for schizophrenia participated in this study. All were in a stable phase of the disorder and able to live in

the community with antipsychotic therapy provided by the outpatient facilities of the Villa Serena Medical Centre.

The sample consisted of 21 males and 9 female participants. Ages ranged from 21-66 years, with a mean of 37.8 (SD 10.7). Mean education level was 9.9 years (SD 2.8). All were in a post-acute phase of illness defined by no changes in medication with no changes for at least six months. None of the patients had ever been hospitalised for more than six consecutive months. The average participant had had 10.03 (SD 7.15) lifetime psychiatric hospitalisations, with a length of illness of 13.87 years (SD 6.20).

Exclusion criteria were major physical illness requiring constant medical care, neurological disease, alcohol or substance abuse, and mental retardation (IQ < 75). All participants provided written informed consent after a complete description of the study, in accordance with the local ethics committee which approved the study.

Procedures

Testing was conducted in two sessions, by a resident clinical psychologist (MDA), in which tasks were presented in a random order.

Empathy Quotient – short form (EQ-s) – Italian version. The EQ-s is a self-report questionnaire developed by Baron-Cohen to measure empathising capacity³⁰. The original form contained 60 items, which Wakabayashi et al.³¹ shortened to a more efficient 22-item scale. The EQ empathy questions target both the emotional and cognitive components of empathy. The EQ has a forced choice format; the participant must choose one of four responses. The item is scored two points if the respondent records the behaviour strongly or one point if the respondent records the behaviour mildly.

Pictures of Facial Affect (POFA) system³². Thirty-six slides of human faces portraying surprise, happiness, fear, disgust, sadness and anger were presented in a random order that was the same from participant to participant. Each participant was first shown six cards on which each of the emotions was written down. After insuring that the participant knew what the words meant, he was told that he would see a face for a few seconds and then asked to answer what kind of emotion was displayed. Stimulus exposure was set at 10 seconds.

Irony appreciation task. We used a version of 30 visual jokes from the Marjoram et al.³³ paradigm. Two sets of jokes were shown: a 'Physical set' of slapstick humour that did not require ToM capabilities to understand the joke contained within the picture and a 'ToM set' in which an appreciation of the mental states of the characters (i.e. false belief and deception) were required; the 'Physical set' is used as a control condition of the ToM

irony task. Fifteen single-image cartoon jokes were presented one at a time for each condition (an example of the two conditions is reported in Figure 1). The participant was instructed to indicate when he understood the jokes' meaning: the interval from vignette administration and appreciation constitutes the 'Time for correct response'. The participant was then required to report his interpretation. For the interpretation response to be considered correct, the participant had to appropriately interpret the characters' mental state for ToM jokes, or describe the scenario for Physical joke. The examiner scored one for a correct answer and zero for an incorrect one. The sum of the reported scores and time spent to give the correct response for each condition (i.e., ToM and Physical) constituted the scores.

Wisconsin Card Sorting Test (WCST), for the executive functions evaluation. This is a neuropsychological test of strategic planning, organised searching, utilising environmental feedback to shift cognitive sets, directing behaviour toward achieving a goal, and modulating impulsive responding. A number of stimulus cards are presented to the participant telling him/her to match the cards, but not how to match; however, the subject is told whether the match is right or wrong. It was administered with the standard instructions described by Heaton³⁴ using a computerised version. Performances were automatically scored by the computer and were based on number of stages achieved, number of total and perseverative errors.

Clinical evaluation

A senior psychiatrist (A.R.) and a clinical psychologist (I.R.) blind to performances on the tasks clinically evaluated participants for symptomatology and global functioning. The current symptoms of the patients with schizophrenia were assessed using the PANSS³⁵, a 30-item, 7-point rating instrument, in Italian version. Each item on the PANSS is accompanied by a complete definition as well as detailed anchoring criteria for all seven rating points, which represent increasing levels of psychopathology. Of the 30 psychiatric parameters assessed on the PANSS, seven constitute a Positive Scale, seven a Negative Scale and the remaining 16 a General Psychopathology Scale. The PANSS cognitive component was calculated by summing the 7 items according to Bell et al. (1994) and Daneluzzo et al.³⁶.

Patient's functioning was rated using Italian version of The Global Assessment of Functioning (GAF) Scale³⁷ as the Axis V of DSM-IV reflects global functioning. The GAF is the standard method for representing a clinician's judgment of a patient's overall level psychological, social, and occupational functioning. In *DSM-IV*, the rating is made on a scale from 1 to 100, from severe impairment to superior functioning.

Statistical analysis

Because some continuous measures were not normally distributed (Kolmogorov-Smirnov test: $p < .01$), Spearman's correlation was used. The level of significance was set at $p = .05$.

Results

The data (means and standard deviations) of the sample are reported in Table I. No significant correlations were found between EQ-s and any other cognitive or clinical variable.

PoFA total score correlated with time spent to give a correct response to the ToM irony comprehension and with

TABLE I.
Cognitive and clinical characteristics of the sample.

	Mean	SD	Range
EQ-s	22.10	6.6	0-44
PoFA (correct answers)			
Total	65.9	16.2	0-100
Happiness	93.9	13.5	0-100
Sadness	45.5	28.7	0-100
Fear	51.6	25.2	0-100
Anger	61.6	26.7	0-100
Surprise	75	25	0-100
Disgust	70.5	29.6	0-100
Irony comprehension			
ToM (correct answers)	5	2	0-15
ToM time	52.3	34.2	-
Phy (correct answers)	7.23	3.3	0-15
Phy time	45.5	35.4	-
WCST			
Correct stages	3.3	2.2	0-6
Tot Errors	17.9	12.4	0-63
Perseverative Errors	30.4	13.8	0-63
PANSS			
Total score	95.1	19.4	30-210
Positive cluster	19.9	4.6	7-49
Negative cluster	21.5	6	7-49
Cognitive cluster	20	6.1	7-49
GAF	55.6	9.1	0-100

EQ-s: Empathy Quotient short; PoFA: Pictures of Facial Affect; Irony comprehension: ToM, theory of mind condition; Phy: physical condition; WCST: Wisconsin Card Sorting Test; PANSS: Positive and Negative Syndromes Scale; GAF: Global Assessment of Functioning.

appreciation of humour in the physical vignettes (Table II). Observing the coefficients for single emotions, recognition of fear correlated with time spent (ToM irony comprehension), while anger correlated with appreciation of physical irony (irony not requiring ToM ability). No other significant correlations were seen for the remaining emotions.

ToM irony comprehension score correlated with WCST index. This correlation reached statistical significance even partialling out for education level (vs. WCST number of stages $\rho = 0.41$ $p < 0.05$).

With regard to symptoms and functioning, time spent to correctly respond to both ToM and physical vignettes correlated with negative symptoms ($\rho = 0.46$

and $\rho = 0.40$, $p < 0.05$). Positive, negative and cognitive clusters of the PANSS correlated with the GAF ($\rho = -0.39$, $\rho = -.41$ and -0.46 , $p < 0.05$ respectively).

Discussion

In this study, we sought to explore if some relations between different abilities, i.e. empathy, ToM and emotion recognition, exist, and if these abilities are correlated to symptomatology and global functioning.

The hypothesis we made of a relationship between empathy, emotional processing and cognitive processing speed and the readiness required by the environment

TABLE II.

Correlations between participants demographics. Clinical/functional characteristics and tasks measures.

	Ys III ^a (1)	Age (2)	Edu ^b (3)	Gender (4)	PANSS ^c (5)	Pos ^d (6)	Neg ^e (7)	Cogn ^f (8)	GAF ^g (9)	ToM ^h (10)	ToMt ⁱ (11)
1	1										
2	.65**	1									
3	-.18	.52**	1								
4	.41*	-.26	.22	1							
5	-.03	-.08	.26	.27	1						
6	-.02	-.30	.51**	.33	.58**	1					
7	.02	.17	.10	.19	.71**	.07	1				
8	.11	.20	.05	.24	.83**	.33	.61**	1			
9	.10	.13	-.17	-.26	-.59**	-.39*	-.41*	-.46*	1		
10	-.36*	-.61**	.62**	.26	.08	.34	-.15	-.02	-.16	1	
11	-.15	.15	-.16	-.06	.38*	.03	.46*	.36	-.19	-.32	1
12	-.39*	-.54**	.64**	.25	.03	.20	-.06	-.09	-.08	.89**	-.30
13	-.17	.00	-.20	.21	.36	.08	.40*	.26	-.23	-.27	.52**
14	.15	.04	.18	-.16	-.06	.11	-.19	-.15	.06	.01	-.11
15	-.15	-.47**	.37*	-.16	.13	.33	-.10	-.05	-.12	.46**	-.02
16	.08	.13	-.10	-.25	-.20	-.23	-.02	-.13	.35	.05	-.30
17	-.17	-.39*	.31	.02	-.14	-.05	-.16	-.28	.26	.01	-.42*
18	-.16	-.25	.31	-.14	.25	.20	.01	.10	-.07	.30	-.06
19	-.12	-.15	.06	.21	-.17	.08	-.17	-.15	-.10	.33	-.21
20	-.20	-.32	.22	.04	-.03	.02	-.09	-.13	.04	.23	-.12
21	-.18	-.33	.26	.06	-.23	-.00	-.22	-.28	.17	.36	-.46*
22	-.07	-.32	.22	.05	-.02	.08	-.17	-.20	-.16	.44*	-.27
23	.21	.24	-.41*	-.09	-.21	-.14	-.11	-.09	.34	-.45*	.02
24	.23	.13	-.40*	-.18	-.07	-.15	-.11	.01	.18	-.27	-.05

* $p < .05$; ** $p < .01$.

^a Duration of the illness-years; ^b Years of education; ^c Positive and Negative Symptoms Scale- Total Score; ^d PANSS Positive Symptoms Cluster; ^e PANSS Negative Symptoms Cluster; ^f PANSS Cognitive Symptoms Cluster; ^g Global Assessment of Functioning; ^h ToM Comprehension – Total score (Irony ToM Task); ⁱ Total Time spent to give correct response to ToM Comprehension; ^j Physical Comprehension-Total score (Irony Physical Task);

to have a good functioning was partially confirmed. Although no correlations were found between self-reported empathy and other variables, emotion recognition and understanding of irony were indeed related, suggesting that affective and cognitive components of understanding the mental state of the others may interact with each other^{30,38}. According to our results of a correlation between time spent to give a correct response to the ToM task and the recognition of emotions, specifically of fear, it seems that a poor 'first glance' intention grasping, i.e. poor emotional recognition, corresponds to a long latency before correctly understanding the mental processes underlying ironic vignettes. If so, the negative correlation between

time spent in irony detection and recognition of emotion in general may tap a possible shared mechanism for fast attributions of intentions to others. It is conceivable that patients with schizophrenia are particularly compromised when they have to “mentalise on the spot” under time pressure, as hypothesised by Corcoran and Frith ²⁷, to grasp both states of mind and some relevant emotional expressions of others. They need to employ ToM and facial emotion recognition to correctly perform ‘on-line’ social tasks ²⁷ as they would in a real-life situation. This lack of steady attributions may contribute to generate the communicative failures these persons suffer from. Of note, on one hand the absence of a significant correla-

Phy ^l (12)	Phyt ^m (13)	EQs ⁿ (14)	Hap ^o (15)	Sad ^p (16)	Fear ^q (17)	Ang ^r (18)	Sur ^s (19)	Dis ^t (20)	PoFA ^u (21)	Stages ^v (22)	NTotErr ^w (23)	NErrPers ^x (24)
1												
-.23	1											
.07	-.18	1										
.36	-.09	.33	1									
.20	.04	.15	.07	1								
.24	-.28	.05	-.01	.32	1							
.47**	-.12	.14	.32	.42*	.38*	1						
.30	-.26	-.33	.32	-.05	-.13	.01	1					
.31	-.17	-.08	.35	.12	.41*	.46*	.18	1				
.47**	-.32	-.04	.42*	.51**	.58**	.59**	.43*	.65**	1			
.42*	-.23	.24	.33	-.08	-.01	.10	.31	.13	.17	1		
-.31	-.19	-.00	-.20	.23	.23	.15	.04	.21	.26	-.43*	1	
-.17	-.28	.17	-.06	.23	.21	.30	-.01	.22	.22	-.11	.85**	1

^m Total Time spent to give correct response to Physical Comprehension; ⁿ Empathy Quotient short version; ^o Happiness (Pictures Of Facial Affects); ^p Sadness (Pictures Of Facial Affects); ^q Fear (Pictures Of Facial Affects); ^r Anger (Pictures Of Facial Affects); ^s Surprise (Pictures Of Facial Affects); ^t Disgust (Pictures Of Facial Affects); ^u Pictures Of Facial Affects – Total Score; ^v Number of Stages-Wisconsin Cards Sorting Task; ^w Number of Total Errors-Wisconsin Cards Sorting Task; ^x Number of Perseverative Errors-Wisconsin Cards Sorting Task.

tion between ToM comprehension and emotions recognition we found is in line with ³⁹ and could be interpreted in a way as supporting Frith and Frith's ^{40 41} neurocognitive model of social interaction. On the other hand, the relation between time spent to give a correct ToM response and emotion recognition is in line with Besche-Richard et al. ⁴² who found that performances in the facial emotion recognition are the best predictor of performances in the attribution of beliefs. Regarding the correlation specifically with fear, data exists on an impairment of facial expression of fear, anger and disgust in people with schizophrenia ^{43 44}, but to the best of our knowledge, there are no studies about the possible relation between impairments of specific emotions and ToM ability. Accordingly, this issue deserves further research.

Exploring the correlations between self-reported empathy and other variables, we found it was neither related to facial emotion recognition nor to comprehension of irony, supporting previous evidence of these elements being dissociable ^{7 19 45 46}. This may be due to empathy being a complex ability that includes more than recognition of mental states. One may fully understand what the other is feeling and thinking, but be cold, detached, or even hostile, preventing the individual from being able to fully assume the other's perspective.

Correlations between cognitive ToM performance and poor mental flexibility (i.e. WCST) is a result consistent with previous literature findings suggesting that intact neurocognition is needed for at least the more basic aspects of the mentalistic system to work appropriately ^{7 15 47-49}. Some studies did not find, however, such a link ⁵⁰.

Considering correlations with symptoms and social functioning, we found a significant correlation between time spent in appreciating both ToM or physical irony and negative symptoms. This may suggest that even if these patients can understand irony and the character's mental states, their slowing down is associated with symptomatology, interfering with the fast and natural interactions that social functioning requires. These patients are likely to require an extra-reasoning effort that would make them feel constantly out of synchrony with the rapid shifts between serious statements and jokes that form everyday conversations with relatives and peers. This delay in understanding mental states hampers the ability to maintain and support social contact during the demanding challenges of real-life social situations ⁵¹. Alternative or integrative hypothesis may be that avolition, anhedonia and passivity could be an indirect sign of depression that would reduce the sensitivity to funny stories, and a possible marker of less desire for social contact.

Self-reported empathy did not show any significant correlations with the symptom cluster and global functionality. This result is consistent with previous findings: Derntl and

colleagues ⁶ found no significant correlations between empathy deficits and clinical symptoms, though a subgroup of patients with prominent negative symptoms had better empathic performance than other groups with predominant positive or mixed symptomatology. In any case, our results are in line with Brune and colleagues ²³, who failed to find significant correlations of this type.

The relationships we found among the variables considered can suggest that empathic processing acts on functionality improving the mentalisation efficiency, in terms of readiness and rapidity. Given that emotion perception in particular has been connected to social competence, independent living and community functioning ⁵², it is conceivable that emotion processing within empathy may be a potential catalyst within the process of comprehension of the minds of others, which can have an impact both on symptomatology and functioning ⁵³.

There are some limitations to our study. First, the sample size is relatively small, but could be sufficient for a preliminary test of heuristic value hypotheses. Second, there was no control group so the difference in the battery we adopted that would have emerged in comparison to a non-clinical population has not been assessed. Third, the correlations between empathy and ToM need to be further investigated possibly using information from relatives or specific tasks for empathy performance involving affective responsiveness simulating real-life situations.

A fourth limitation is the use of self-report instrument, instead of the rating of the clinician, in order to detect empathy abilities. It is possible that a measure of such a complex mentalistic ability, self-reported by people who often do not have good self-reflection ^{47 48} could generate a biased description of true empathic ability even if some self-report questionnaires to measure self reflection abilities are widely used (e.g. Toronto Alexithymia Scale ⁵⁴).

Further, we did not apply a correction for multiple correlations. Nevertheless, due to the exploratory intent of the study supported by hypotheses derived from the literature, in which data are collected with an objective although with the *a priori* key hypothesis we stated, multiple test adjustments may not be strictly required with a flexible approach for design and analysis. Moreover, each variable we considered was of interest in its own, so we chose to report all individual p-values and make separate considerations in relation to our hypotheses. When multiple test results have implications on specific responses, correction for multiple comparisons can be unnecessary, as it is more relevant to know the strength of evidence for testing individual hypotheses ⁵⁵.

This was a correlational study, so that no causal links can be derived from this experimental design. These findings, however, can be of heuristic value for the hypothesis of a parallel intervention of different constructs in the social adaptation.

Further studies are needed, possibly with multi-modal assessment of empathy, to better understand the role of an empathy deficit in schizophrenia and its relation to aspects of the mental state understanding systems, as well as its possible role in explaining the social dysfunction from which these persons suffer.

Conflicts of interest

None.

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Sleep disorders in adult ADHD: a key feature

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Summary

Objectives

Attention deficit hyperactivity disorder (ADHD) is a neuropsychiatric disorder affecting individuals across the life span, and the relationship between ADHD and sleep poses several challenges in clinical practice. As ADHD symptoms overlap with those of sleep disorders, the aim of this paper is to summarise the state of art regarding the relationship between these conditions, in order to provide suggestions for future research and key elements to take into account during the diagnostic assessment of ADHD as well its clinical management.

Methods

We performed a PubMed search for articles published from 2005 to 2016, using the following key words: attention deficit disorder, ADHD, sleep disorders. The literature search was conducted in March 2016. Only articles written in English and providing data on adult population were considered.

Results

We found 773 articles matching keywords. Applying the above-mentioned exclusion criteria, only 30 resulted pertinent to our aim. Other articles from other databases were selected accord-

ing to their importance, and then further filtered according to their capability in answering our research objectives. A total of 35 articles allowed us to identify the most frequently reported sleep disorders in adult ADHD, the potential neurobiological substrates at the basis of the similarities in symptomatology and the most important implications for clinical and research settings.

Conclusions

A poor sleep can worsen ADHD symptomatology, resulting in an increasing risk for accidents and health problems. An increased risk for depression has also been documented. Because of the overlapping symptomatology, the presence of a sleep disorder should be adequately screened during ADHD assessment and during the clinical management of the disorder. The similarities between symptoms of ADHD and those of a sleep disorder suggest certain basic disturbances in a potential common circuitry that require further exploration. The understanding of the causes accounting for the frequent co-occurrence of sleep disorders in people affected by ADHD may help to implement an effective treatment for improving quality of life of these patients.

Key words

ADHD • Attention deficit disorder • Sleep disorders

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a common neurobiological condition with childhood onset characterised by developmentally inadequate symptoms of inattention, impulsivity and hyperactivity causing impairment in several domains (e.g. school, home, social and sentimental relationships, work etc.). For a long time, ADHD has been considered a clinical condition affecting only childhood, but now there is consensus about its frequent persistence over the lifespan.

It is widely known that both children and adults with ADHD may also meet criteria for other psychiatric disorders, and patients with both ADHD and comorbidities may experience greater impairment than people with ADHD alone ¹. Mood, anxiety and substance use dis-

orders have been reported as co-occurring conditions of adult ADHD in several study and international surveys, but recently greater attention has been given to sleep disorders. Research data show a prevalence rate of adult ADHD of 3.4% ², and up to 83% of adults with ADHD reports sleep complaints ³. Adults with ADHD frequently report difficulties in falling asleep, problems in awakening in the morning and may present daytime sleepiness ⁴. However, it would be noted that daytime sleepiness, impaired cognitive performance and behavioural problems are usually reported also by patients with sleep disorders ⁴.

The relationship between sleep problems and ADHD has been described as extremely complex. In fact, it has been suggested a bidirectional association between sleep dif-

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difficulties and ADHD, so that poor sleep may exacerbate ADHD symptomatology and viceversa ⁵.

Moreover, sleep difficulties, such as restless sleep, bedtime resistance and nocturnal awakenings, have been proposed as a risk factor for the subsequent development of ADHD ⁶: sleep problems in infancy have been found to be associated to attentional and behavioural problems at age 15 ⁷, and short sleep duration was significantly related to increased externalising symptoms ⁸.

Because several studies show how sleep restriction may affect cognition and behaviour in a way that may mimic ADHD ⁸, the intricate nature of such relationship requires an adequate consideration in the diagnostic assessment process for ADHD, in order to avoid an incorrect (or partial) diagnosis.

The relationship between sleep disturbances and ADHD symptoms and its negative impact on functioning have been largely examined in children. With the recognition of the persistence of ADHD in adulthood, research on interaction between sleep and adult ADHD is necessary. The aim of this paper is to provide the state of art regarding:

1. the most reported sleep disorders in adults with ADHD;
2. neurobiological mechanisms underlying the relationship between sleep and ADHD;
3. implications for clinical practice and suggestions for research.

Materials and methods

We performed a PubMed search for articles published from 2005 to 2016, using the following key words: attention deficit disorder, ADHD, sleep disorders. The literature search was conducted in March 2016.

The titles and abstracts of identified papers were screened. We excluded all articles not written in English, and not considering the adult population. Articles so filtered were read in full and examined according to their relevance in the field.

Results

We found 773 articles matching keywords. Applying the exclusion criteria before mentioned, only 30 resulted pertinent to our aim. Additional articles from other databases were selected according to their importance and then further filtered according to their capability in answering our research objectives.

Our search of the most recent literature allowed us to identify: the most frequently reported sleep disorders in adult ADHD, the suggested neurobiological substrates at the basis of the similarities in symptomatology and the most important implications for clinical and research settings.

Obstructive sleep apnea (OSA)

Both individuals with ADHD and those suffering from an obstructive sleep apnea complain of daytime inattentiveness and impaired concentration. Attention deficits, poor planning activities, restlessness and irritability are very well documented in these populations, especially in children ⁹. In consideration of previous research ¹⁰ that found the presence of OSA in 5% of subjects affected by relevant symptoms of ADHD, in 26% of people with a mild symptomatology and in 5% of people without the disorder, it has been suggested that the overlap of symptoms between OSA and ADHD may lead patients with OSA to be misdiagnosed as having ADHD ⁹.

In case of co-occurrence of both disorders, higher anxiety levels and a greater deterioration in daytime functions have been described, and the treatment of only OSA was considered of limited efficacy in improving daytime functioning ¹¹.

Restless legs syndrome

Another sleep disorder frequently reported in ADHD population is restless legs syndrome (RLS). RLS is a sensorimotor condition characterised by discomfort and tension in the lower limbs with the urge to move them ¹². Children and adults with RLS have problems falling asleep due to aching, cramping, or tingling leg sensations that cause bedtime resistance until late at night. RLS has been found frequently associated with periodic limb movement disorder (PLMD), which is characterised by periodic and sustained contractions in legs, occurring mainly in non-rapid eye movement (REM) sleep. This interruption of sleep seems to determine irritability, frustration and angry outbursts in the daytime. Growing evidence suggests a link between RLS and PLMD, so that it has been suggested that periodic limb movement may also be a marker for a genotype of RLS ¹³. It is worth noting that in both RLS and PLMD, there is a frequent diagnosis of ADHD in the patient's history ¹². However, much of our knowledge on the relationship between RLS/PLMD and ADHD derives from studies performed on children and adolescents. Up until now there is still a paucity of data regarding the prevalence of RLS and PLMD in the adult population with symptoms of ADHD, and about their impact on quality of life of affected individuals. As a positive association between RLS and the severity of ADHD symptoms has been found in children ⁶, we believe that such conditions need to be adequately investigated in the adult population with a diagnosis with ADHD.

Alterations in circadian rhythms

Adults with ADHD commonly present delayed bedtimes and frequently show a sleep pattern consistent with a de-

layed sleep phase disorder (DSPD)¹⁴. DSPS is a circadian rhythm sleep disorder characterised by a shift in the circadian biological clock for which people fall asleep in the early morning hours. However, their sleep structure seems to be near normal¹⁵. Evidence shows that people with DSPS present a delay in the time of evening in which melatonin levels reach the threshold defined dim-light melatonin onset (DLMO), causing a subsequent delay in the sleep onset¹⁶. Since associations between delayed sleep and symptoms of hyperactivity and impulsivity have been found in both patients and controls¹⁷, a recent study examined the potential associations between other circadian abnormalities, such as alterations in the core body temperature (CBT) and skin temperature with the melatonin profiles in individuals with ADHD and matched controls¹⁸. It was found that individuals with ADHD and DSPS were characterised by large intra-individual day-to-day variability in bedtimes that was not related to the time of melatonin release in the body. Interestingly, dim-light melatonin onset, activity and temperature parameters were all delayed in ADHD + DSPS subjects, and even their profiles were not related to the onset of melatonin release. Moreover, subjects with ADHD and DSPS are characterised by alterations in core and skin temperatures¹⁸. The nature and meaning of such findings require further exploration.

Neurobiology of sleep and ADHD: suggested overlap in SNC systems and neurotransmission

It is worth to note that notwithstanding the great interest in sleep disorders affecting ADHD individuals, their impact on the severity of ADHD symptomatology and management of the disorder, the underlying mechanisms explaining such frequent overlapping conditions have not been clarified.

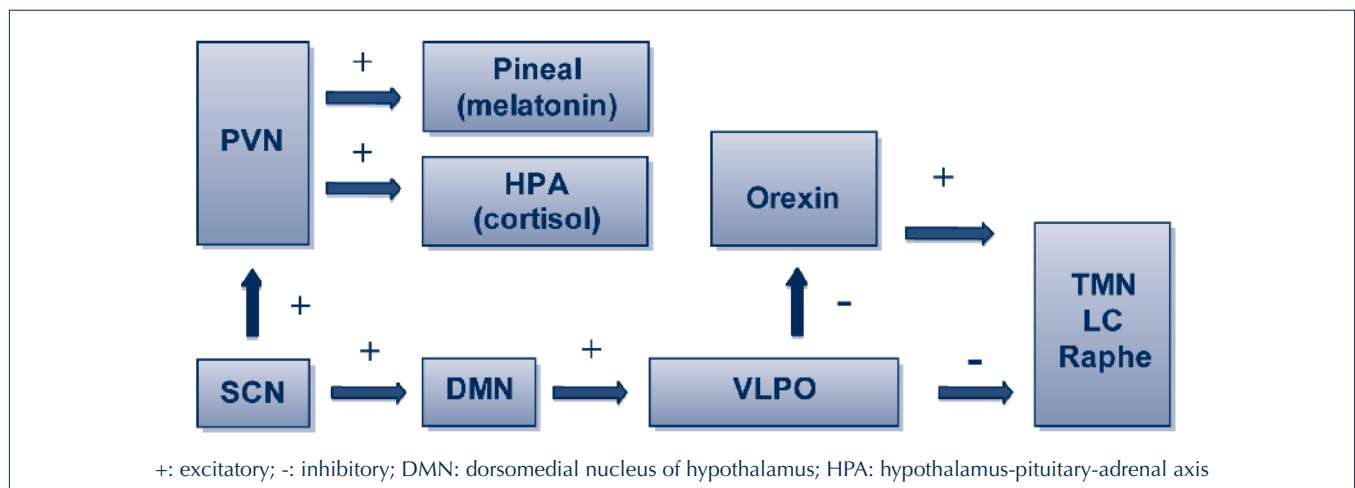
Data regarding the neuroanatomy of ADHD emphasise the role of a dysfunction in dorsolateral prefrontal (DLPFC) and dorsal anterior cingulate cortices (dACC), which are implicated in the neural circuitry underlying executive functioning. Other abnormalities have been found in the inferior parietal cortex and corticostriatal system¹⁹. Indeed, growing evidence from neuroimaging studies in the ADHD population shows the presence of alterations in the cortico-striatal network at the basis of the deficits in motor control, causing excessive moving or talking in subjects affected by the disorder¹⁹.

Sleep deprivation seems to affect the functional connectivity of prefrontal cortical areas²⁰, as well connectivity with subcortical areas²¹, with a reduction in functional connectivity between the thalamus and frontal and temporal gyri.

Cortese et al. (2008)¹² suggested disruptions in dopaminergic neurotransmission as a common brain dysfunction

at the basis of comorbid RLS and ADHD. Altered dopaminergic neurotransmission in people with ADHD has been found in the mid-brain, frontal and pre-frontal areas, whereas dopamine deficiency has been proposed in RLS²². As Owens suggested (2009)⁸, taking into account the interrelations between brain areas implicated in both ADHD and sleep disorders, it is very likely that disruption in one system may adversely affect the other. This consideration is not trivial, particularly for pharmacological management of adult ADHD. Dopamine is implicated in sleep disturbance, whereas noradrenaline plays a role in arousal. Acting by the synaptic release of dopamine and noradrenaline and by blocking their reuptake, stimulants have been considered a potential cause of insomnia and have been found to increase sleep-onset latency by more than 3-fold in children on treatment with methylphenidate, in respect with those on atomoxetine²³. However, data on adults show that methylphenidate has beneficial effects on sleep in adults with ADHD²⁴.

The findings regarding the absence of differences in sleep architecture between subjects with ADHD and controls²⁵, and of similar melatonin levels, activity and temperature parameters in people with and without ADHD¹⁸, demonstrate how challenging clarification of the intricate relationship between ADHD and sleep may be. The master clock of the circadian rhythms is housed in the suprachiasmatic nucleus of the anterior hypothalamus (SCN), a genetically based clock, which is reset by the day light cycle. The SCN drives other circadian rhythms such as that of melatonin and cortisol, a process mediated by the paraventricular nucleus at the tuberal hypothalamus (PVN). Another key brain structure for the sleep circuitry is the ventrolateral preoptic nucleus (VLPO), the neurons of which inhibit such neurons in the posterior hypothalamus as histaminergic neurons of the tuberomammillary nucleus (TMN), orexin neurons in the lateral hypothalamic area, glutamatergic neurons in the supramammillary region, serotonergic neurons at the mesencephalic raphe and noradrenergic neurons at the locus coeruleus (LC) that promote wakefulness^{26,27} as summarised in Figure 1. Sleep circadian rhythm disruption (SCRD) is a common dimension in severe psychiatric disorders such as bipolar disorder, schizophrenia and major depression, where 80% of patients report sleep abnormalities. Although ADHD has been associated with sleep abnormalities, the nature of the association between sleep and the pathophysiology of ADHD has not been clarified at a mechanistic level. At a circuitry level of explanation, there are a few studies in ADHD indicating that the circadian clock circuitry may be affected within the domains of melatonin, cortisol and consequently the HPA axis as well as dopamine (see Review by Coogan et al., 2016)²⁸. Furthermore, another vulnerable node of the circadian circuitry

**FIGURE 1.**

Diagrammatic representation of sleep circuitry. The suprachiasmatic nucleus (SCN) drives other circadian rhythms such as that of melatonin and cortisol, a process mediated by the paraventricular nucleus at the tuberal hypothalamus (PVN). Another key brain structure for the sleep circuitry is the ventrolateral preoptic nucleus (VLPO), the neurons of which inhibit such neurons in the posterior hypothalamus as histaminergic neurons of the tuberomammillary nucleus (TMN), orexin neurons in the lateral hypothalamic area, glutamatergic neurons in the supramammillary region, serotonergic neurons at the mesencephalic raphe and noradrenergic neurons at the locus coeruleus (LC) that promote wakefulness (from Saper, 2013; Rihel and Schier, 2013, mod.)^{26,27}.

in ADHD may be the noradrenergic system housed at the locus coeruleus in the midbrain.

Exploring the potential involvement of such brain circuits in adult ADHD is of great value, also considering evidence emerged from a recent study describing excessive daytime sleepiness in adults with ADHD associated to a great vulnerability to accidents, with the authors indicating the implication of dysregulation of waking system as more important than the typical lacking of attention of ADHD subjects in such adverse events²⁹.

Discussion

There is compelling evidence of the interrelation between symptoms of ADHD and disordered sleep. The increasing data show how individuals affected by both ADHD and a chronic sleep disorder are at risk of several health problems, such as mood disorders, obesity and cardiovascular disease, as well as diabetes and metabolic syndrome¹⁶. We believe that the investigation of the interplay between ADHD symptomatology, sleep difficulties and emotional dysregulation in adults with ADHD may provide important information regarding the potential existence of a different adult syndrome that is consistent with ADHD except for childhood onset³⁰⁻³¹. In fact, findings from Moffitt and colleagues (2015)³¹ demonstrated the existence of a substantial number of subjects who received a diagnosis of ADHD in adulthood and did not present signs of the disorder before age 12 years, and

without such neuropsychological deficits characterising those with a childhood onset.

Moreover, it has been pointed out that disrupted sleep in early stages of life can alter brain function by changes in the 5-HT system and in brain structures such as the dorsal striatum, ventral striatum and prefrontal cortex, causing dysfunctions affecting brain development³². Research reports an association between childhood sleeping disturbances and an increased risk for depression at 34 years old³³. In this context, the hypothesis of a common brain system underlying the relationship between ADHD, sleep, mood and emotion regulation finds support in recent data showing an association between depression and ADHD symptoms with a mediating effect on substance use³⁴. Such findings are also in line with previous research reporting sleep problems in ADHD due to comorbidities, such as affective disorders and substance abuse and dependency³⁵.

Because of the evidence regarding the occurrence of sleep problems in adults with ADHD, who frequently report a relevant emotional lability, along with the observation of the paucity of such data collected in adult population, our group is currently involved in a research exploring the clinical impact of sleep disturbances on emotional control and psychosocial impairment in individuals with ADHD, financed by the online crowdfunding platform for ADHD research ADHDFund.com (<http://www.adhdfund.com/en/>).

Not to forget that patients with ADHD have usually a poor

sleep hygiene, sometimes eating at bedtime, or chatting/using social networks until late at night, and we know that circadian clock may be influenced by several factors, such as light exposure, for late sleep timing^{17 18}.

Limitations of our study include the fact that the vast majority of findings differ according to the assessment tools used for evaluating sleep complaints. We know that studies reporting polysomnographic findings do not show consistent results²², and self-reported complaints in adults with ADHD seem to be more related to their frequent nocturnal awakenings, causing a subjective feeling of a poor sleep quality²².

However, there is no doubt about the deleterious impact that sleep deprivation may have on the quality of life of people affected by ADHD. For this reason, we would emphasise the importance of routine screening for the presence of a sleep disorder when assessing adult ADHD or during a follow-up for monitoring treatment response. Such clinical evaluation should take into account the individual's sleep habits, the presence of anxiety or mood disorder and the timing of medication.

A sleep diary and actigraphy may be useful tools for quantifying the variability of sleep patterns, and a polysomnography may be indicated if there are signs of OSA or RLS. Psychoeducation regarding sleep hygiene habits is suggested, and melatonin should also be considered because of its efficacy in reducing sleep onset delay associated or not with stimulant treatment. In light of recent evidence from anatomic and physiologic studies regarding the role of VLPO and its afferents in sleep promotion, further research may help us to define the potential utility of neuromodulation in treating disrupted circuits causing dysfunctional interactions between sleep, circadian and limbic factors, in people affected by ADHD.

Conclusion

ADHD is frequently associated with sleep disorders, and the relationship between such conditions is bidirectional, with several implications for clinical practice. Several studies support that poor sleep can worsen ADHD symptomatology, resulting in an increasing risk for accidents and health problems. Because of the overlapping symptomatology, clinicians should routinely screen for the presence of a sleep disorder when assessing ADHD or vice versa. The bidirectional relationship between ADHD and sleep also need to be considered when choosing for ADHD medications. Further studies should explore underlying neurobiological mechanisms that may account for the frequent co-occurrence of sleep disorders in people affected by ADHD in order to implement effective treatment for improving the quality of life of these patients, and blocking the negative spiral of events deter-

mined by the interaction between poor sleep and ADHD symptomatology.

Conflicts of interest

None.

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Quality of life, alexithymia, and defence mechanisms in patients affected by breast cancer across different stages of illness

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Summary

Objectives

The aim of this study was to evaluate the effect of alexithymia and defence mechanisms on the quality of life of patients affected by breast cancer at different stages of the disease.

Methods

A convenience sample of 110 patients with breast cancer was involved in the study: 41 were receiving adjuvant chemotherapy after surgery, 29 had disease-free survival in follow-up and 40 were receiving chemotherapy for metastatic disease. Quality of life, alexithymia and defence mechanisms were assessed using the following instruments: EORTC QLQ-C30-BR23, Toronto Alexithymia Scale (TAS-20) and Defense Mechanism Inventory (DMI).

Results

Compared to the other groups, patients receiving chemotherapy for metastatic disease reported poorer quality of life in several domains, more severe cancer-related and treatment-related symptoms and higher levels of alexithymia. When the effect of other potential predictors was taken into account, TAS-20 difficulty in identifying feelings was significantly related to all the EORTC functional subscale.

Conclusion

This study underlined the relevance of difficulty in emotional processing and defence mechanisms in modulating psychological adjustment in women affected by breast cancer, suggesting that these might be potential targets of psychological intervention for this population.

Key words

Psycho-oncology • Quality of Life • Alexithymia • Defence mechanisms • Breast Cancer

Introduction

A diagnosis of breast cancer substantially affects patients' quality of life and may produce various psychological consequences, such as changes in self-esteem and personal values and severe disturbances in body image. Consistent evidence has demonstrated that women with breast cancer who underwent to surgical therapy show low self-esteem, greater worries for body image and concerns about the opinions of others¹⁻³.

In the bio-psycho-social perspective, assessing quality of life in oncology is crucial to monitor the adjustment process of cancer patients to family, social and working life and, when needed, to deliver specific intervention programmes⁴. Chemotherapy has been associated with reduced quality in physical and mental domains, together with body image dissatisfaction and reduced sexual functioning^{5,6}. Furthermore, patients experiencing recurrence of disease suffered greater reduction in quality of life, particularly in symptom severity and

physical functioning, than patients with metastatic disease or primary, non-metastatic disease⁷.

Given its specific characteristics of aggressiveness and uncertainty, a diagnosis of cancer rouses anxieties of destruction, triggering extreme and archaic defence mechanisms. According to the literature, denial is the most frequent defence mechanism used by cancer patients to manage a diagnosis of breast cancer and its consequences⁸. While, on the one hand, denial clearly represents a primitive and global strategy, which often leads to gross distortion of reality, on the other hand, denial might be an adaptive strategy to protect the patient against overwhelming events and emotions⁹.

Another well-known feature of cancer patients is the difficulty in identifying feelings and in expressing emotions that is currently defined by the term "alexithymia"¹⁰. Evidence suggests that alexithymia could represent a possible risk factor for medical and psychiatric disorders. Although high levels of alexithymia have been related to

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immune system dysfunctions, lower quality of life, and anxiety and depression symptoms, the role of alexithymia in the onset and course of breast cancer patients is not fully clear^{11 12}. Indeed, some authors consider alexithymia a dynamic reaction to the illness in recently diagnosed patients, declining during subsequent phases^{13 14}. In this view, cancer patients' inhibited behaviour can be regarded as a time-limited reaction rather than a stable personality trait¹⁵. Alexithymia can be defined as a reaction to unpleasant emotional states in which individuals restrict their emotional range to mitigate painful experiences. By contrast, others suggested a distinction between primary alexithymia, as a stable personality trait, and secondary alexithymia, as a transitory reaction and a coping mechanism through which individuals avoid unpleasant emotional states by severely restricting emotional range^{16 17}. For instance, an Italian survey of women with breast cancer suggested that these patients may have something in common with so-called psychosomatic patients in terms of constrained imagination and fantasy, and difficulty in verbalising emotions¹⁸.

Our study aims to compare psychological adjustment and cancer- and treatment- related symptoms between patients with breast cancer at different stages of the disease (i.e. receiving chemotherapy for metastatic disease, receiving adjuvant chemotherapy and in disease-free follow-up). Additionally, the study seeks to investigate, whether, besides the effect of the illness stage, quality of life is also affected by alexithymia and defence mechanisms.

Materials and methods

Participants

A convenience sample was recruited among women affected by breast cancer, who were previously treated with surgical therapy, admitted to the outpatient clinic of the Cancer Surgery Department of a private hospital of Palermo. The study was approved by the clinical team. Patients were recruited on voluntary basis, were fully informed about the aims and the risks and benefits of the study and signed an informed consent sheet. Patients were divided into three groups according to disease stage: the first group consisted in patients who were receiving adjuvant chemotherapy after surgery (chemotherapy), the second group in patients in follow-up after treatment of neoplastic disease (disease-free survival/follow-up) and the third group of patients was undergoing chemotherapy treatment for metastatic disease (metastatic).

Instruments

The following instruments were administered to participants by clinical psychologists.

- *The European Organization for Research and Treatment for Cancer Quality of Life* (EORTC QLQ-C30)¹⁹: a self-report questionnaire used to study the quality of life in cancer patients. It investigates the stage of illness through nine scales: five functional scales (physical, role, cognitive, emotional, social), three symptom scales (fatigue, pain, nausea/vomiting) and a global health status scale. Moreover, it includes six single-item scales assessing symptoms typically associated with cancer and with cancer treatment, such as dyspnoea, insomnia, loss of appetite, constipation, diarrhoea and financial difficulties; there are also some items inquiring sexuality. To better understand the specific conditions of breast cancer patients, the module EORTC BR23 was also administered that covers the effects of therapy, body perception, sphere of sexuality and vision of the future in this specific population.
- *The Toronto Alexithymia Scale* (TAS-20)²⁰: a self-report questionnaire consisting in 20 items assessing alexithymia, and specifically difficulty in identifying feelings and distinguishing them from somatic sensations (F1), difficulty in describing feelings (F2) and externally oriented thinking, i.e. the tendency of individuals to focus their attention on external events rather than internal thoughts and emotions (F3).
- *The Defense Mechanisms Inventory* (DMI)²¹: a paper-and-pencil test that evaluates the defence mechanisms, classified according to five defensive styles: Turning Against Object (TAO) that means dealing with internal or external conflicts by attacking an external frustrating object; Projection (PRO) meaning projecting out unacceptable characteristics of the subjects to an external object; Principalisation (PRN) that is isolating, intellectualising and rationalising unacceptable emotions, thoughts, or behaviours; Turning Against Self (TAS), i.e. dealing with frustrating experience by turning aggression against oneself; Reversal (REV), a mechanism by which negative emotions are managed by enacting positive or neutral behaviour in response to frustrating objects, which normally evoke a negative reaction: defences such as negation, denial, reaction formation and repression are subsumed under this category.

In addition to the above, a socio-demographic questionnaire was also administered to collect socio-demographic data.

Statistical analysis

Analyses were carried out using SPSS version 18.0. Comparisons between groups were performed using one-way ANOVA and post-hoc Bonferroni and Dunnett's C tests. When appropriate, analyses were controlled for possible confounders (i.e. any variable that was associated both with

the disease stage and with any of the psychological variables) using ANCOVA. The correlation between variables was tested using bivariate Pearson's correlation. Finally, the combined effect of groups, alexithymia and defence mechanism on quality of life domains was assessed using linear regression models.

Results

Our sample consisted of 110 subjects. 41 patients were receiving adjuvant chemotherapy (Chemotherapy), 40 patients chemotherapy for metastatic disease (Metastatic) and 29 were disease-free patients in follow-up (Follow-up). The description of sample is reported in Table I. The three groups were different only in terms of education with the follow-up group that achieved higher education level (meaning more than 9 years spent at school) than the other two groups.

Mean score of the quality of life (EORTC QLQ-C30, Global Health Status QOL) scale and mean scores at the physical, role, emotional and social functional scales were significantly lower in metastatic patients than in disease-free patients. Furthermore, the former showed more severe symptoms of fatigue, nausea, pain and appetite loss than patients in follow-up. In addition, financial difficulties were less pronounced in the follow-up patients compared to the other groups (Table IIa).

Regarding the specific features of QoL in breast cancer patients, persons with metastatic cancer showed lower body image satisfaction compared to persons in the follow-up stage. This group was, obviously, less upset by side effects and hair loss than the other two groups. In addition, patients undergoing adjuvant chemotherapy ex-

perienced worse sexual functioning than the metastatic (Table IIb). For these QOL domains (i.e. social functioning) or symptoms (i.e. pain, and side effects) that were also associated with education level, analyses were repeated using ANCOVA: the effect of group remained significant and, additionally, higher education was also associated with poorer social functioning ($B = -14.582$, 95% CI -23.082 to -6.082 , $t = -3.402$, $p = 0.001$).

Alexithymia total score and, specifically, difficulty in identifying feelings (TAS-20 F1) and externally oriented thinking (TAS-20 F3) were higher in patients with progressive disease compared to the other groups, which showed similar mean scores. Furthermore, difficulty in expressing feelings (TAS-20 F2) was higher in the metastatic group only compared to the adjuvant chemotherapy group (see Table III). Since in this sample alexithymia was associated with lower education, analyses were covariates for education levels: the effect of group remained significant, but, in addition, higher education achievement was associated with lower alexithymia total score ($B = -5.988$, 95% CI -10.515 to -1.460 , $t = -2.622$, $p = 0.010$), reduced F2 difficulty in expressing feelings ($B = -8.894$, 95% CI -16.887 to -0.902 , $t = -2.206$, $p = 0.030$) and lower F3 externally oriented thinking ($B = 7.433$, 95% CI -12.323 to -2.543 , $t = -3.014$, $p = 0.003$).

We found that the TAS-20 difficulty in identifying feeling negatively correlated with all the functional scales of EORTC (physical functioning Pearson's $r = -0.419$, $p < 0.001$; role functioning $r = -0.312$, $p = 0.001$; emotional functioning $r = -0.422$, $p < 0.001$; cognitive functioning $r = -0.318$, $p = 0.001$; social functioning $r = -0.412$, $p < 0.001$). However, TAS-20 F2 difficulty in expressing feelings was only related to physical functioning ($r = -0.276$, $p = 0.004$) and

TABLE I.
Demographic features of the sample.

	Follow-up n = 29	Chemotherapy n = 41	Metastatic n = 40	Anova's F test/ chi square	p
Age mean (sd)	54.1 (10.2)	54.2 (9.2)	57.9 (9.9)	1.589	0.209
Education					
Lower education (< 8 ys) n (%)	11 (27.5%)	24 (58.5%)	17 (58.6%)	9.859	0.007
Higher education (> 9 ys) n (%)	29 (72.5%)	17 (41.5%)	12 (41.4%)		
Occupation					
Unoccupied n (%)	23 (57.5%)	25 (61.0%)	18 (62.1%)	0.172	0.918
Occupied n (%)	17 (42.5%)	16 (39.0%)	11 (37.9%)		
Marital status					
Married n (%)	35 (87.5%)	33 (80.5%)	22 (75.9%)	1.608	0.447
Unmarried n (%)	5 (12.5%)	8 (19.5%)	7 (24.1%)		

sd: Standard deviation; ys: Years of instruction.

TABLE IIA.
EORTC QLQ-C30 scores across groups.

	Follow-up	Chemotherapy	Metastatic	Crude Anova's F test (p value)	Adjusted Anova's F test (p value)	Comparison between groups
Global Health Status QoL M (sd)	76.7 (17.4)	71.4 (19.8)	63.4 (18.8)	4.253 (0.017)		M < C*
Functional scales						
Physical functioning (PF2) M (sd)	86.4 (15.2)	80.5 (15.3)	62.5 (26.9)	9.224 (< 0.001)		M < C; M < FU**
Role functioning (RF2) M (sd)	89.4 (17.9)	82.8 (20.6)	60.9 (38.8)	7.772 (0.001)		M < C; M < FU**
Emotional functioning (EF) M (sd)	79.8 (19.5)	75.1 (20.5)	60.6 (27.5)	6.530 (0.002)		M < C; M < FU*
Cognitive functioning (CF) M (sd)	83.7 (18.2)	82.7 (19.1)	82.2 (27.4)	0.044 (0.957)		
Social functioning (SF) M (sd)	91.7 (13.4)	83.1 (22.0)	74.6 (31.0)	5.037 (0.010)	8.110 (0.001)	M < FU**
Symptom scales						
Fatigue (FA) M (sd)	19.7 (24.4)	27.0 (22.8)	43.0 (28.7)	7.308 (0.001)		M > C; M > FU*
Nausea and vomiting (NV) M (sd)	3.4 (12.6)	8.3 (14.8)	19.3 (29.1)	4.251 (0.019)		M > FU**
Pain (PA) M (sd)	13.4 (16.4)	18.8 (19.4)	30.5 (30.2)	3.952 (0.024)	3.970 (0.022)	M > FU**
Dyspnoea (DY) M (sd)	10.1 (17.1)	9.6 (18.4)	26.3 (34.9)	2.900 (0.063)		
Insomnia (SL) M (sd)	15.2 (21.2)	26.6 (29.8)	31.9 (33.8)	3.204 (0.045)		
Appetite loss (AP) M (sd)	4.2 (11.1)	3.2 (9.9)	22.8 (30.9)	5.401 (0.007)		M > C; M > FU**
Constipation (CO) M (sd)	9.3 (22.7)	16.1 (24.6)	23.9 (33.0)	2.255 (0.113)		
Diarrhoea (DI) M (sd)	4.2 (13.5)	4.8 (13.9)	10.3 (21.9)	0.881 (0.419)		
Financial difficulties (FI) M (sd)	5.8 (14.8)	19.3 (24.4)	26.3 (35.9)	7.289 (0.002)		FU < C; FU < M**
* Bonferroni's test significant at 0.05 level; ** Dunnett C's test significant at 0.05 level; M: Metastatic group; C: Chemotherapy group; FU: Follow-up group; m: Mean; sd: Standard deviation.						

role functioning ($r = -0.224$, $p = 0.019$), and TAS-20 externally oriented thinking only correlated with physical functioning ($r = -0.215$, $p = 0.025$).

All the groups scored higher in the principalisation (PRN) defensive style than in the other defensive styles, with no differences between groups (see Table IV). Furthermore, turning against the object (TAO) was positively related to EORTC physical functioning (Pearson's $r = 0.273$ $p = 0.004$) and role functioning (Pearson's $r = 0.234$ $p = 0.014$), while principalisation (PRN) negatively correlated with EORTC emotional functioning (Pearson's $r = -0.217$ $p = 0.023$). Finally, considering the results of the univariate analyses, we assessed the combined effect of the groups, TAS-20 alexithymia scales, and DMI defence styles on the EORTC functional scales. Independent variables were entered in three blocks: in the first block we included stage of the illness and education level; in the second block the TAS-20 subscales that correlated with EORTC scales; in the third block the DMI defence styles that correlated with EORTC scales. As described in Table V, controlling for effect of the other psychological variables, the stage of the illness significantly predicted only the social functioning score.

In contrast, TAS-20 F1, difficulty in identifying feelings predicted lower quality of life in all EORTC domain and DMI TAO better physical functioning and role functioning. Overall, the final models explained between 8% and 26% of the variance in quality of life.

Discussion and conclusion

Although EORTC global health status (range 63.4 - 76.7) and functional domains score (range 60.6 - 91.7) show that – on average – our sample describe their quality of life as medium-high¹⁹, the different stages of breast cancer were related to specific issues in psychological adjustment and physical symptoms.

Compared to the other groups, patients receiving chemotherapy for metastatic disease showed higher global impairment, poorer quality of life in several domains and experienced more severe cancer-related and treatment-related symptoms. Specifically, after controlling for the effect of multiple testing, metastatic patients showed greater physical impairment and greater diffi-

TABLE IIB.
EORTC BR23 scores across the three groups.

	Follow-up	Chemotherapy	Metastatic	Crude Anova's F (p value)	Adjusted Anova's F test (p value)	Comparison between groups
Functional scales						
Body image (BRBI) M (sd)	86.5 (22.9)	74.2 (24.1)	72.1 (24.1)	4.013 (0.023)		M < FU**
Sexual functioning (BRSEF) M (sd)	25.9 (26.3)	15.6 (19.1)	36.7 (40.4)	4.649 (0.012)		C < M*
Sexual enjoyment (BRSEE) M (sd)	23.8 (27.4)	12.9 (21.9)	20.6 (34.9)	1.633 (0.200)		
Future perspective (BRFU) M (sd)	66.6 (30.8)	59.6 (31.0)	48.3 (28.9)	3.139 (0.053)		
Symptom scales						
Systemic therapy side effects (BRST) M (sd)	8.1 (9.3)	21.9 (14.5)	29.7 (20.3)	19.017 (< 0.001)	15.802 (< 0.001)	C > F; M > F*
Breast symptoms (BRBS) M (sd)	8.2 (14.0)	13.3 (12.8)	9.6 (12.7)	1.549 (0.220)		
Arms symptoms (BRAS) M (sd)	16.0 (20.5)	21.6 (20.9)	20.4 (20.5)	0.798 (0.454)		
Upset by hair loss (BRHL) M (sd)	0.6 (3.5)	31.5 (38.5)	25.1 (36.2)	11.399 (< 0.001)		C > F; M > F*

* Bonferroni's test significant at 0.05 level; ** Dunnett C's test significant at 0.05 level; M: Metastatic group; C: Chemotherapy group; FU: Follow-up group; m: Mean; sd: Standard deviation.

TABLE III.
Toronto Alexithymia Scale-20 scores across the three groups.

	Follow-up	Chemotherapy	Metastatic	Crude Anova's F test (p value)	Adjusted Anova's F test (p value)	Comparison between groups*
TAS-20 M (sd)	42.5 (10.9)	44.2 (11.0)	57.6 (13.3)	15.917 (< 0.001)	14.208 (< 0.001)	M > C M > FU
F1 M (sd)	39.8 (17.2)	41.5 (15.9)	55.3 (22.8)	6.772 (0.002)	6.209 (0.003)	M > C M > FU
F2 M (sd)	47.9 (19.9)	46.2 (19.8)	58.9 (22.1)	3.624 (0.030)	3.367 (0.038)	M > C
F3 M (sd)	43.2 (13.4)	46.9 (13.4)	58.5 (10.5)	12.692 (< 0.001)	10.479 (< 0.001)	M > C M > FU

* Bonferroni's test significant at 0.05 level; TAS-20: Alexithymia total score; F1: Difficulty in identifying feelings; F2: Difficulty in expressing emotions; F3: Externally oriented thinking; m: Mean; sd: Standard deviation; M: Metastatic group; C: Chemotherapy group; FU: Follow-up group.

culty in daily life activities and employment. Moreover, they reported more often than the other groups to feel anxious, worried, or depressed and to be less satisfied of their body image than patients in follow-up. All the

above are obviously related to the greater impact of cancer on family and social life. When the other personality features were taken in account, illness stage significantly predicted EORTC social functioning. This confirms the

TABLE IV.
DMI scores across the three groups.

	Follow-up	Chemotherapy	Metastatic	Crude Anova's F (p value)
TAO M (sd)	32.7 (8.1)	33.5 (9.0)	33.9 (10.5)	0.959 (0.386)
PRO M (sd)	38.4 (6.3)	38.7 (6.3)	33.1 (4.6)	0.707 (0.495)
PRN M (sd)	51.0 (6.3)	49.9 (7.5)	50.5 (6.8)	0.279 (0.757)
TAS M (sd)	37.0 (7.7)	35.0 (6.7)	36.6 (7.0)	0.883 (0.416)
REV M (sd)	41.1 (7.5)	40.2 (9.0)	41.7 (7.7)	0.294 (0.746)

TAO: Turning Against Object; PRO: Projection; PRN: Principalisation; TAS: Turning Against Self; REV: Reversal; m: Mean; sd: Standard deviation..

TABLE V.
Effect of stage of the illness, education level, alexithymia, defence style and the functional scale of EORTC.

	Predictors	B (95% CI)	Anova's F (p value)	R2	Adj. R2
Physical functioning	TAS-20 F1 DMI TAO	-0.358 (-0.586 – -0.194) 0.298 (0.293 – 1.086)	6.920 (< 0.001)	0.289	0.247
Role functioning	TAS-20 F1 DMI TAO	-2.720 (-0.631 – - 0.099) 2.904 (0.250 – 1.329)	4.795 (0.001)	0.189	0.149
Emotional functioning	TAS-20 F1	-0.460 (-0.780 – -0.328)	6.502 (< 0.001)	0.200	0.169
Cognitive functioning	TAS-20 F1	-0.318 (-0.547 – -0.145)	3.941 (0.010)	0.101	0.076
Social functioning	Group education level TAS-20 F1	0.215 (1.193 – 10.411) 0.315 (6.484 – 22.684) -0.456 (-0.758 – -0.332)	10.460 (< 0.001)	0.287	0.259

crucial impact of cancer on the interpersonal and social relationship²² as well as on sexual functioning^{23,24}. In fact, sexual functioning scores were very low across groups and, particularly, in the group receiving adjuvant chemotherapy. In addition, as expected, both patients undertaking chemotherapy for primary or metastatic disease were more upset by cancer-related (i.e. fatigue, nausea, pain, and appetite loss) and treatment-related symptoms (i.e. systemic therapy side effects and hair loss) than disease-free patients.

Self-reported alexithymia was significantly higher in the metastatic patients group than in the other two, being in the range 52-60 that is classified as "possible alexithymia"²⁰. Although several longitudinal studies have indicated alexithymia as a stable personality trait^{25,26}, some research pointed out secondary, or reactive, alexithymia in breast cancer patients²⁷ as a defensive reaction to stressful events. Furthermore, several studies on different

clinical populations, including oncologic cohorts, support the view that alexithymia is mainly a relatively stable personality trait, but to a small extent, it is susceptible to be increased under psychological distress²⁸⁻³⁰. In this perspective, and with the limitation of a cross-sectional study (i.e. lack of information about alexithymia before the onset of cancer disease), the higher score in the metastatic group might be interpreted as a reaction to the stress conveyed by the progression of the disease.

In addition to the course of the disease, TAS-20 factor 1, difficulty in identifying feelings, was significantly related to all the EORTC functional subscales, even when the effect of other potential predictors was taken into account, contributing to considerably lowering the quality of life of patients affected by breast cancer, independently of their illness stage. The finding is consistent with a previous study on cancer patients showing that, together with abnormal illness behaviour, difficulty in identifying

and describing feelings predicted cancer pain, which in turn was related to cancer status and adjustment to the disease³¹. Furthermore, another study on HIV-infected men attending a cancer screening program found that, after controlling for baseline mental health, TAS-20 F1 predicted lower physical and mental quality of life and higher levels of anxiety and depression³². It was suggested that difficulty in identifying and processing feelings tend to increase sensitivity to pain and use of maladaptive coping strategies to manage negative emotions, with important consequences on the quality of life^{31,32}. Besides difficulty in processing emotions, patients affected by breast cancer share a similar defence profile characterised by the use of defensive strategies linked to the denial cluster, such as DMI principalisation (i.e. managing unacceptable emotions and stressful experiences by isolating their intellectual meaning, including isolation and rationalisation) and, to lesser extent, reversal (i.e. dealing with unacceptable emotions and stressful experiences by giving them a neutral or positive connotation (including denial, reaction formation, and repression)). Moreover, more intensive use of principalisation was related to poorer EORTC emotional functioning, namely greater depression, anxiety and worries. This is consistent with studies claiming that women affected by breast cancer have a strong propensity to inhibit their own affection and to be emotionally over-controlled, even when this implies to give up to their personal needs^{33,34}. Furthermore, additional evidence suggests that among oncologic patients the so-called "type D (distressed) personality", characterised by negative effects and social inhibition, might be associated with impaired quality of life, higher psychological distress and increased risk for mental health problems, including somatic symptoms^{35,36}. However, caution is needed in interpreting the association between principalisation and quality of life, since in linear regression model, the effect of this mechanism became non significant once that the effect of the other variables was taken into account. On the other hand, we found a positive correlation and a positive effect of DMI turning against the object (i.e. dealing internal or external conflicts by attacking an external frustrating object, including displacement) on EORTC physical and role functioning. This seems counterintuitive, since turning against the object is considered as a primitive, immature defence that was associated with more severe psychopathology in the general population³⁷ and poor social support in women with a possible diagnosis of breast cancer³⁸. However, it could be speculated that, for some patients and in particular time of the disease course, the outward expression of anger might be less impairing than its repression (i.e. reversal) or its inward expression (i.e.

turning against self). Moreover, turning against the object might be related with higher level of energy and, indirectly, with reduced physical impairment and lower disability in performing working and daily life tasks. Unfortunately, the cross-sectional design prevents any conclusion regarding direction of causality.

In summary, this study underlined the relevance of difficulty in emotional processing and defence mechanisms in modulating psychological adjustment in women affected by breast cancer, suggesting that these might represent targets of psychological intervention for this population. However, the study has several limitations: the use of a cross-sectional design does not allow to establish whether difficulty in identifying feelings and TAO defence profile might be regarded as liability factors for poor quality of life, rather than its effects. Furthermore, the use of a convenience sample may limit, to some extent, the generalisability of the findings. Since this study relied on self-reported information, the effect of recall bias cannot be fully excluded, though the effect of TAS-20 F1 and DMI TAO were still significant after adjusting for stage of illness. Finally, it cannot be excluded that the relation between quality of life and personality factors was influenced by other non-assessed variables (including characteristics of the tumour, stressful events, social support and psychiatric comorbidities). Therefore, further investigations are warranted.

Conflicts of interest

None.

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Development, cross-cultural adaptation process and preliminary validation of the Italian version of the Nepean Dysphoria Scale

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Summary

Objectives

Dysphoria is a complex emotional state that is prevalent in the clinical setting but very vague in its precise meaning. The aim of this study was to develop and validate the Italian version of the Nepean Dysphoria Scale (NDS-I), a self-report questionnaire developed to measure the severity of dysphoria.

Methods

The NDS was translated into Italian and subjected to a cross-cultural adaptation process according to standard guidelines. The scale was then administered to 132 psychology students, together with other conceptually similar (Beck Depression Inventory II, Dysfunctional Attitude Scale – Form A, Toronto Alexithymia Scale) and conceptually different (Anxiety Sensitivity Index – 3) instruments.

Introduction

Dysphoria is a term that is becoming increasingly popular in clinical parlance, but its meaning is still surrounded by a halo of vagueness. It appears in the context of many psychiatric disorders, especially borderline personality disorder, mood and anxiety disorders and delusional disorder. In DSM-5, dysphoria is deemed to be a cardinal feature of gender dysphoria and premenstrual dysphoric disorder, but such use of the term has been criticised as perpetuating the notion that dysphoria is vague and non-specific¹.

The term “dysphoria” is usually used as a synonym for sadness or subthreshold forms of depression and to describe a mixture of negative and unpleasant emotions. Thus, dysphoria seems to denote a general dissatisfaction and consists of anxiety and depression, without any specific features^{2,3}. However, these attempts to define dysphoria do no justice to the complexity of this emotional state and, in order to better understand dysphoria, it is essential to describe its fundamental characteristics: one general and three specific^{4,5}.

Results

The NDS-I demonstrated excellent internal consistency (Cronbach $\alpha = 0.949$). Factor analysis confirmed four factors related to irritability, discontent, interpersonal resentment and surrender. There were medium to strong correlations between the scores on the NDS-I and its subscales and the scores on the Beck Depression Inventory II, and weak to medium but still significant correlations with the scores on the other instruments.

Conclusions

The NDS-I has good psychometric properties, thus supporting the validity of the original scale. Further research in clinical samples is needed to test it as a tool for routine clinical practice.

Key words

Dysphoria • Cross-cultural adaptation • Psychometric properties • Borderline personality disorder

From a general point of view, dysphoria is a mood condition that is characterised by intense distress, unease, unhappiness and/or discontent and that is experienced as an uncomfortable state, devoid of an object to which it refers, difficult to articulate and permeating the whole person. In addition, dysphoria is characterised by at least three specific emotional features: *tension*, *irritability* and *urge*. *Tension* is a state of great inner pressure underlying “bad” mood, chronic and unidentifiable unhappiness and widespread and tenacious discontent, with a tendency to give up; *irritability* refers to a state of constant and annoying restlessness, worry and unceasing anxiety; *urge* is characterised by impatience and intolerance that are subsequently experienced as an irresistible need to act, often taking the form of self-injurious behaviours, typically seen in borderline patients.

From a similar perspective, Starcevic (2007)⁶ argued that “dysphoria can be conceptualized as a process, within a dynamic definition. It is [...] characterized by intense discontent and/or unhappiness and accompanied by inner tension or a ‘driven’ feeling to resort to some action to alleviate discontent or unhappiness. Outwardly, the ten-

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sion and 'drivenness' are often manifested through irritability, hostility, anger, agitation, and a tendency to blame others for one's discontent or unhappiness; the latter can sometimes reach delusional (paranoid) proportions and/or lead to aggressive behaviour" (p. 11). In order to explore the complexity of the construct of dysphoria, Berle and Starcevic (2012)⁷ developed a self-report instrument, the Nepean Dysphoria Scale (NDS), which measures the severity of dysphoria through four subscales. After initial validation⁷, the NDS was used in a clinical sample, with findings supporting a notion that dysphoria is a complex emotional state with both non-specific and specific relationships with related domains of psychopathology⁸.

The aims of this study were to highlight the process of developing the Italian version of the NDS (NDS-I) and test its psychometric properties. With good indicators of reliability and validity, the NDS-I could be used in Italy to further study the proposed conceptualisation of dysphoria.

Method

Participants

In order to replicate the original validation of the NDS, first and second year psychology students from the University of Urbino (Italy) and University of Bologna, Cesena Campus (Italy) were selected. The sample consisted of 132 students, 99 (75%) of whom were female. Their mean age was 21.44 years ($SD = 4.66$). After describing the study to the participants, written informed consent was obtained. The study was approved by the local ethics committees.

Measures

A total of 5 self-report instruments were administered to the participants. The key instrument was the NDS-I. The original NDS is a questionnaire developed by David Berle and Vladan Starcevic at the Sydney Medical School – Nepean, University of Sydney, Australia⁷. It consists of 24 items, which are rated for frequency on a five-point Likert scale, from 0 ("not at all") to 4 ("always"). A total score is obtained by calculating the mean of the scores on all the items. The NDS also provides separate scores on four subscales of dysphoria, as follows: *irritability*, *discontent*, *surrender* and *interpersonal resentment*. Every item (except for items 2, 4, 13 and 24) starts with the phrase: "Have you felt..." and is followed by a specific feeling (e.g., "...discontent?", "...on edge?", "...cranky?"). The validity of the NDS was tested in 134 first-year psychology students (mean age = 19.43 years) in Australia. It was administered in association with three conceptually related instruments (Beck Depression Inventory II [BDI-II], Dysfunctional Attitude Scale – Form A [DAS] and

Toronto Alexithymia Scale [TAS]) and one conceptually unrelated scale (Anxiety Sensitivity Index [ASI]). Results showed that the 24-item NDS had an excellent internal consistency (Cronbach $\alpha = 0.91$); there were medium to strong correlations between the scores on the NDS and its subscales and depressive symptoms as measured by the BDI-II (r s 0.36 to 0.65) and weaker, but still significant, correlations with the scores on the DAS (r s 0.21 to 0.45), TAS (r s 0.24 to 0.38) and ASI (r s 0.23 to 0.36)⁷.

To replicate the original validation of the NDS and examine the convergent and divergent validity of the NDS-I, Italian versions of the same instruments were administered to the Italian participants: BDI-II, DAS, TAS and the Anxiety Sensitivity Index – 3 (ASI-3, a more recent and psychometrically more sound version of the ASI). We expected strong positive correlations between scores on the NDS-I and scores on the measures of depression (BDI-II) and cognitive vulnerability to depression (DAS) because of the important conceptual links between dysphoria and depression. We also expected similar correlations between scores on the NDS-I and those on the measure of alexithymia (TAS) due to a well-documented relationship between alexithymia and depression⁹⁻¹² and conceptual overlap between emotional complexities (e.g., difficulties in emotional articulation) inherent to both dysphoria and alexithymia. In contrast, we expected weaker correlations between scores on the NDS-I and those on the ASI-3 due to a much closer relationship between predisposition to anxiety and panic as well as to anxiety disorders.

The BDI-II measures the severity of depression. This instrument consists of 21 items rated on a four-point scale from 0 to 3, according to increasing intensity. The total score is obtained by adding up item scores. The BDI-II has shown very good internal consistency (Cronbach $\alpha = 0.91-0.93$), excellent short-term test-retest reliability ($r = 0.93-0.96$) and good convergent and criterion validity¹³⁻¹⁵. The Italian version of the BDI-II has been shown to have excellent psychometric properties¹⁶.

The DAS evaluates beliefs denoting a cognitive vulnerability to depression. Originally developed by Weissman and Beck¹⁷ and consisting of 100 items, the DAS was reconfigured into two 40-item versions (i.e., DAS-A and DAS-B) by Weissman (1979; unpublished thesis). Previous research has essentially relied on the DAS-A; as a result, most research on the psychometric properties of the DAS has been conducted with the DAS-A¹⁸. Each item is rated on a seven-point Likert scale (7 = fully agree; 1 = fully disagree) and total score is the sum of the scores on each item. It has been shown that the DAS-A has excellent internal consistency (Cronbach $\alpha = 0.89-0.94$), good six-week test-retest reliability ($r = 0.73$) and adequate convergent and divergent validity^{19 20}. The Italian version of the DAS-A differs from the original in terms of

the items being rated on a five-point Likert scale (5 = fully agree; 1 = fully disagree); it has also demonstrated very good psychometric properties ²¹.

The TAS consists of 20 items that assess the difficulties in the awareness and identification of emotions. Subjects respond on a five-point Likert scale from 1 (strongly disagree) to 5 (strongly agree). Factor analysis of the TAS revealed three factors: 1) difficulty in identifying feelings; 2) difficulty in describing feelings; 3) externally oriented thinking. The TAS has demonstrated good internal consistency (Cronbach α = 0.79-0.82) and adequate three-week (r = 0.77) and three-month (r = 0.74) test-retest-reliability; it has also proved to have good levels of convergent, divergent and concurrent validity ²²⁻²⁴. The Italian version of the TAS was reported to have very good psychometric properties ²⁵.

The ASI-3 contains 18 items and measures the fear of anxiety-related symptoms. Each item is rated on a five-point Likert scale from 0 (very little) to 4 (very much) and total score is obtained by adding up item scores. Confirmatory factor analysis revealed a three-factor model: physical, social and cognitive concerns ²⁶. The factorial validity of the ASI-3 was stronger than that of the original ASI. Cronbach's alpha values for each of the ASI-3 subscales ranged between acceptable and good (the range for physical concerns was 0.73-0.90, for cognitive concerns it was 0.77-0.93 and for social concerns the range was 0.69-0.89) ²⁶. Studies also suggest very good convergent, divergent and criterion validity of the ASI-3 ²⁶. The Italian version of the ASI-3 has shown excellent psychometric properties ²⁷.

Procedure involving the translation and validation of the NDS

This was a two-stage procedure. Stage 1 involved the Italian translation and cross-cultural adaptation of the NDS. Stage 2 was a preliminary validation of the NDS-I.

Stage 1. Translation and cross-cultural adaptation

The NDS was translated into Italian and subjected to a cross-cultural adaptation process, according to the standard guidelines for self-report measures ²⁸. At the beginning, two translators with the target language (Italian) as their mother tongue translated the NDS from the original language (English) to the target language (*forward translation*). The two translators had different profiles: one with a background in clinical psychology to ensure equivalence from a measurement perspective, the other with no background in clinical psychology to ensure equivalence from a semantic perspective. The translators worked independently of each other, writing down ambiguous phrases or uncertain meanings and producing two different Italian versions of the NDS: T1 and T2.

Subsequently, the two translators compared their translations with the goal of reaching a consensus (in the presence of an observer). A synthesis of T1 and T2 was produced and one joint translation was created: T-12 (*synthesis of the translations*).

Completely blind to the original NDS, two translators with the original language (English) as their mother tongue translated the T-12 back into English (*backward translation*). The two translators were not aware of the concepts examined by the questionnaire, and their background was not in clinical psychology. Again, the translators worked independently from each other, highlighting conceptual errors or unclear words in the T-12 and producing two different English versions: BT1 and BT2.

Next, an expert committee, composed of psychiatrists, clinical psychologists, methodologists, language professionals and translators involved in the cross-cultural adaptation process (forward and backward translators), revised all the materials produced (T1, T2, T-12, BT1, BT2) to achieve semantic, idiomatic, experiential and conceptual equivalence between the source and target versions, thus creating a pre-final version of the translation (*expert committee review*).

A pre-final version was then administered to a group of 34 second-year psychology students (mean age = 21.91 years) of the University of Urbino, Italy (*pre-testing*). Students were also asked to write comments on comprehensibility and clarity of items and provide any suggestions for improving item presentation.

Finally, after a careful consideration of the comments made by the students during pretesting, the final version was created (NDS-I) and submitted to the authors of the NDS for final approval (*final appraisal*).

Stage 2. Establishing psychometric properties

Analysis of the psychometric properties of the NDS-I first entailed use of a parallel analysis with the syntax of O'Connor ²⁹ rather than the Kaiser's criterion (eigenvalues > 1) or Scree plot method. This procedure has been chosen for two reasons. First, we intended to replicate the process used in the original validation of the NDS. Secondly, there are significant limitations of Kaiser's criterion and Scree plot method ³⁰⁻³².

In order to decide how many factors to retain, a parallel analysis was conducted through a syntax program called "rawpar.sps" that runs on SPSS software. This procedure extracts eigenvalues from random data sets based on the number of cases and variables, and these are then compared with the actual eigenvalues derived from a regular factor analysis ²⁹. A good practice is to specify the desired percentile (usually 95th) and the number of random data sets. Factors or components that are to be retained (i.e., the eigenvalues derived from actual data) should

be greater than the eigenvalues from random data at the 95th percentile, based on the number of random data sets generated²⁹.

In the SPSS syntax for parallel analysis, the number of cases (i.e., 132 in our sample), the number of variables (i.e., 24 items of the NDS), the number of random data sets generated (100) and the percentile (95) were then entered. Subsequently, the factor analysis was repeated with the principal axis factoring solution, promax rotation and the number of factors constrained to four. A value of at least 0.3 was set as the criterion for factor loading. Item-total correlations and the coefficient of internal consistency (Cronbach's α value) for the whole NDS-I and for each factor were also calculated. Convergent and divergent validity of the NDS-I were examined by means of Pearson's parametric and Spearman-Brown non-parametric correlations between the scores on the NDS-I and its subscales and scores on the other self-report instruments. All statistical analyses were conducted using SPSS for Windows, version 19.0.

Results

Cross-cultural adaptation process

Some difficulties emerged during the cross-cultural adaptation process that were mainly due to the colloquial nature of certain items. In fact, during the forward translation the translators did not agree on two NDS items, so in both cases a clarification by the authors of the NDS was necessary. Item 3 ("Have you felt that others have messed up things for you") was translated in two ways: with a phrase indicating a relatively benign meaning (corresponding to "complicating things") and with a phrase indicating a more serious meaning (corresponding to "spoiling everything"). The authors of the NDS clarified that the meaning of the item was neither catastrophic nor too "mild", but rather that it pertained to a sense of being prevented from doing something important in life or from just moving on with life because of the actions taken by others. Therefore, the translators agreed to translate item 3 with a phrase indicating a more "intermediate" meaning (corresponding to "blowing up things"). Item 21 ("Have you felt miserable?") was also translated in two ways: with an adjective indicating a generic meaning (corresponding to "wretched") and with an adjective indicating a specific meaning – in use in Scotland, Australia and New Zealand (corresponding to "mean/stingy"). The authors of the NDS clarified that the meaning of the item broadly corresponded to profound emotional suffering, distress and/or unhappiness and the translators agreed to translate it with an adjective indicating a more shared meaning (corresponding to "depressed"). Similar issues emerged during pretesting. In fact, in the

final comments many subjects pointed out that item 2 ("Have things got the better of you?") was not clear. So, a change in the phrase was needed, but in order to avoid interpretation of the item that would be semantically too far from the original, a clarification was requested again. The authors of the NDS proposed the following examples in English as a substitute for item 2: "Have you felt that people or responsibilities wore you out (or over-ran you, exhausted you or used up all of your energy and resources)?", "Have you felt like you have nothing left to offer?" (or "Have you felt like you have nothing left to offer because you were exhausted by 'things' in your life?") and "Have you felt that coping with ordinary things is too hard?". The translators carefully evaluated the alternatives, and agreed not to change the colloquial form "get the better of" (also in use in Italy and equally effective), but replace "things" with a more specific wording (corresponding to "events of life"). Moreover, some participants suggested that item 21 lacked clarity and emphasised that the adjective "depressed" had become too popular in the contemporary language and had lost its depth in clinical terms. The translators took this into account, but decided this time not to change anything in the translation, because any alternative adjective would not have the same broad meaning of the original wording ("miserable").

Factor analysis

Our study confirmed the results of the original parallel analysis, i.e., we also found that the first four eigenvalues derived from actual data of the factor analysis were greater than the first four 95th percentile random data eigenvalues. Therefore, four factors were retained. Subsequently, factor analysis was carried out again with the number of factors forced to four: the residual correlation matrix revealed that four-factor solution was appropriate. The pattern matrix showed cross loadings with small differences (less than 0.1) between loadings on each factor for two items: item 4 ("Has it been hard to relax?") had loadings of 0.36 and 0.42 on the first and second factors, respectively, while item 8 ("Have you felt as if nothing seemed right?") had loadings of 0.37 and 0.43 on the second and fourth factors, respectively. The two items were assigned to the factors with higher loadings, as their removal changed internal consistency of the total scale only minimally (i.e., Cronbach alpha for the full, 24-item NDS-I was 0.949, it was 0.948 when item 4 was removed and 0.946 when item 8 was removed). This is in accordance with the item-analysis criterion for item retention/deletion stipulated in the recommendations for best practices in using exploratory factor analysis in scale development³³.

Item means, standard deviations, item-total score correlations and pattern matrix of the principal axis factoring so-

lution are reported in Table I. The proportion of variance accounted for by the four-factor solution was greater for the NDS-I (58.63%) than it was for the NDS (46.57%). However, unlike the NDS, more variance in the NDS-I was accounted for by the factor "interpersonal resentment" than by the factor "surrender". The four factors corresponded to the subscales of the NDS-I and components of dysphoria.

Correlations among the NDS-I factors reported in Table

II were strong and ranged between 0.57 and 0.70. This suggests that factors are representative of the underlying construct (dysphoria).

Comparisons between factor structures of the NDS-I and NDS showed that 15 (62.5%) scale items loaded on the same factors in the two studies ("common items"). Among these, 7 loaded on factor 1 ("Irritability"), 4 loaded on factor 3 ("Interpersonal Resentment"), 3 loaded on factor 2 ("Discontent") and 1 loaded on factor 4

TABLE I.

Item means, standard deviations, item-total score correlations and pattern matrix of principal axis factoring solution with Promax rotation constrained to four factors.

	Mean	SD	Item-total score correlation	Factor*			
				1	2	3	4
Proportion of variance accounted for (%)				45.45	6.26	4.19	2.73
13. Have you been losing your temper?	0.89	0.95	0.50	0.85			
16. Have you felt cranky?	1.86	1.03	0.68	0.78			
11. Have you felt on edge?	1.80	1.18	0.71	0.74			
7. Have you felt that you might lose control and hit someone?	0.84	1.17	0.60	0.66			
18. Have you been feeling angry towards other people?	1.37	1.10	0.64	0.62		0.44	
20. Have you felt easily annoyed by what others say or do?	1.80	1.07	0.62	0.56			
14. Have you felt that everything was too much?	1.27	1.18	0.80	0.55			
24. Has everything been getting on your nerves?	1.06	1.05	0.73	0.53			
5. Have you felt impatient with other people?	1.59	1.22	0.56	0.43		0.30	
1. Have you felt discontent?	1.52	0.92	0.54		0.96		
19. Have you felt unhappy?	1.42	1.07	0.70		0.76		
21. Have you felt miserable?	1.26	1.04	0.74		0.75		
2. Have things got the better of you?	1.17	1.03	0.53		0.52		
22. Have you felt overwhelmed by life?	0.95	1.13	0.74		0.52		0.36
4. Has it been hard to relax?	1.98	1.19	0.63	0.36	0.43		
23. Have you felt that people are against you?	0.88	1.02	0.65			0.81	
9. Have you felt that people shouldn't be trusted?	1.63	1.17	0.54			0.81	
15. Have you felt that people are not fair towards you?	1.11	1.02	0.77			0.72	
3. Have you felt others have messed up things for you?	1.03	1.07	0.50			0.62	
12. Have you felt that people don't care about you?	1.20	1.12	0.70			0.54	
10. Have you felt like giving up?	1.02	1.19	0.69				0.96
17. Have you felt like you couldn't cope anymore?	1.16	1.12	0.75				0.57
8. Have you felt as if nothing seemed right?	1.42	1.17	0.78		0.37		0.43
6. Have you felt that you achieved nothing?	1.64	1.17	0.55				0.41
Cronbach α value				0.90	0.87	0.85	0.86
Mean				1.39	1.38	1.17	1.31

* Factor loadings of at least 0.30 are reported.

Factor 1: "Irritability"; **Factor 2:** "Discontent"; **Factor 3:** "Interpersonal resentment"; **Factor 4:** "Surrender".

Total scale Cronbach α = 0.949; total scale mean = 1.19, SD = 0.68.

("Surrender") in both studies. Common items constituted 80% of Interpersonal Resentment items, 78% of Irritability items, 50% of Discontent items and 25% of Surrender items in the NDS-I.

Other psychometric properties

The Cronbach α value for the full 24-item NDS-I was 0.949, while it was 0.904 for the first, 0.868 for the second, 0.851 for the third and 0.865 for the fourth factor, respectively. These values demonstrate an excellent internal consistency (Table I). Item-total score correlations (Table I) were all adequate, since they were above the usual cut-off of 0.30 (the lowest value was 0.50), suggesting that all items of the NDS-I are related with the content of the whole scale ³⁴.

The correlations between scores on the NDS-I and its subscales and scores on the other self-report instruments are reported in Table III. All correlation coefficients were statistically significant. The NDS-I total score and scores on its subscales showed medium to strong correlations with BDI-II scores (r s ranging from 0.51 to 0.67). The correlations with TAS-20 total scores (r s ranging between 0.38 and 0.49), DAS scores (r s ranging between 0.21 and 0.36) and ASI-3 scores (r s ranging between 0.32 and 0.43) were weaker, but still noteworthy.

The final version of the NDS-I consists of 24 items, which are rated for frequency over a 1-week period preceding its administration on a five-point Likert scale, from 0 to 4. As in the NDS, a brief guide is provided to standardise responses: score 0 means "not at all"; score 1 denotes occasional frequency defined as "1 day for up to 3-4 hours"; score 2 corresponds to "often", defined as "up to 4 days for up to 3-4 hours"; score 3 means "very often" or a frequency of "every day for up to 3-4 hours"; score 4 denotes "always" or "every day, most of the time". Total score is calculated by determining the mean of the scores on all the items. Like the NDS, the NDS-I provides separate scores on four subscales, which are also the main components of dysphoria, i.e., irritability, discontent, interpersonal resentment and surrender.

Discussion

We have described the process of translating the NDS into Italian to create the NDS-I. This process was in accordance with the cross-cultural adaptation principles and involved several stages. We have shown how to successfully address the problems and complexities arising in the course of translating instruments for use in mental health research, which is one of the strengths of the present study and has implications for similar endeavours by other research teams working cross-nationally. In the sample of Italian university students, the NDS-I

had a 4-factor structure, similar to the structure reported for the NDS. This is noteworthy, considering the cultural differences between Italy and the country in which the NDS was developed (Australia). In addition, the factors identified are consistent with the theoretical concepts of dysphoria proposed by Starcevic (2007) ⁶ and Rossi Monti (2012) ⁴. With regards to the scale items and factors, the greatest concordance between the NDS-I and NDS was for "Interpersonal Resentment" and "Irritability", followed by "Discontent". This suggests that these factors might be the core elements of dysphoria and that its externalising components (interpersonal resentment and irritability) might be more conceptually sound. Lower concordance rates between the NDS-I and NDS for internalising aspects of dysphoria (discontent and surrender) call for scale refinement, but they do not necessarily undermine the internal coherence of the NDS-I and conceptual validity of dysphoria because of the strong correlations between all NDS-I factors (Table II).

The NDS-I was found to have an excellent internal consistency (total scale Cronbach α = 0.949), similar to that reported for the NDS (total scale Cronbach α = 0.91). In addition, moderate to strong item-total scale correlations for all scale items suggest that the NDS-I, like the NDS, is conceptually coherent.

The strength of the correlations between the scores on the NDS-I and its subscales and the scores on the BDI-II, TAS and DAS indicates convergent validity of the NDS-I. The strongest correlations were between the scores on the NDS-I and its subscales and the scores on the BDI-II, suggesting that dysphoria is related to the symptoms of depression, but not identical with the concept of depression. The weaker but still significant correlations between the scores on the NDS-I and its subscales and the scores on the ASI-3 are in accordance with our expectation, but they do not support a clear differentiation between dysphoria and anxiety. This suggests the need to include other anxiety measures in further studies of the psychometric properties of the NDS to better delineate the relationship between dysphoria and anxiety. For example, Starcevic et al.'s most recent study (2015) ⁸ revealed a significant pre-

TABLE II.

Factor correlation matrix of the Nepean Dysphoria Scale, Italian version (NDS-I).

Factor	1	2	3	4
1. Irritability	1.00	0.62	0.68	0.60
2. Discontent		1.00	0.64	0.70
3. Interpersonal resentment			1.00	0.57
4. Surrender				1.00

TABLE III.

Correlations between scores on the NDS-I and its subscales and scores on other measures.

		Pearson's Correlations								
		1.	2.	3.	4.	5.	6.	7.	8.	9.
Spearman-Brown Correlations	1. NDS-I Irritability	1	0.68 [†]	0.75 [†]	0.65 [†]	0.90 [†]	0.37 [†]	0.65 [†]	0.21 [†]	0.41 [†]
	2. NDS-I Discontent	0.68 [†]	1	0.70 [†]	0.77 [†]	0.89 [†]	0.39 [†]	0.59 [†]	0.34 [†]	0.44 [†]
	3. NDS-I Interpersonal resentment	0.76 [†]	0.68 [†]	1	0.63 [†]	0.88 [†]	0.38 [†]	0.53 [†]	0.26 [†]	0.38 [†]
	4. NDS-I Surrender	0.62 [†]	0.75 [†]	0.62 [†]	1	0.82 [†]	0.32 [†]	0.64 [†]	0.36 [†]	0.40 [†]
	5. NDS total score	0.90 [†]	0.88 [†]	0.87 [†]	0.79 [†]	1	0.43 [†]	0.68 [†]	0.32 [†]	0.47 [†]
	6. ASI-3	0.36 [†]	0.42 [†]	0.37 [†]	0.33 [†]	0.43 [†]	1	0.46 [†]	0.56 [†]	0.56 [†]
	7. BDI-II	0.60 [†]	0.63 [†]	0.51 [†]	0.62 [†]	0.67 [†]	0.44 [†]	1	0.45 [†]	0.51 [†]
	8. DAS	0.21 [†]	0.31 [†]	0.22 [†]	0.31 [†]	0.30 [†]	0.51 [†]	0.36 [†]	1	0.41 [†]
	9. TAS – total score	0.40 [†]	0.46 [†]	0.38 [†]	0.41 [†]	0.48 [†]	0.58 [†]	0.48 [†]	0.37 [†]	1

* $p < 0.05$; [†] $p < 0.01$.

Pearson's correlations are above the diagonal, Spearman-Brown correlations are below the diagonal.

NDS-I: Nepean Dysphoria Scale, Italian version; ASI-3: Anxiety Sensitivity Index – 3; BDI-II: Beck Depression Inventory II; DAS: Dysfunctional Attitude Scale – Form A; TAS: Toronto Alexithymia Scale (20-item version).

dictive relationship between the somatic and cognitive negative effects of anxiety and the “Discontent” factor. This is a further evidence of the usefulness of confirmatory analysis of the NDS-I scale.

This study has a number of limitations. Firstly, our sample was non-clinical, which limits generalisations of the findings and their applicability to clinical populations. Therefore, there is a need to further validate the NDS-I in treatment-seeking individuals with a variety of conditions (e.g., borderline personality disorder, depressive disorders, bipolar disorders, posttraumatic stress disorder, generalised anxiety disorder and psychotic disorders) in which dysphoria has been hypothesised to play a role. Secondly, considering that test-retest reliability and divergent validity of the NDS-I have not been examined and confirmed, the NDS-I should undergo further testing of its psychometric properties.

In conclusion, the NDS was carefully translated into Italian and preliminary validation of the NDS-I replicated to a large extent the results of the preliminary validation of the NDS. This confirms solid psychometric properties of the instrument and allows use of the NDS-I in Italy to measure the severity of dysphoria. The adoption of the NDS/NDS-I is expected to improve understanding of the construct of dysphoria, but there is still a need for further studies of the NDS-I in clinical samples similar to the clinical investigation already performed with the NDS⁸.

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Conflicts of interest

None.

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Development and validation of an abridged version of the Social Provisions Scale (SPS-10) in Italian

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Summary

The Social Provisions Scale-10 item (SPS-10) is a shortened version of the 24-item Social Provisions Scale developed by Cutrona and Russell in 1987. The SPS-24 originally consisted of six subscales that measure the availability of social support: emotional support or attachment, social integration, reassurance of worth, material help, orientation and opportunity for nurturance. Each subscale comprises four items, two formulated positively and two negatively, for a total of 24 items. The SPS-10 retains the original subscales, except for opportunity for nurturance, and includes only negatively worded items. The aim of this paper is to present the validation of the Italian version of this instrument. The study population consisted of 483 pregnant Italian women with a mean age of 33 years recruited from two large hospitals of northwestern Italy from January 2010 to February 2012 during scheduled routine follow-up visits or when they attended the antenatal classes. The SPS-10 showed a strong concurrent validity with the original SPS-24 scale ($r = 0.896$). All its items were highly correlated with the total score and its internal consistency was high (Cronbach's $\alpha = 0.809$).

The construct validity was investigated using a two-level confirmatory factor analysis (CFA). This analysis confirmed that the items conform to a structure consisting of 5 first-level dimensions (subscales) and one second-level dimension that measures the overall perception of social support. The CFA model had excellent goodness of fit to the data.

The total score of SPS-10 was significantly associated with the presence of antenatal depressive symptoms (ADS) in a logistic regression model, and this association was stronger than that found between the total SPS-24 and ADS. Overall, these analyses suggest that the SPS-10 is a reliable and valid instrument for measuring the availability of social support with the advantage of shorter administration time compared with the original SPS-24 scale. It is therefore ideal for administration in busy clinical settings for screening purposes and in epidemiological studies.

Key words

Pregnancy • Social support • Attachment • Depression

Introduction

Maternity is condition in which new mothers experience a loss of routines and prior identity, have to face a number of challenges and have to acquire new skills. Social support may ease this transition through exposure to models already experienced and contact with others who share values and priorities associated with motherhood and may provide positive reinforcement^{1,2}. Many studies have reported that the lack of social support, i.e. lack of emotional and practical help from the partner and family members, is strongly associated with depressive symptoms both during pregnancy or/and in the postpartum period and with negative maternal emotional well-being³⁻⁵. Thus, early identification of lack of social support during pregnancy, mainly if associated with depressive symptoms, may orient professionals on psychosocial interventions to prevent perinatal disorders. In the framework of a large Italian project aimed to pre-

vent depression in women during pregnancy and in the postpartum period, we carried out a broad assessment of the risk factors of depression. Among the available instruments to assess social support, we choose the Social Provision Scale (SPS) by Cutrona & Russell⁶ that includes six subscales based on social needs identified by Weiss in 1973: attachment, reassurance of worth, reliable alliance, social integration, guidance, opportunity for nurturance. The SPS has been shown to have excellent psychometric properties in several studies^{7,8} carried out in different fields, which suggest that the perception of social support is one of the best predictors of mental distress and quality of life.

Notably, in a study of first-time mothers, Cutrona² found that the provisions of reliable alliance, reassurance of worth, social integration and guidance were predictive of postpartum depression. Women without these provisions were more likely to become depressed after their pregnancy.

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In the original validation study⁶, the instrument showed good concurrent validity with several instruments: the satisfaction with support received, the size of social network and support behavior and attitudes towards the support. However, this scale had a weak correlation with social desirability $r = 0.12$. As to its construct validity, the instrument was negatively related to the Beck Depression Inventory⁹ and neurosis as measured by the Eysenck Personality Inventory. The Social Provisions Scale (SPS) has been translated and validated in Quebec by Caron¹⁰ on a sample of 790 people. The internal consistency of the instrument was excellent ($\alpha = 0.96$) and for the subscales it varied between 0.73 and 0.88. The temporal stability (test-retest reliability) of the instrument was very good ($r = 0.86$). Factor analyses carried out in the population of Quebec confirmed the multidimensional structure of the instrument.

The SPS has been used in many studies in Canada in the general population¹¹, in low-income people, in people with schizophrenia and their families, in people with a previous suicidal attempt and families with children in the nursery school⁷. These studies showed that social support measured with this scale was one of the best predictors of psychological distress and quality of life.

The aim of this paper is to illustrate the validation process of an abridged version of that scale (SPS-10) in Italian, obtained by reducing it from 24 items to 10 items to produce a reliable and valid instrument for measuring the perceived availability of social support.

Methods

Participants

The study population consisted of pregnant Italian women recruited from two large hospitals of northwestern Italy from January 2010 to February 2012. Women were assessed on a single occasion during scheduled routine follow-up visits or when they attended antenatal classes. In the first case, women were invited to an interview, and in the second case women filled out the study instruments after a group intervention in which they received information about postpartum depression. The study procedures were approved by the Ethics Committee of Niguarda-Ca' Granda Hospital, Italy.

Measures

The study assessments included an ad hoc form to collect socio-demographic information, distressing life events, past psychiatric history and past psychological and/or pharmacological treatment and family history for psychological problems and psychiatric disorders and pregnancy-related variables.

In addition, the Social Provisions Scale (SPS), the Edinburgh Post-natal Depression Scale (EPDS) and Beck Depression Inventory, Short Form (BDI-SF) were administered. The SPS⁶ measures the perception of social support and consists of 24 items expressed as statements, with responses coded on a 4-point scale from strongly disagree (= 1) to strongly agree (= 4). The factor structure was examined in the original paper⁶ and consisted of six first-level factors (attachment, social integration, reassurance of worth, reliable alliance, guidance, opportunity for nurturance) and one second-level general factor. Each factor includes 4 items, 2 with a negative and 2 with a positive formulation. This structure was subsequently confirmed by Perera¹² using a bi-factor structural equation model. The instrument was shown to have a good convergent and discriminant validity. The six factor scores range from 4 to 16 and the total score ranges from 24 to 96. Higher scores denote better perceived support.

The Italian version, translated from the English version, was initially tested by our group in a small pilot sample of women to examine its face validity. Based on the suggestions that emerged during the administration of the instrument, the anchor points of the scale were defined as false (= 1) or true (= 4) and the formulation of some items was improved to make them more comprehensible.

The EPDS¹³ is the most widely used measure of post-partum depression symptoms and is commonly used as a screening tool for prenatal depression symptoms as well¹⁴. The 10 EPDS items do not directly correspond to DSM criteria. They do not include somatic depressive symptoms (appetite change and fatigue) psychomotor agitation/retardation or reduced concentration. Participants based ratings on their experiences and feelings over the previous week. Each item is scored on a 4-point Likert scale from 0 to 3 with possible total scores ranging from 0-30. A higher score indicates higher reported frequency or severity of symptoms.

A systematic review¹⁵ has confirmed that the screening accuracy of the EPDS in diagnosing depression during pregnancy is satisfactory and that the EPDS can be recommended for use for this purpose.

The EPDS was validated in Italian and shown to have a good internal consistency (Cronbach $\alpha = 0.747$); a sensitivity of 0.556 and a specificity of 0.989 were associated with the cut-off score of 11/12¹⁶.

The BDI⁹ is one of the most widely used self-rating scales for measuring depression. Beck and Steer proposed that this scale could be divided in two subscales: cognitive-affective (items 1 to 13) and somatic-performance (items 14 to 21). In the present study, we used the cognitive-affective subscale alone (the so-called BDI short-form (BDI-SF)) to assess depression. Each answer is scored from 0 to 3. Higher total scores indicate more severe depressive symptoms.

Development of the SPS-10

The short version was obtained by retaining five of the six original SPS subscales: emotional support (attachment), social integration, reassurance of worth, material support (reliable alliance) and guidance, which includes advice and information. In the original instrument, each of these scales comprises 4 items - 2 with a positive and 2 with a negative formulation. We kept only negatively worded items because we found that they allow to better capture the lack of social support, while items with a positive formulation elicit stereotypical responses. The total score ranges from 10 to 40. Item scores are inverted so that the higher the score, the stronger the perceived provision of social support.

Consistent with Caron⁷, the subscale that measures the need to feel useful (opportunity for nurturance) was not retained because this dimension of social provisions measures the support provided rather than the support received and because previous studies showed that this dimension has a weaker association with mental health compared with the other subscales. The SPS-10 is provided in the appendix.

Statistical analyses

Descriptive statistics of the total score of the SPS-10 and of the SPS-24 were calculated. To determine the concurrent validity of SPS-10, we calculated Pearson's correlations between each of the 10 items of the SPS-10, its total score and score of the original 24-item scale. In order to verify the fidelity of the SPS-10, the internal consistency was assessed by Cronbach's alpha and compared with that of the original 24 item scale. Then, to investigate the construct validity of the scale, a two-level confirmatory factor analysis of items was carried out.

Each item was specified to load onto only the factor it was designed to measure, with correlations among the six factors freely estimated. The six factors were specified to index a higher-order general factor, in line with previous research^{6,12}. In order to test the goodness of fit of the model, three approximate fit indices were considered: comparative fit index (CFI) and Tucker-Lewis index (TLI), > 0.900 and 0.950 for acceptable and excellent fit, respectively; and root mean square error of approximation (RMSEA), < 0.050 and 0.080 for close and reasonable fit, respectively¹⁷.

Bivariate and multivariate logistic regression models were used to analyse the association between antenatal depressive symptoms (ADS) and SPS total scores and subscale scores. ADS were defined as an EPDS score ≥ 12 or a BDI-SF score ≥ 9 , and/or a score > 0 on item EPDS item 10 or BDI-SF item 7, that assess suicidality, in line with Corbani et al. (2016, submitted). In multiple logistic regression, a forward stepwise procedure was used to include only variables significantly associated with ADS at $p < 0.05$.

Analyses were conducted using IBM SPSS Statistics, version 23.0 and MPLUS, version 7.

Results

The study sample consists of 483 women who completed the SPS questionnaire. Mean age was 33 years, the large majority was married, had a high school diploma or a university degree and had paid maternity leave (Table I). Fewer than 10% reported distressing life events, unemployment and change in work. About one in four reported that pregnancy was unplanned and 12.8% had an at-risk pregnancy. Figure 1 shows the frequency distributions of SPS-10 and

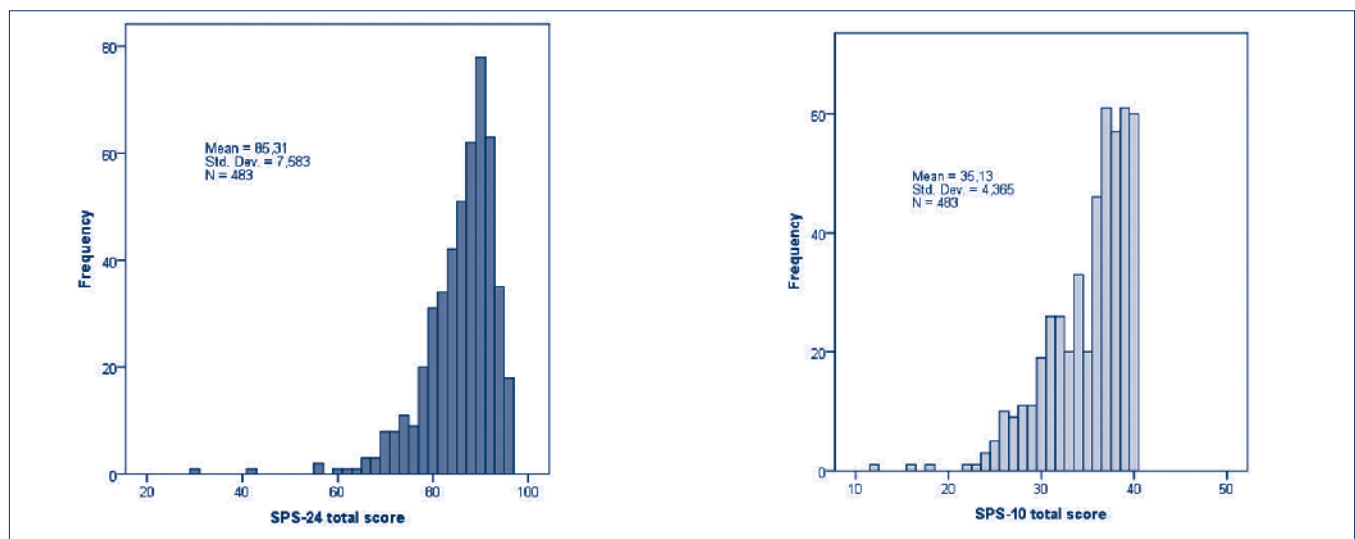


FIGURE 1.
Frequency distribution of SPS-10 and SPS-24 scores.

TABLE I.
Characteristics of the study sample (N = 483).

Age, mean (SD)	33.0 (4.4)
Marital status	
Married, n (%)	460 (95.5)
Educational level, n (%)	
None	0
Primary school	0
Middle school	52 (10.8)
High school	240 (49.7)
University degree	189 (39.1)
Missing	2 (0.4)
Living condition, n (%)	
Alone	8 (1.7)
With partner and/or children	449 (93.5)
With original family	12 (2.5)
Other	11 (2.3)
Work, n (%)	
Paid maternity leave	423 (87.6)
Unemployed	30 (6.2)
Change in work	23 (4.8)
Distressing life events, n (%)	
Marital problems	30 (6.2)
Financial problems	36 (7.5)
Bereavement	30 (6.2)
Change of residence	34 (7.0)
Pregnancy-related variables, n (%)	
Planned	343 (71.0)
Unplanned	110 (22.8)
Assisted reproduction	20 (4.1)
Missing	10 (2.1)
Trimester	
First	18 (3.7)
Second	79 (16.4)
Third	383 (79.3)
Missing	3 (0.6)
At risk pregnancy, n (%)	62 (12.8)
Any previous abortion, n(%)	114 (23.6)
Number of children, median (range)	0 (0-5)
Number of pregnancies, median (range)	0 (0-6)
Psychiatric history, n (%)	128 (26.5)
Past treatment n (%)	
Psychological treatment	64 (13.3)
Pharmacological treatment	9 (1.9)
Both	30 (6.2)
None	380 (78.6)
Family history of psychiatric disorders, n(%)	126 (26.1)

SPS-24 scores. The histograms are skewed to the left, indicating that the large majority of the sample perceived strong social support. The SPS-10 score ranged from 12 to 40, mean = 35.1, SD = 4.4, median = 36 and the SPS-24 score ranged from 30 to 96, mean = 85.3, SD = 7.6, median = 87.

Table II shows the correlation of the 10 negative items with the total SPS-10 score and the total SPS-24 score. Notably, the correlation between the total scores of the SPS-10 and SPS-24 was 0.896, denoting an excellent concurrent validity. All the items had medium to strong correlations with the SPS-10, ranging from 0.465 to 0.674 according to Cohen's definition, which sets a threshold of 0.5 for strong correlation (Cohen, 1988).

The internal consistency of SPS-10 scale was very good (Cronbach's alpha = 0.809) and not much inferior to that of the SPS-24 scale (alpha = 0.847).

The confirmatory factor analysis model had a very good fit to the data (CFI = 0.989, TFI = 0.983, RMSEA = 0.049), indicating that the a priori defined structure held true in the study sample (Figure 2). All items had high loadings on the respective factors, ranging from 0.48 to 0.88. We also fitted a model including only first-level factors, and the fit to the data was similar (CFI = 0.99, TFI = 0.982, RMSEA = 0.051).

We then examined the relationship between social support and ADS (Table III). Forty-nine women (10.1%) screened positive for ADS. Three logistic regression models were fit, in which the variables used to predict ADS were the total SPS-10 score, the total SPS-24 score and the SPS-10 subscales, respectively. High levels of perceived social support significantly contributed to decreasing the likelihood of having ADS in each model. Notably, among the five SPS-10 subscales only reassurance of worth was significantly associated with ADS and none of the other scales contributed additional independent information to the prediction of ADS.

Discussion

The present study reports on the validation of an abridged version of the social provisions scale obtained by reducing it from 24 items to 10 items, so as to produce a reliable and valid instrument for measuring the perception of the availability of social support that requires a shorter time to be completed.

The analyses indicate that the SPS-10 possesses excellent psychometric properties. First, it had a strong concurrent validity with the SPS-24, as indicated by the correlation between the total scores of the two scales.

The fidelity of the short version, examined in terms of internal consistency, was satisfactory. The overall alpha of the SPS-10 was slightly lower than the original scale, but still very high.

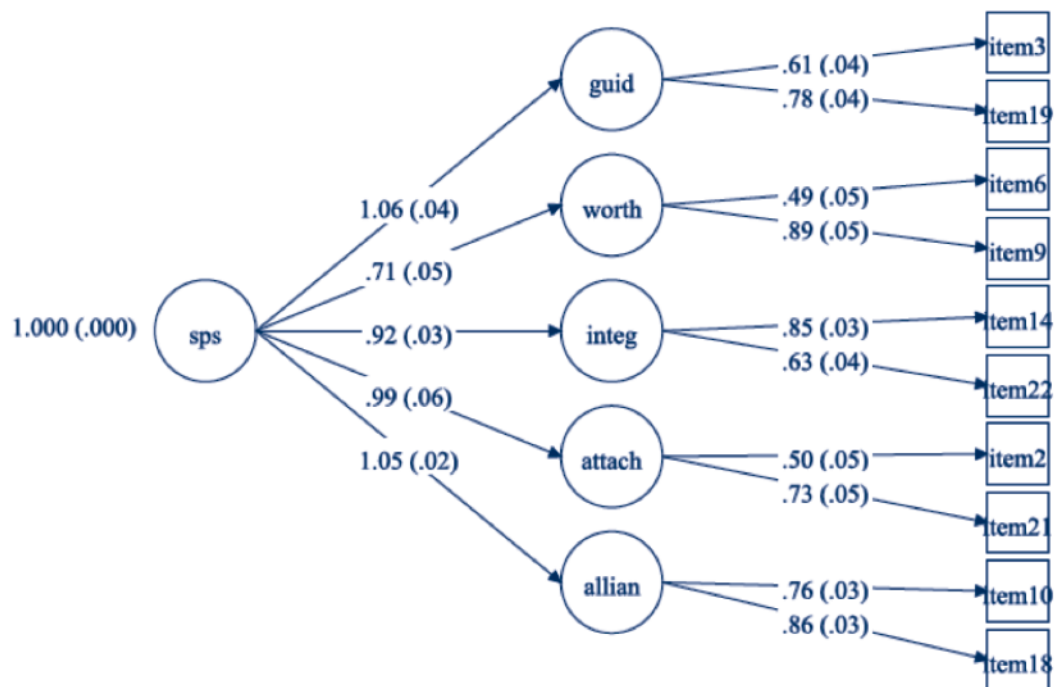
The structure of the scale was robust and consistent with that found in previous studies. Although the fit to the data was similar for the two models comprising only first-level factors (the subscales) and first-level + a second-level factor (the overall perception of social support), the second

TABLE II.

Correlation of the 10 items with SPS-10 and SPS-24 total scores.

	Item2	Item3	Item6	Item9	Item10	Item14	Item18	Item19	Item21	Item22	Total SPS-10	Total SPS-24
Item2	1											
Item3	,285**	1										
Item6	,146**	,168**	1									
Item9	,243**	,306**	,358**	1								
Item10	,257**	,378**	,182**	,349**	1							
Item14	,219**	,318**	,162**	,371**	,380**	1						
Item18	,214**	,266**	,147**	,321**	,365**	,559**	1					
Item19	,222**	,253**	,152**	,276**	,346**	,473**	,597**	1				
Item21	,275**	,277**	,168**	,397**	,358**	,386**	,337**	,398**	1			
Item22	,200**	,154**	,115*	,265**	,259**	,350**	,252**	,298**	,290**	1		
Total SPS-10	,522**	,557**	,465**	,648**	,595**	,674**	,629**	,625**	,663**	,509**	1	
Total SPS-24	,437**	,458**	,395**	,544**	,478**	,661**	,622**	,556**	,584**	,450**	,896**	1

**. Correlation is significant at the 0.01 level (2-tailed).

**FIGURE 2.**

SPS-10 two-level structure. Results from confirmatory factor analysis.

model is more relevant from a clinical point of view because it supports the use of the total score and facilitates clinicians in the interpretation of the scale. The results should be interpreted in light of strengths

and limitations. The strength includes the availability of data from a large sample of women recruited at different trimesters of pregnancy, which can be considered representative of the populations of women that undergo

TABLE III.

Relationship between perceived social support and the presence of antenatal depressive symptoms. Results from 3 logistic regression models.

	B	OR	95% CI	p-value
Model 1				
SPS-10 total score	-0.095	0.910	0.858-0.965	0.002
Model 2				
SPS-24 total score	-0.039	0.962	0.932-0.994	0.019
Model 3				
Reassurance of worth	-0.391	0.677	0.552-0.830	< 0.001

scheduled follow-up visits or attend antenatal classes. Limitations include the cross-sectional study design, which prevents drawing conclusions about impact of the social support on the course of depressive symptoms during the perinatal period, and the restricted range of SPS scores, that are on average higher than those reported for the general population. Fleury et al.¹¹ reported a mean SPS-24 score of 80.7 ($\pm$ 9.0) in a large population sample, which is about five points lower than that found in the present study. A possible interpretation of our results is that social desirability issues may come into play when women are asked to report on possible lack of support from the partner or family members during pregnancy. Alternatively, our results may be genuine, suggesting that pregnant women perceive that their condition takes on a special significance and elicits a strong support from the family and friends. This is likely because in Italy birth rates are very low and families tend to have just one child. An additional limitation is that our sample includes only females, therefore validation in a sample including both genders is warranted.

The availability of a valid Italian short and highly informative instrument to measure the perception of social support has a number of advantages.

First, the perception of poor social support is an important risk factor for depression during pregnancy, affects the sense of well-being¹⁸ and may decrease the ability of the woman to cope with stressful events and the needs of the newborn¹⁹. Thus, the SPS-10 can be a useful screening tool to be administered together with other instruments measuring anxious-depressive symptoms in pregnant women. Information on the lack of social support can be valuable to inform decisions about psychosocial interventions to prevent post-partum depression and its disruptive consequences on women and their newborns. In addition, the SPS-10 might be easily used in other screening contexts such as pre-natal classes, vaccination centres, counselling services provided by different health professionals (paediatricians, midwives, nurses) allowing

to reach a larger number of women and thus strengthening primary prevention measures.

Lastly, social support is acknowledged to be both a protecting factor against mental disorders and a strong predictor of healthcare service utilisation for mental health reasons in general population studies¹¹. Therefore, the SPS-10 can be a useful clinical and research tool to assess perceived social support not only in perinatal and paediatric settings, but also in general medical and mental health settings.

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Conflicts of interest

None.

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ALLEGATO

Scala del Supporto Sociale (SPS-10)

Le chiediamo di rispondere a questo questionario nel modo più sincero possibile, indicando quanto ritiene vera o falsa ogni affermazione. Non ci sono risposte giuste o sbagliate; nel rispondere, pensi alle persone che la circondano.

Per ogni affermazione, segni con una croce la risposta che meglio descrive i suoi rapporti con gli altri utilizzando questo punteggio: 1= vero; 2= in parte vero; 3= in parte falso; 4= falso

	Vero	In parte vero	In parte falso	Falso
2. Non ho rapporti stretti con altre persone	1	2	3	4
3. Non c'è nessuno a cui posso rivolgermi nei periodi di stress	1	2	3	4
6. Gli altri pensano che io sia incapace in quello che faccio	1	2	3	4
9. Non penso che gli altri non rispettino ciò che faccio	1	2	3	4
10. Se qualcosa andasse storto, nessuno mi aiuterebbe	1	2	3	4
14. Nessuno condivide i miei interessi e le mie preoccupazioni	1	2	3	4
18. Non potrei chiedere aiuto a nessuno, se davvero ne avessi bisogno	1	2	3	4
19. Non c'è nessuno con cui parlerei tranquillamente dei miei problemi	1	2	3	4
21. Non mi sento vicino a nessuno	1	2	3	4
22. A nessuno piace fare le cose che piacciono a me	1	2	3	4

