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Editorial

Massimo Di Giannantonio, Enrico Zanalda

Presidents of the Italian Psychiatric Association (SIP)

This second and third volume of Evidence-Based Psychiatric Cares (EBPC) is published after the publication of some supplements in Italian, namely the one on the guidelines published at the national conference of the Italian Psychiatric Association (SIP) in Florence on 21/23 June 2019, the one on the antipsychotic cariprazine released in summer 2019 and, finally, the one on heterofamily supported adult insertions (IESA) published in December. These editorial choices were made to disseminate scientific information of national interest in Italian through the supplements, as they are intended for operators in our country, while the magazine continues to be published in English.

During the year 2019, the executive committee of SIP took some important organizational decisions, such as the change of the company's operational headquarters and the modification of the timing of national congresses.

Since the beginning of October 2019, SIP's head office has become a room in Hall 26 of the Compendio Immobiliare di Santa Maria della Pietà (former Psychiatric Hospital) in Rome owned by the Azienda Sanitaria Locale (ASL) Roma 1. This historic place of Italian psychiatry represents the return to Rome of our society which was founded here as the Società Freniatria Italiana back in 1873. The important thing is not so much the return to the capital city but the fact that, by virtue of its long tradition, it had its headquarters in a historical place such as the former Santa Maria della Pietà Psychiatric Hospital in Rome with the possibility of remaining there in the future thanks to a favorable contract for the concession of space by the ASL Roma 1.


The passage to the annual National Congress allows maintaining closer contact with the members and especially with the regional sections that will be more strongly involved in the organization of the event locally. In 2020 it will be the turn of the Ligurian section to participate in the organization of the national congress in Genoa that will take place.

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Alexithymia, childhood maltreatment and suicide risk: an update



Domenico De Berardis

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Summary

It is well known that persons with alexithymia may suffer from severe anxiety and depression, usually experiencing somewhat more significant psychological distress. There is growing evidence that alexithymia may be considered a risk factor for suicide, even basically increase the risk of development of depressive symptoms or per se. The role of childhood maltreatment seems to be a significant factor in the developing of alexithymic features and increased suicide risk. Therefore, the objective of this narrative review was to elucidate the possible relationships between alexithymia, childhood maltreatment and suicide risk. Taken together, almost all reviewed studies have pointed out a strong correlation between alexithymia, childhood maltreatment and increased suicide risk. In conclusion, the significance of alexithymia screening in daily clinical practice and the assessment of clinical correlates of alexithymic traits and childhood maltreatment should be essential parts of all illness managing programs and, particularly, of suicide prevention strategies and interventions. Moreover, clinical attention appears necessary concerning childhood maltreatment, preferably assisting such subjects in scaffolding and normalizing safe disclosure of childhood maltreatment, and delivering earlier interventions to protect against current mood and suicide risk symptoms.

Key words: alexithymia, childhood maltreatment, suicide risk, psychiatric disorders

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Introduction

It has been extensively proven that subjects with alexithymia may show affective dysregulation as well as the incapacity to self relieve and deal with emotions due to a relative lack of emotional consciousness¹. Therefore, these subjects may suffer from severe anxiety and depression, usually suffering from a relatively higher psychological pain, and may be at risk of developing both inexplicable somatic symptoms and symptoms of emotional distress as they are, on a psychological point of view, inadequately furnished^{2,3}.

Besides, numerous studies showed that alexithymics might insufficiently respond both to psychopharmacotherapy and psychotherapy. The typical characteristics of alexithymic behavior are mostly evident in social relationships with high emotional connotations⁴. A persistent affect-avoiding in interpersonal behaviors are rather distressing and may produce instability and struggles in

such significant relationships, subsidizing the increase of symptoms of anxiety and depression, thus increasing the possibility of suicidal ideation and behavior⁵. Likewise, it has been proven that alexithymia should be considered as a relative constant personality feature^{6,7}, increasing susceptibility to depressive symptoms^{8,9} and is mostly associated with a higher risk of death for numerous causes (accidents, injury, or violence)¹⁰.

There is growing evidence that alexithymia may be a risk factor for suicide, even basically increase the risk of development of depressive symptoms or per se¹¹. This evidence comes out from the results of several studies conducted on both the general population¹² and clinical samples of patients with psychiatric disorders or medical conditions. Moreover, childhood maltreatment has been often associated with alexithymia and seems to be a risk factor for both developing alexithymia and suicide ideation. Therefore, the objective of this narrative review was to elucidate the possible relationships between alexithymia, childhood maltreatment, and suicide risk.

Alexithymia, childhood maltreatment and suicide risk

Childhood maltreatment, such as sexual abuse, physical abuse, emotional abuse, and neglect, is an essential predictor of risky behaviors such as the increased risk of drug abuse, pathological gambling, substance abuse, dangerous sexual practices, and impulse dyscontrol. Furthermore, childhood maltreatment is one of the most critical risk factors for developing psychiatric disorders and suicide ideation and behaviors.

The relationships between alexithymia and childhood maltreatment were explored in numerous studies.

Yates et al.¹³ demonstrated that experiences of child maltreatment were related to increased problematic Internet use (PIU) in a large sample of 1470 college students, and mediation analyses showed that this relation was partially explained by alexithymia. Swannel et al.¹⁴ pointed out that child maltreatment, and in particular, physical abuse, was strongly related to the development of non-suicidal self-injury (NSSI), and this association was mediated by dissociation, alexithymia, and self-blame for females. The Authors concluded that altering attributional style (through cognitive therapy or emotion-focused therapy) and improving the capacity to regulate emotions (through dialectical behavior therapy) may contribute to the reduction or interruption of NSSI.

Ogrodniczuk et al.¹⁵ collected data of 188 persons at three urban outpatient psychiatric clinics in Canada pointed out the role of alexithymia as a mediating factor between childhood maltreatment and somatic complaints in maturity. The results showed that the mediated relationship was specific to maltreatment involving physical abuse, sexual abuse, and physical neglect, and a core dimension of alexithymia (difficulty identifying feelings, DIF). Another study demonstrated that growing up in a punishing environment (such as being hit or beat or expected to obey to an austere code of behaviour) was indirectly associated with negative urgency via DIF dimension of alexithymia, suggesting that excessive use of punishment during

childhood may shrink the development of the capacity to identify and give an explanation to feeling states¹⁶. This trouble in emotional processing may, in turn, lead to acting impulsively when emotionally stimulated. It has also been demonstrated that alexithymia may partially explain the associations between emotional neglect and symptoms of depression, anxiety, and loneliness that may be linked with increased suicide ideation¹⁷. Adverse experiences early in life can impair an individual's emotional processing, and these deficiencies in emotional functioning contribute to behavioral and interpersonal dysregulation, resulting in increased impulsivity and risk-taking that may further contribute to NSSI or suicidal behaviors¹⁸.

Concerning individuals with Bipolar I Disorder (BD-I), the results of a case-control study showed that patients with BD-I reported significantly more frequent abusive experiences in childhood, higher levels of attachment insecurities, more severe pathological and somatoform dissociation, as well as higher scores on measures of alexithymia¹⁹.

In conclusion, taken together, the results of the above-reviewed studies point out a close relationship between childhood maltreatment and alexithymia that may predispose the individual to an increased susceptibility to develop suicide ideation and behaviors.

Moreover, childhood maltreatment may also be directly linked to increased suicide ideation independently from alexithymia and this was demonstrated by several studies. The findings of a cross-sectional study by Pompili et al.²⁰ on 163 consecutively admitted adult inpatients suggested that exposure to abuse and neglect as a child may increase the risk of subsequent symptoms of more severe externalizing "male depression" (characterized by abrupt lowered stress tolerance, irritability, impulsive, aggressive, and/or psychopathic behavior, such as alcohol and/or drug abuse or abusive equivalents), which has been associated with higher suicidal risk. Falgares et al.²¹ suggested that the combined effect of specific forms of dysfunctional parental behavior during childhood (such as lack of care and psychological abuse) and the development of rigid and dysfunctional negative personality traits may increase the risk for suicidal ideation and behavior during adulthood. Moreover, it is well known that impulsivity and childhood maltreatment may independently increase the risk of suicide attempts, self-injury, and interpersonal violence²². Childhood maltreatment may have a stronger effect on violence directed towards the self than on interpersonal violence, and this is valid in both genders²³. Paul and Ortin²⁴ investigated self-harm behavior and suicidal ideation in children at the age of 9 years; childhood abuse and neglect had already been investigated at the children's age of 3 years within this longitudinal cohort, which adhered to a strictly prospective design. Most interestingly, they investigated potential pathways from early maltreatment to self-harm via different types of psychopathology. While neglect predicted both suicidal ideation and self-harm via internalizing psychopathology, physical and psychological abuse only predicted self-harm via more externalizing mental health problems.

In a study on a national sample of 530 Canadian men,

younger men exposed to childhood maltreatment reported significantly higher depression and suicide risk scores than their older peers who also had a maltreatment history²⁵. Therefore the mood-related impact of childhood maltreatment is most significant during men's younger years. Recently, Goldberg et al.²⁶ assessed 165 patients with a principal diagnosis of major depressive disorder (MDD) and found that childhood maltreatment was a precise predictor of suicidal behavior among such patients, with a significant effect even after controlling for potential confounders.

Studies on relationships between alexithymia and suicide risk in psychiatric disorders

Several studies on clinical samples of patients with mental disorders have confirmed the hypothesis that alexithymia may increase the suicide risk, primarily through the development of depressive symptoms.

The prevalence of alexithymia is relatively higher in subjects with psychiatric disorders²⁷. Therefore, the studies on relationships between alexithymia and suicide risk on clinical samples of patients with mental disorders are fascinating as alexithymia may predispose to their development or worsen an existing one^{8,9,28,29}.

The presence of alexithymic traits in patients with Anxiety Disorders (ADs) may be a risk factor of suicide, merely worsening the AD itself per se or leading to the development of depressive symptoms or even a comorbid Major Depressive Episode (MDE)^{2,30,31}.

Regarding Obsessive-Compulsive Disorder (OCD), it has been found that alexithymia and depressive symptoms were considerably associated with OCD patients¹¹. De Berardis et al. have demonstrated that OCD patients with alexithymia showed higher disorder severity, less insight, and inflated responsibility attitude, all related to suicide ideation, independently from depressive symptoms³². Again, in this research, the DIF subscale of TAS-20 was associated with higher SSI scores. Moreover, alexithymia and perfectionism have been found related to higher suicide ideation in patients with OCD³³.

Also in patients with Panic Disorder (PD), a relationship between alexithymia and increased suicidal ideation has been found associated with a serum lipid dysregulation³⁴. This positive correlation between alexithymia and increased suicidal ideation was substantially confirmed also in patients with Generalized Anxiety Disorder (GAD) (35). Only one study directly evaluated alexithymia and suicide risk in Posttraumatic Stress Disorder (PTSD), even if a relationship between alexithymia and post-traumatic symptoms has been revealed in other studies^{27,36-40}. Kusevic et al.⁴¹ evaluated 127 veterans from the 1991-1995 war in Croatia, and the study's results suggested that alexithymia can be considered as a risk factor for attempted suicide among war veterans with PTSD.

Despite the high number of studies that have evaluated the presence and clinical correlates of alexithymia in Affective Disorders such as MDD⁴²⁻⁴⁵, surprisingly, relatively few studies have directly investigated its relationships with suicide risk. Alexithymia may be a risk factor of suicide

in adolescent depression especially in presence of maladaptive early schemas⁴⁶. Concerning adults, De Berardis et al.⁴⁴ evaluated 145 drug-naive adult outpatients with a DSM-IV diagnosis of MD and found that alexithymic patients showed higher scores on SSI, thus indicating a higher suicide risk. In a linear regression model, lower high-density lipoprotein levels, DIF, and "Difficulty in Describing Feelings" (DDF) dimensions of TAS-20 were associated with higher suicide risk. Serafini et al. (47) recruited 281 euthymic participants of which 62.3% with unipolar MD and 37.7% with bipolar disorder and showed that such patients with affective disorders might suffer from constant difficulties in processing sensory input which has been significantly linked with higher depression, impulsivity, alexithymia, and hopelessness. Lower registration of sensory input referring to hyposensitivity and sensation avoiding relating to hypersensitivity correlated considerably with higher alexithymia and, in particular, with DIF and DDF dimensions of TAS-20, accounting for higher impulsivity and hopelessness (that may be risk factors of suicide). Moreover, alexithymic subjects with MDD may characterize for homocysteine dysregulation that may be somewhat linked to suicide ideation, regardless depression' severity⁴⁸. Finally, alexithymia and low resilience were significant predictors of increased suicide ideation in a sample of patient at first MD episode⁴⁹.

Positive correlations between alexithymia and increased suicide risk have been found in other several psychiatric disorders. Somatoform disorder patients with lifetime suicide attempts might have more significant difficulties in identifying and describing emotions, and a propensity to intensely feel and express anger (50). Moreover, in patients with conversion disorder (CD), alexithymia is higher in suicide attempters⁵¹.

Several shreds of evidence point out that alexithymia may be a risk factor of suicide in Eating Disorders (EDs). For example, Carano et al.⁵² demonstrated that individuals with Binge Eating Disorder (BED) might experience higher suicide ideation, particularly in the presence of alexithymia and depressive symptoms, even if these latter symptoms are subclinical. Alpaslan et al.⁵³ evaluated 381 female students in Turkey and found that disordered eating attitudes (DEAs) were frequently found among female students, and alexithymia was often correlated with increased suicide risk in adolescents with DEAs. However, no studies have been conducted to estimate the association between alexithymia and increased suicidal ideation in patients with anorexia nervosa and bulimia.

Moreover, several studies have pointed out that alexithymia can be a potential factor enhancing suicide and self-harm risk in individuals with Substance Use Disorders⁵⁴⁻⁵⁶.

To our knowledge, only one study has evaluated the relationships between alexithymia and suicide risk in schizophrenia and study results showed that alexithymia in schizophrenia was associated with more severe suicide ideation and depressive symptoms, regardless of the severity of both positive and negative symptoms⁵⁷.

Conclusions

Taken together, almost all studies have pointed out a direct or indirect relationship between alexithymia, childhood maltreatment and increased suicide risk.

These findings may be explained in several ways. One is in accordance to the Freyberger's theory of acute "secondary alexithymia" as a response to stressful events⁵⁸. Acute secondary alexithymia is considered a momentary, state-dependent experience that may be a consequence of subjective distress, that decrease when an acute disease episode has resolved⁵⁹. As the presence of alexithymia may worsen an existing psychiatric or medical disease, this worsening may be related to the development of suicidal ideation per se or through the development of depressive symptoms or even a comorbid clinically relevant MDE⁴. The presence of childhood maltreatment may exacerbate the acute "secondary alexithymia," maybe through an increased stress sensitivity. As a consequence, it is possible to argue that higher state-dependent alexithymia may enhance the severity of underlying psychiatric disorders, thus increasing the risk of suicide.

Nevertheless, even if alexithymia may be a state-dependent phenomenon, it should be considered a relatively stable personality trait that may also be existing even before the onset of a psychiatric disorder or a medical disease^{6,7}. Thus, our review findings are also in accordance with the "stress-alexithymia hypothesis"⁶⁰. Alexithymia may be a chronic disorder (maybe with an onset during infancy or early adolescence and often in consequence of childhood abuse or neglect)^{14,54} characterized by a marked inflammatory state with an impaired Hypothalamic-pituitary-adrenal (HPA) axis reactivity to even minor or modest life stressors⁶¹. Therefore, it should be considered as a chronic state reaction in reaction to stressful circumstances that may invariably complicate a psychiatric disorder or a medical illness⁶². As well as it happens in secondary alexithymia, childhood maltreatment may increase the perceived stress in the alexithymic subjects and may further increase chronic HPA reactivity, thus leading to a possible heightening of suicidal ideation and behaviors^{63,64}.

In conclusion, the importance of alexithymia screening in everyday "real world" clinical practice and the assessment of quantifiable correlates of alexithymic traits should be essential parts of all illness management plans and, especially, of suicide prevention. Accordingly, focused clinical attention appears necessary for people with a history of childhood maltreatment, preferably assisting in scaffolding and normalizing safe disclosure of childhood maltreatment, and delivering earlier interventions to buffer against current mood and suicide risk symptoms.

References

- 1 Taylor GJ, Bagby RM, Parker JDA. *Disorders of affect regulation: alexithymia in medical and psychiatric illness*. Cambridge, UK: Cambridge University Press 1997.
- 2 De Berardis D, Campanella D, Serroni N, et al. *The impact of alexithymia on anxiety disorders: a review of the literature*. *Current Psychiatry Reviews* 2008;4:80-8.
- 3 De Berardis D, Di Giannantonio M. *Alessitimia (I parte)*:
Noos, aggiornamenti in Psichiatria. Rome: Il Pensiero Scientifico Editore 2010.
- 4 Taylor GJ, Bagby RM. *New trends in alexithymia research*. *Psychother Psychosom* 2004;73:68-77.
- 5 Lester D. *Alexithymia, depression, and suicidal preoccupation*. *Perceptual and motor skills* 1991;72:1058.
- 6 Luminet O, Bagby RM, Taylor GJ. *An evaluation of the absolute and relative stability of alexithymia in patients with major depression*. *Psychother Psychosom* 2001;70:254-60.
- 7 Luminet O, Rokbani L, Ogez D, et al. *An evaluation of the absolute and relative stability of alexithymia in women with breast cancer*. *J Psychosom Res* 2007;62:641-8.
- 8 Honkalampi K, Koivumaa-Honkanen H, Lehto SM, et al. *Is alexithymia a risk factor for major depression, personality disorder, or alcohol use disorders? A prospective population-based study*. *J Psychosom Res* 2010;68:269-73.
- 9 Tolmunen T, Heliste M, Lehto SM, et al. *Stability of alexithymia in the general population: an 11-year follow-up*. *Compr Psychiatry* 2011;52:536-41.
- 10 Kauhanen J, Kaplan GA, Cohen RD, et al. *Alexithymia and risk of death in middle-aged men*. *J Psychosom Res* 1996;41:541-9.
- 11 De Berardis D, Campanella D, Gambi F, et al. *Insight and alexithymia in adult outpatients with obsessive-compulsive disorder*. *Eur Arch Psychiatry Clin Neurosci* 2005;255:350-8.
- 12 Haatainen K, Tanskanen A, Kylma J, et al. *Factors associated with hopelessness: a population study*. *Int J Soc Psychiatry* 2004;50:142-52.
- 13 Yates TM, Gregor MA, Haviland MG. *Child maltreatment, alexithymia, and problematic internet use in young adulthood*. *Cyberpsychol Behav Soc Netw* 2012;15:219-25.
- 14 Swannell S, Martin G, Page A, et al. *Child maltreatment, subsequent non-suicidal self-injury and the mediating roles of dissociation, alexithymia and self-blame*. *Child Abuse Negl* 2012;36:572-84.
- 15 Ogrodniczuk JS, Joyce AS, Abbass AA. *Childhood maltreatment and somatic complaints among adult psychiatric outpatients: exploring the mediating role of alexithymia*. *Psychother Psychosom* 2014;83:322-4.
- 16 Gaher RM, Arens AM, Shishido H. *Alexithymia as a mediator between childhood maltreatment and impulsivity*. *Stress Health* 2015;31:274-80.
- 17 Brown S, Fite PJ, Stone K, et al. *Accounting for the associations between child maltreatment and internalizing problems: the role of alexithymia*. *Child Abuse Negl* 2016;52:20-8.
- 18 Hahn AM, Simons RM, Simons JS. *Childhood maltreatment and sexual risk taking: the mediating role of alexithymia*. *Arch Sex Behav* 2016;45:53-62.
- 19 Kefeli MC, Turow RG, Yildirim A, et al. *Childhood maltreatment is associated with attachment insecurities, dissociation and alexithymia in bipolar disorder*. *Psychiatry Res* 2018;260:391-9.
- 20 Pompili M, Innamorati M, Lamis DA, et al. *The associations among childhood maltreatment, "male depression" and suicide risk in psychiatric patients*. *Psychiatry Res* 2014;220:571-8.
- 21 Falgares G, Marchetti D, Manna G, et al. *Childhood maltreatment, pathological personality dimensions, and suicide risk in young adults*. *Front Psychol* 2018;9:806.
- 22 McMahon K, Hoertel N, Olfson M, et al. *Childhood maltreatment and impulsivity as predictors of interpersonal violence, self-injury and suicide attempts: a national study*. *Psychiatry Res* 2018;269:386-93.
- 23 Torchalla I, Strehlau V, Li K, Schuetz C, Krausz M. *The association between childhood maltreatment subtypes and cur-*

- rent suicide risk among homeless men and women. *Child Maltreat*. 2012;17:132-143.
- ²⁴ Paul E, Ortin A. *Psychopathological mechanisms of early neglect and abuse on suicidal ideation and self-harm in middle childhood*. *Eur Child Adolesc Psychiatry* 2019;28:1311-9.
- ²⁵ Rice SM, Kealy D, Olliffe JL, et al. *Childhood maltreatment and age effects on depression and suicide risk among Canadian men*. *Psychiatry Res* 2018;270:887-9.
- ²⁶ Goldberg X, Serra-Blasco M, Vicent-Gil M, et al. *Childhood maltreatment and risk for suicide attempts in major depression: a sex-specific approach*. *Eur J Psychotraumatol* 2019;10:1603557.
- ²⁷ Leweke F, Leichsenring F, Kruse J, et al. *Is alexithymia associated with specific mental disorders?* *Psychopathology* 2012;45:22-8.
- ²⁸ Saarijarvi S, Salminen JK, Toikka T. *Temporal stability of alexithymia over a five-year period in outpatients with major depression*. *Psychother Psychosom* 2006;75:107-12.
- ²⁹ Conrad R, Wegener I, Imbierowicz K, et al. *Alexithymia, temperament and character as predictors of psychopathology in patients with major depression*. *Psychiatry Res* 2009;165:137-44.
- ³⁰ Loas G, Dalleau E, Lecointe H, et al. *Relationships between anhedonia, alexithymia, impulsivity, suicidal ideation, recent suicide attempt, C-reactive protein and serum lipid levels among 122 inpatients with mood or anxious disorders*. *Psychiatry Res* 2016;246:296-302.
- ³¹ De Berardis D, Campanella D, Gambi F, et al. *Alexithymia, fear of bodily sensations, and somatosensory amplification in young outpatients with panic disorder*. *Psychosomatics* 2007;48:239-46.
- ³² De Berardis D, Serroni N, Campanella D, et al. *Alexithymia, responsibility attitudes and suicide ideation among outpatients with obsessive-compulsive disorder: an exploratory study*. *Compr Psychiatry* 2015;58:82-7.
- ³³ Kim H, Seo J, Namkoong K, et al. *Alexithymia and perfectionism traits are associated with suicidal risk in patients with obsessive-compulsive disorder*. *J Affect Disord* 2016;192:50-5.
- ³⁴ De Berardis D, Campanella D, Serroni N, et al. *Alexithymia, suicide risk and serum lipid levels among adult outpatients with panic disorder*. *Compr Psychiatry* 2013;54:517-22.
- ³⁵ De Berardis D, Serroni N, Campanella D, et al. *Alexithymia, suicide ideation, C-reactive protein, and serum lipid levels among outpatients with generalized anxiety disorder*. *Arch Suicide Res* 2017;21:100-12.
- ³⁶ Yehuda R, Steiner A, Kahana B, et al. *Alexithymia in Holocaust survivors with and without PTSD*. *J Trauma Stress* 1997;10:93-100.
- ³⁷ Sondergaard HP, Theorell T. *Alexithymia, emotions and PTSD; findings from a longitudinal study of refugees*. *Nord J Psychiatry* 2004;58:185-91.
- ³⁸ Evren C, Dalbudak E, Cetin R, et al. *Relationship of alexithymia and temperament and character dimensions with lifetime post-traumatic stress disorder in male alcohol-dependent inpatients*. *Psychiatry Clin Neurosci* 2010;64:111-9.
- ³⁹ Park J, Jun JY, Lee YJ, et al. *The association between alexithymia and posttraumatic stress symptoms following multiple exposures to traumatic events in North Korean refugees*. *J Psychosom Res* 2015;78:77-81.
- ⁴⁰ Terock J, Van der Auwera S, Janowitz D, et al. *From childhood trauma to adult dissociation: the role of PTSD and alexithymia*. *Psychopathology* 2016;49:374-82.
- ⁴¹ Kusevic Z, Cusa BV, Babic G, et al. *Could alexithymia predict suicide attempts - a study of Croatian war veterans with post-traumatic stress disorder*. *Psychiatria Danubina* 2015;27:420-3.
- ⁴² Marchesi C, Ossola P, Tonna M, et al. *The TAS-20 more likely measures negative affects rather than alexithymia itself in patients with major depression, panic disorder, eating disorders and substance use disorders*. *Compr Psychiatry* 2014;55:972-8.
- ⁴³ Li S, Zhang B, Guo Y, et al. *The association between alexithymia as assessed by the 20-item Toronto Alexithymia Scale and depression: a meta-analysis*. *Psychiatry Res* 2015;227:1-9.
- ⁴⁴ De Berardis D, Serroni N, Campanella D, et al. *Alexithymia and its relationships with C-reactive protein and serum lipid levels among drug naive adult outpatients with major depression*. *Prog Neuropsychopharmacol Biol Psychiatry* 2008;32:1982-6.
- ⁴⁵ Saarijarvi S, Salminen JK, Toikka TB. *Alexithymia and depression: a 1-year follow-up study in outpatients with major depression*. *J Psychosom Res* 2001;51:729-33.
- ⁴⁶ Hirsch N, Hautekeete M, Kochman F. *Early maladaptive processes, depression and alexithymia in suicidal hospitalized adolescents*. *Encephale* 2001;27:61-70.
- ⁴⁷ Serafini G, Gonda X, Canepa G, et al. *Extreme sensory processing patterns show a complex association with depression, and impulsivity, alexithymia, and hopelessness*. *J Affect Disord* 2016;210:249-57.
- ⁴⁸ De Berardis D, Olivieri L, Rapini G, et al. *Alexithymia, suicide ideation and homocysteine levels in drug naive patients with major depression: a study in the "real world" clinical practice*. *Clin Psychopharmacol Neurosci* 2019;17:318-22.
- ⁴⁹ De Berardis D, Fornaro M, Valchera A, et al. *Alexithymia, resilience, somatic sensations and their relationships with suicide ideation in drug naive patients with first-episode major depression: an exploratory study in the "real world" everyday clinical practice*. *Early Interv Psychiatry* 2019.
- ⁵⁰ Kampfer N, Staufienbiel S, Wegener I, et al. *Suicidality in patients with somatoform disorder - the speechless expression of anger?* *Psychiatry Res* 2016;246:485-91.
- ⁵¹ Gulec MY, Ynanc L, Yanartathorn O, Uzer A, et al. *Predictors of suicide in patients with conversion disorder*. *Compr Psychiatry* 2014;55:457-62.
- ⁵² Carano A, De Berardis D, Campanella D, et al. *Alexithymia and suicide ideation in a sample of patients with binge eating disorder*. *J Psychiatr Pract* 2012;18:5-11.
- ⁵³ Alpaslan AH, Soyulu N, Avci K, et al. *Disordered eating attitudes, alexithymia and suicide probability among Turkish high school girls*. *Psychiatry Res* 2015;226:224-9.
- ⁵⁴ Evren C, Evren B, Dalbudak E, et al. *Childhood abuse and neglect as a risk factor for alexithymia in adult male substance dependent inpatients*. *J Psychoactive Drugs* 2009;41:85-92.
- ⁵⁵ Sakuraba S, Kubo M, Komoda T, et al. *Suicidal ideation and alexithymia in patients with alcoholism: a pilot study*. *Subst Use Misuse* 2005;40:823-30.
- ⁵⁶ Evren C, Evren B. *Self-mutilation in substance-dependent patients and relationship with childhood abuse and neglect, alexithymia and temperament and character dimensions of personality*. *Drug Alcohol Depend* 2005;80:15-22.
- ⁵⁷ Marasco V, De Berardis D, Serroni N, et al. *Alexithymia and suicide risk among patients with schizophrenia: preliminary findings of a cross-sectional study*. *Riv Psichiatr* 2011;46:31-7.
- ⁵⁸ Freyberger H. *Supportive psychotherapeutic techniques in primary and secondary alexithymia*. *Psychother Psychosom* 1977;28:337-42.
- ⁵⁹ Kim HW, Rim HD, Kim JH, et al. *Alexithymia and stress response patterns among patients with depressive disorders in Korea*. *Psychiatry Investig* 2009;6:13-8.
- ⁶⁰ Martin JB, Pihl RO. *The stress-alexithymia hypothesis: theo-*

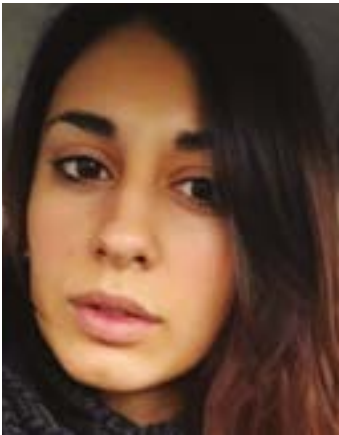
- rectical and empirical considerations*. *Psychother Psychosom* 1985;43:169-76.
- ⁶¹ Honkalampi K, Lehto SM, Koivumaa-Honkanen H, et al. *Alexithymia and tissue inflammation*. *Psychother Psychosom* 2011;80:359-64.
- ⁶² De Berardis D, Conti C, Iasevoli F, et al. *Alexithymia and its relationships with acute phase proteins and cytokine release: an updated review*. *J Biol Regul Homeost Agents* 2014;28:795-9.
- ⁶³ Ouellet-Morin I, Robitaille MP, Langevin S, et al. *Enduring effect of childhood maltreatment on cortisol and heart rate responses to stress: the moderating role of severity of experiences*. *Dev Psychopathol* 2019;31:497-508.
- ⁶⁴ Gerritsen L, Milaneschi Y, Vinkers CH, et al. *HPA axis genes, and their interaction with childhood maltreatment, are related to cortisol levels and stress-related phenotypes*. *Neuropsychopharmacology* 2017;42:2446-55.



The role of structured exercise in psychiatric rehabilitation

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Sport based rehabilitation final goal is not just an agonistic performance or just social inclusion, but the promotion of structured physical activities that through sport techniques is addressed to fight main psychopathological symptoms in the frame of every individual rehabilitative program.

The evidence connecting physical activity with improving wellbeing and mental health is well recognized and published ¹. The Royal College of Psychiatrists recognise exercise prescription as a treatment modality for a wide range of mental health conditions ².

Several studies ³ indicate that sport may positively influence the prognosis of some mental disorders that represent the most frequent causes of mental disability – including major depression, schizophrenia and Alzheimer's disease ⁴.

Sedentary life-style determines an important change of biological factors that support the good balance between mental and body functions and mood. In our body there is a sophisticated system of molecules performing as extracellular messengers mostly belonging to the nervous, endocrine, immune and muscular systems. Skeletal muscle would also be a sort of endocrine organ that, through contraction, stimulates the release of extracellular messengers (BDNF, dopamine, irisin, thermogenin, cytokine) influencing metabolism and modifying their production in tissues and organs. These substances stimulate the development of new nerve cells and increase the number of synapses, enhancing memory, learning and cognitive abilities.

Sport has a bio-psycho-social perspective and an important impact throughout life. Physical activity promotes neuroendocrine changes with antidepressant and anti-stress effects, improving mood and reducing arousal excess, constantly stimulating the sympathetic and parasympathetic neuro-vegetative system ⁵. Physical exercise raises the levels of norepinephrine and dopamine and the release of endorphins.

Many studies suggest the strong correlation between mental disorders and metabolic syndrome, due to the sedentary lifestyle of people suffering from these problems, which is an important risk factor for the onset of cardiovascular diseases, diabetes and cancer. In this regard, a study published in *Neuropsychiatric Disease and Treatment* in 2014 highlighted the prevalence of metabolic syndrome in schizophrenic individuals compared to the general population, and some recent meta-analyses have estimated that this percentage is 32.5% ⁶.

International scientific literature and guidelines on the treatment for mental disorders suggest to integrate pharmacological treatments with psychological and psychosocial interventions aimed at the prevention of risk factors and the modification of lifestyles ⁷.

Just as there are risk factors for mental disorders and mental suffering there are also protective factors: among these factors physical activity and sport are very important.

Sport represents an opportunity to observe the close relationship linking the three dimensions that characterize the psychophysical health of the human being: mind, body and social life; on the other hand it represents a place of action and of the relationship opposed to the "non-places" of mental distress and isolation.

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From the mid-1990s to the present, numerous “practices” of sport-based rehabilitation have developed in many Italian Mental Health Departments. Rehabilitation activities are carried out by various community-based facilities, sometimes in collaboration with amateur sport companies or sport promotion bodies. The territorial distribution of these sport-based rehabilitation programs is not uniform, resulting in a so called “patchy leopard” situation.

Furthermore, it is clear that a fragmented and episodic sports treatment, as Liberman states⁸, available only at the time of the exacerbation of symptoms or relapse, is incompatible with rehabilitation and recovery: for this reason, exercise should be continuous and included in every rehabilitation program.

The project *SPHERE - Sport Healing Rehabilitation*, coordinated by the *European Culture and Sport Organization* (ECOS) and co-funded by the *European Commission under the Erasmus + Sport 2018 Programme*, fits into this context and aims to define and validate a scientific sports protocol – implemented by psychiatrists, academic researchers and sports professionals – which will allow to identify virtuous models of rehabilitation through sport for psychiatric patients with different diagnoses and needs in order to improve their psychophysical well-being. The direct beneficiaries are the psychiatric patients in care at the national mental health departments of the various partner countries. The indirect beneficiaries are all the relevant stakeholders interested in promoting physical activity in psychiatric rehabilitation programs (gyms, coaches, sports federations, clinics, decision makers etc.). The main project outputs will be:

- review and digital map of good practices at European level on the use of sport in psychiatric rehabilitation;
- guidelines for the training of coaches involved in the pilot actions of the project;
- review of all data collected and analysed during the pilot actions with related monitoring indicators;
- scientific sports protocol to identify the most appropriate physical activity for psychiatric patients with different clinical situations;
- project documentary.

The definition and validation of the protocol, and in general of all the activities that will be implemented, will be supervised by a scientific committee appointed within the project, chaired by the psychiatrist Dr. Santo Rullo, who will coordinate the work, and composed of Dr. Stefania Cerino, psychiatrist and professional sports instructor, of Prof. Diane Crone, professor of Exercise and Health at *Cardiff Metropolitan University* (UK), and of Prof. Jürgen Beckmann, head of the Sports Psychology Department at the *Technical University of Munich* (Germany).

After an initial phase of mapping, study and analysis of European “practices” related to sport and psychiatric rehabilitation, the pilot actions will be carried out in Italy, Finland, Croatia and the United Kingdom. ECOS will identify a series of sports programs for the patients of the Italian rehabilitation experiences; the same will be done by 3 other

European partners (*Everton in the Community* in the United Kingdom, the *Finnish Sport Federation Tampere Region* in Finland, and the *Rijeka Sports Association for Persons with Disabilities* in Croatia) to involve a total of about 50 psychiatric patients.

Patients will be followed by a team composed of health professionals and qualified coaches of different sports and will follow programs defined specifically with the help of psychiatrists, while the coaches followed a course of “basic psychiatric approach” that took place in Brussels in October 2019. The psychiatrist who is in charge of the patients, assisted by his/her work group, will monitor sports activities according to indicators approved and defined by the scientific committee.

All the data collected and analysed during the pilot actions will contribute to the definition of the final scientific sports protocol.

In conclusion, the main objective of the project is to promote sport and physical activity in psychiatric rehabilitation programs according to a well defined evidence based approach at national and European level, in order to improve the social and psychophysical well-being of people suffering from mental disorders, thus fighting the stigma still existing around mental illness while improving social cohesion.

To this end, it becomes desirable that mental health specialists, including sports psychologists and psychiatric rehabilitation technicians, also collaborate with sports professionals to create psychiatric rehabilitation programs focused on structured physical activity.

References

- 1 Harvey SB, Øverland S, Hatch SL, et al. *Exercise and the prevention of depression: results of the HUNT cohort study*. *Am J Psychiatry* 2018;175:28-36.
- 2 Psychiatrists Royal College. *Physical activity and mental health*. www.rcpsych.ac.uk/healthadvice/treatmentwellbeing/physicalactivity.aspx.
- 3 Blumenthal JA, Sherwood A, Rogers SD, et al. *Understanding prognostic benefits of exercise and antidepressant therapy for persons with depression and heart disease: the UPBEAT study - rationale, design, and methodological issues*. *Clinical Trials* 2007;4:548-59.
- 4 Rössler W, Salize HJ, van Os J, et al. *Size of burden of schizophrenia and psychotic disorders*. *Eur Neuropsychopharmacol* 2005;15:399-409.
- 5 Corsale B. *Lo sport una palestra per la psiche*. *Strenght and Conditioning* 2012;5:81-4.
- 6 Mitchell AJ, Vancampfort D, De Herdt A, et al. *Is the prevalence of metabolic syndrome and metabolic abnormalities increased in early schizophrenia? A comparative meta-analysis of first episode, untreated and treated patients*. *Schizophrenia bulletin* 2013;39:295-305.
- 7 World Health Organization. *Mental health action plan 2013-2020 - 2013*, p. 14.
- 8 Liberman RP. *Il recovery dalla disabilità*. Roma: Giovanni Fioriti Editore 2012.



Treatment of Attention Deficit/ Hyperactivity Disorder and comorbid Bipolar Disorder: a brief review and preliminary clinical data

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Treatment of Attention Deficit/Hyperactivity Disorder (ADHD) and Bipolar Disorder (BD) are closely related, and adults with ADHD are four times more likely to have any mood disorder¹. Rates of ADHD comorbidity in bipolar disorder are between 9.5% and 21.2%, and rates of comorbid bipolar disorder in ADHD at 5.1% and 47.1% in some studies². Several studies suggest that adults with ADHD and BD may have worse outcomes and more severe clinical presentations compared to subjects without this comorbidity. In particular they usually display earlier age of onset of bipolar disorder³, more frequent affective episodes^{4,5}, more severe affective symptoms, shorter duration of wellness, lower educational achievement, more suicide attempts and more legal problems⁶⁻⁸. Due to a substantial overlap between mood and ADHD symptoms, it could be difficult to differentiate between the two conditions and some authors speculate that this large comorbidity is artifactual⁹. However ADHD symptoms generally do not respond to mood-stabilizers, persist after mood episodes have resolved, and improve with the administration of ADHD treatments⁹⁻¹³. Moreover neurobiologic studies suggest that BD + ADHD and MDD + ADHD are subtypes of BD and MDD that are heritable, have overlapping pathophysiologies, and are distinguishable from BD and MDD on a number of neurobiologic features⁹.

Even if data on literature and some expert opinion seems to clarify that the use of certain antidepressant and antipsychotic drugs used to control BD symptoms may worsen ADHD¹⁴, it has pointed out that specific treatments for ADHD symptoms (stimulants and atomoxetine) may be destabilizing for BD due to induction of psychotic and manic-like symptoms or Hypo/manic switches¹⁵. In a randomized, double-blind, crossover study Dorrego et al.¹⁶, compared lithium and MPH in the treatment of ADHD core symptoms. The results suggest that lithium is less effective than MPH.

At the best of our knowledge, only a few studies have been conducted in order to test the efficacy and/or safety of ADHD medications in adult populations with comorbid BD. Some evidences can be taken from studies on pediatric populations or on prescription of stimulants in patients with affective disorder without ADHD. More conclusions came from case report and case series.

McIntyre et al.¹⁷, conducted an open-label study of adjunctive flexible dose of LDX in the treatment of adults with stable bipolar I/II disorder and comorbid ADHD. 40 subjects received adjunctive LDX (mean dose = 60 ± 10 mg/day) to conventional pharmacotherapy and psychosocial interventions for BD. After 4 weeks, there was a significant reduction from baseline in the *ADHD Self-Report Scale* and in the *Montgomery-Åsberg Depression Rating Scale* total scores as well as the Clinical Global Impression Severity and Improvement score.

Two controlled studies were performed in pediatric populations with ADHD and BD. In the first, 40 subjects (6-17 years) with bipolar I disorder or bipolar II disorder (*Young Mania Rating Scale* score ≥ 14) were treated with divalproex sodium. 32 subjects achieved ≥ 50% reduction in YMRS baseline scores,

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no significant improvement in ADHD symptoms was observed. In placebo-controlled crossover phase, Mixed amphetamine salts was significantly more effective than placebo for ADHD symptoms. No significant side effects or worsening of manic symptoms was observed¹⁰. In the second, 16 patients (5-17 years) with ADHD and comorbid BD currently euthymic and treated with at least a mood stabilizer where randomized to receive placebo or MPH. At the endpoint, patient on MPH showed an improvement in ADHD symptomatology. Authors concluded that the addition of MPH did not cause a destabilization of mood symptoms¹¹.

Recently Viktorin et al.¹⁸, identified 2,307 adults with bipolar disorder who initiated therapy with methylphenidate and compare the rate of mania between subjects with and without concomitant mood-stabilizing treatment. Patients on methylphenidate without a concomitant mood-stabilizer showed an increased rate of manic episodes both within 3 months of medication initiation and between 3 and 6 months. Conversely, patients taking mood stabilizers had a significantly lower risk of mania after starting methylphenidate.

In 2000 another open label study try to demonstrate the efficacy and safety of methylphenidate in adult BD patients, type I and II, with a moderate depressive episode and without ADHD. 14 patient received MPH added to mood stabilizers and/or antipsychotics. At week 1 no proper (Hypo)manic switches were reported and half of the patients showed a decrease of severity of depressive symptoms¹⁹.

Few other naturalistic studies provide more evidence supporting a safe use of stimulants in adult BD patients without comorbid ADHD. Lydon and EL-Mallakh²⁰ found that MPH was well tolerated and efficacious for the treatment of depressive symptoms in 16 BD subjects observed after a long-term period (14 months). Similar results were reported by Carlson based on 8 charts of BD patients²¹. In a naturalistic trial 27 bipolar patients with treatment resistant depression were treated with stimulants. 5 experienced transient mood elevation and one reported a manic episode²².

Many authors point out the risk of stimulant induced psychotic and manic like symptoms. It has been estimated that such reactions are infrequent in children at therapeutic doses and they are dose dependent and of brief duration^{23,24}. However they could not be preventable²⁵, so patient treated with stimulant should be carefully monitored and comorbid conditions, such as BD, should be treated firstly^{2,26}.

At the date no RCT or other clinical studies on Atomoxetine (ATX) treatment in adult with ADHD and BD were published. Only one open label study exists in a pediatric population of 12 ADHD children and adolescents with ADHD and comorbid type I or II BD. ATX was added to mood stabilizer or antipsychotic, 8 subjects showed a good response and no one developed mania or mixed state even if 2 patients discontinued ATX due to worsening of mood symptoms¹³.

There are some reports of ATX-induced mania in pediatric populations²⁷⁻³⁰ and one in adults³¹. In a report of 153 pediatric patients treated with ATX, after a follow up (aver-

age time 6.39 weeks) 33% reported extreme irritability, aggression, mania, or hypomania. The concomitant treatment with mood stabilizers or antipsychotics did not protect or delay the onset of mood symptoms. Interestingly, 80% of patients showing "activation" had a prior personal history for mood symptoms, 61% had a positive family history for mood disorders, and 53% reported both³².

A naturalistic study has been conducted on a cohort of 168 adults diagnosed with ADHD, followed-up on an average of 6 years after first evaluation. 57 (51%) were still on treatment with methylphenidate (MPH) at follow-up. The second most common reason for discontinuation of treatment was the onset of affective symptoms. None of the subjects who had reported elevated mood or hypomania had been diagnosed with a bipolar disorder (BD) at baseline³³.

As regards non-first-line pharmacological treatments for ADHD in adults, Wilens et al. reported efficacy of bupropion on ADHD symptoms in a 6 week open trial on ADHD-BP adults patients without evidence of (hypo)manic switches.

Some authors tried to investigate whether the use of ADHD treatments (methylphenidate and atomoxetine) during childhood influence the risks of developing BD. Wng et al.³⁴, found that, in a cohort of 144,920 patients diagnosed with ADHD, patients with long-term use of methylphenidate were less likely to be diagnosed with BD compared to ADHD patients that had never taken methylphenidate.

Taken together, the results previously exposed seem to support some preliminary conclusions. First, in patients with ADHD and comorbid Bipolar Disorder the treatment of BD alone may result in residual symptoms of ADHD¹⁵. Second, patient should be treated hierarchically: when present, BD should be treated first while ADHD should be treated whenever a sufficient euthymic state is reached^{10,35}, combining ADHD medications and mood stabilizers¹⁵.

As regards our clinical experience, starting in 2015 we assessed 152 subjects at the S. Andrea Hospital's outpatients psychiatric service. The subjects were referred to our service in order to confirm a diagnostic hypothesis of persistent ADHD in adulthood. In a naturalistic setting, we started an observational study on ADHD-BP comorbidity and its treatment (paper in preparation). It was possible to confirm the diagnosis in 130 subjects through DIVA 2.0 clinical semi-structured interview. 90 of these subjects were subsequently treated and followed up at our services according to clinical needs. After achieving adequate mood stabilization, it was possible to treat with atomoxetine or methylphenidate 20 subjects with a diagnosis of bipolar disorder type II and comorbid ADHD. These subjects were matched to 20 subjects with a diagnosis of persistent ADHD and without bipolar comorbidity. Both in ADHD and in BP-II/ADHD subjects the choice between atomoxetine and methylphenidate was based on the efficacy/tolerability profile for each subject, including the presence of previous effective treatments with atomoxetine or methylphenidate in childhood and/or adolescence. The mean dose of atomoxetine was 65 ± 25 mg/day, while the mean dose of methylphenidate was 45 ± 15 mg/day.

As regards ADHD subjects 12 were males and 8 females,

13 were treated with atomoxetine and 7 with methylphenidate. As regards BP-II/ADHD subjects 7 were males and 13 females, 9 were treated with atomoxetine and 11 with methylphenidate. The mean age of the sample was 27.56 years.

After a three-months follow-up no manic, mixed or psychotic symptoms emerged and all the subjects remained clinically stable. Moreover, a one way ANOVA for repeated measures showed a significant decrease in the severity of ADHD symptoms as measured through ASRS in both groups ($F = 11.94$; $p = 0.003$). The BP-II diagnosis did not significantly influence the decrease in ADHD symptom severity at 3 months. This is in line with previous literature results, and supports a response-specificity of ADHD symptom severity and the possibility to effectively treat subjects with a BP-ADHD comorbidity once adequate mood stabilization is achieved.

References

- Kessler RC, Adler L, Barkley R, et al. *The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication*. Am J Psychiatry 2006;163:716-23. doi: 10.1176/ajp.2006.163.4.716.
- Wingo AP, Ghaemi SN. *A systematic review of rates and diagnostic validity of comorbid adult attention-deficit/hyperactivity disorder and bipolar disorder*. J Clin Psychiatry 2007;68:1776-84.
- Tamam L, Karakus G, Ozpoyraz N. *Comorbidity of adult attention-deficit hyperactivity disorder and bipolar disorder: prevalence and clinical correlates*. Eur Arch Psychiatry Clin Neurosci 2008;258:385-93. doi: 10.1007/s00406-008-0807-x.
- Tamam L, Tuglu C, Karatas G, et al. *Adult attention-deficit hyperactivity disorder in patients with bipolar I disorder in remission: preliminary study*. Psychiatry Clin Neurosci 2006;60:480-5. doi: 10.1111/j.1440-1819.2006.01535.x.
- Ryden E, Thase ME, Straht D, et al. *A history of childhood attention-deficit hyperactivity disorder (ADHD) impacts clinical outcome in adult bipolar patients regardless of current ADHD*. Acta Psychiatr Scand 2009;120:239-46. doi: 10.1111/j.1600-0447.2009.01399.x.
- Klassen LJ, Katzman MA, Chokka P. *Adult ADHD and its comorbidities, with a focus on bipolar disorder*. J Affect Disord 2010;124:1-8. doi: 10.1016/j.jad.2009.06.036.
- Karahmet E, Konuk N, Dalkilic A, et al. *The comorbidity of adult attention-deficit/hyperactivity disorder in bipolar disorder patients*. Compr Psychiatry 2013;54:549-55. doi: 10.1016/j.comppsy.2012.11.005.
- Nierenberg AA, Miyahara S, Spencer T, et al. *Clinical and diagnostic implications of lifetime attention-deficit/hyperactivity disorder comorbidity in adults with bipolar disorder: data from the first 1000 STEP-BD participants*. Biol Psychiatry 2005;57:1467-73. doi: 10.1016/j.biopsych.2005.01.036.
- Bond DJ, Hadjipavlou G, Lam RW, et al. *The Canadian Network for Mood and Anxiety Treatments (CANMAT) task force recommendations for the management of patients with mood disorders and comorbid attention-deficit/hyperactivity disorder*. Ann Clin Psychiatry 2012;24:23-37.
- Scheffer RE, Kowatch RA, Carmody T, et al. *Randomized, placebo-controlled trial of mixed amphetamine salts for symptoms of comorbid ADHD in pediatric bipolar disorder after mood stabilization with divalproex sodium*. Am J Psychiatry 2005;162:58-64. doi: 10.1176/appi.ajp.162.1.58.
- Findling RL, Short EJ, McNamara NK, et al. *Methylphenidate in the treatment of children and adolescents with bipolar disorder and attention-deficit/hyperactivity disorder*. J Am Acad Child Adolesc Psychiatry 2007;46:1445-53. doi: 10.1097/chi.0b013e31814b8d3b.
- Tramontina S, Zeni CP, Ketzner CR, et al. *Aripiprazole in children and adolescents with bipolar disorder comorbid with attention-deficit/hyperactivity disorder: a pilot randomized clinical trial*. J Clin Psychiatry 2009;70:756-64. doi: 10.4088/JCP.08m04726.
- Chang K, Nayar D, Howe M, et al. *Atomoxetine as an adjunct therapy in the treatment of co-morbid attention-deficit/hyperactivity disorder in children and adolescents with bipolar I or II disorder*. J Child Adolesc Psychopharmacol 2009;19:547-51. doi: 10.1089/cap.2009.0030.
- Perugi G, Ceraudo G, Vannucchi G, et al. *Attention deficit/hyperactivity disorder symptoms in Italian bipolar adult patients: a preliminary report*. J Affect Disord 2013;149:430-4. doi: 10.1016/j.jad.2012.12.010.
- Perugi G, Vannucchi G. *The use of stimulants and atomoxetine in adults with comorbid ADHD and bipolar disorder*. Expert Opin Pharmacother 2015;16:2193-204. doi: 10.1517/14656566.2015.1079620.
- Dorrego MF, Canevaro L, Kuzis G, et al. *A randomized, double-blind, crossover study of methylphenidate and lithium in adults with attention-deficit/hyperactivity disorder: preliminary findings*. J Neuropsychiatry Clin Neurosci 2002;14:289-95. doi: 10.1176/jnp.14.3.289.
- McIntyre RS, Alsuwaidan M, Soczynska JK, et al. *The effect of lisdexamfetamine dimesylate on body weight, metabolic parameters, and attention deficit hyperactivity disorder symptomatology in adults with bipolar III disorder*. Hum Psychopharmacol 2013;28:421-7. doi: 10.1002/hup.2325.
- Viktorin A, Ryden E, Thase ME, et al. *The risk of treatment-emergent mania with methylphenidate in bipolar disorder*. Am J Psychiatry 2017;174:341-8. doi: 10.1176/appi.ajp.2016.16040467.
- El-Mallakh RS. *An open study of methylphenidate in bipolar depression*. Bipolar Disord 2000;2:56-9.
- Lydon E, El-Mallakh RS. *Naturalistic long-term use of methylphenidate in bipolar disorder*. J Clin Psychopharmacol 2006;26:516-8. doi: 10.1097/01.jcp.0000236655.62920.dc.
- Carlson PJ, Merlock MC, Suppes T. *Adjunctive stimulant use in patients with bipolar disorder: treatment of residual depression and sedation*. Bipolar Disord 2004;6:416-20. doi: 10.1111/j.1399-5618.2004.00132.x.
- Parker G, Brotchie H. *Do the old psychostimulant drugs have a role in managing treatment-resistant depression?* Acta Psychiatr Scand 2010;121:308-14. doi: 10.1111/j.1600-0447.2009.01434.x.
- Ross RG. *Psychotic and manic-like symptoms during stimulant treatment of attention deficit hyperactivity disorder*. Am J Psychiatry 2006;163:1149-52. doi: 10.1176/appi.ajp.163.7.1149.
- Mosholder AD, Gelperin K, Hammad TA, et al. *Hallucinations and other psychotic symptoms associated with the use of attention-deficit/hyperactivity disorder drugs in children*. Pediatrics 2009;123:611-6. doi: 10.1542/peds.2008-0185.
- Kraemer M, Uekermann J, Wiltfang J, et al. *Methylphenidate-induced psychosis in adult attention-deficit/hyperactivity disorder: report of 3 new cases and review of the literature*. Clin Neuropharmacol 2010;33:204-6. doi: 10.1097/WNF.0b013e3181e29174.
- Schneider BN, Enenbach M. *Managing the risks of ADHD treatments*. Curr Psychiatry Rep 2014;16:479. doi: 10.1007/s11920-014-0479-3.
- Bahali K, Uneri OS, Ipek H. *Atomoxetine-induced mania-like symptoms in an adolescent patient*. Actas Esp Psiquiatr 2013;41:137-8.

- ²⁸ Hah M, Chang K. *Atomoxetine for the treatment of attention-deficit/hyperactivity disorder in children and adolescents with bipolar disorders*. *J Child Adolesc Psychopharmacol* 2005;15:996-1004. doi: 10.1089/cap.2005.15.996.
- ²⁹ Henderson TA. *Mania induction associated with atomoxetine*. *J Clin Psychopharmacol* 2004;24:567-8.
- ³⁰ Steinberg S, Chouinard G. *A case of mania associated with tomoxetine*. *Am J Psychiatry* 1985;142:1517-8. doi: 10.1176/ajp.142.12.1517.
- ³¹ Kumar V, Varambally S. *Atomoxetine induced hypomania in a patient with bipolar disorder and adult attention deficit hyperactivity disorder*. *Indian J Psychol Med* 2017;39:89-91. doi: 10.4103/0253-7176.198954.
- ³² Henderson TA, Hartman K. *Aggression, mania, and hypomania induction associated with atomoxetine*. *Pediatrics* 2004;114:895-6. doi: 10.1542/peds.2004-1140.
- ³³ Edvinsson D, Ekselius L. *Long-term tolerability and safety of pharmacological treatment of adult attention-deficit/hyperactivity disorder: a 6-year prospective naturalistic study*. *J Clin Psychopharmacol* 2018;38:370-5. doi: 10.1097/JCP.0000000000000917.
- ³⁴ Wang LJ, Shyu YC, Yuan SS, et al. *Attention-deficit hyperactivity disorder, its pharmacotherapy, and the risk of developing bipolar disorder: a nationwide population-based study in Taiwan*. *J Psychiatr Res* 2016;72:6-14. doi: 10.1016/j.jpsy-chires.2015.10.014.
- ³⁵ Asherson P, Young AH, Eich-Hochli D, et al. *Differential diagnosis, comorbidity, and treatment of attention-deficit/hyperactivity disorder in relation to bipolar disorder or borderline personality disorder in adults*. *Curr Med Res Opin* 2014;30:1657-72. doi: 10.1185/03007995.2014.915800.



Hypnotic Psychotherapy for Panic Disorder: an empirical comparison with Cognitive Psychotherapy

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Summary

Objective. To increase knowledge about indications for hypnotic psychotherapy in panic disorder.

Method. 39 panic disorder patients with or without agoraphobia were treated with hypnotic psychotherapy (n = 21) and with cognitive psychotherapy (n = 18). Patients were evaluated at baseline, at the end of treatment, and at the end of a 12-month follow-up period.

Results. Hypnotic psychotherapy: 1) promotes a panic free condition in 47% of patients at end of treatment, achieving 89% at 12-month follow-up; 2) is able to improve significantly the quality of life, showing high tolerability and low drop-out rate; 3) is statistically similar to cognitive psychotherapy in relapse/recurrence prevention.

Conclusions. Our data support hypnotic psychotherapy as a promising treatment for management of panic disorder patients.

Key words: hypnotic psychotherapy, cognitive psychotherapy, panic disorder, evidence-based medicine

Introduction

Panic disorder (PD), with a lifetime prevalence in the general population of 1% to 4%, does not describe a homogeneous diagnosis and therefore covers phenotypically discrete patient subtypes with genetic and/or environmental vulnerability^{1,2}. This may justify a range of prognoses and profiles of resistance to change requiring different treatments to respond to different and specific individual patient needs.

Current practice guidelines for the clinical management of PD have broadened the range of therapeutic proposals beyond pharmacological treatment as the only 'first choice' therapy supported by evidence based medicine (EBM) criteria³.

In the 2010 update⁴, the American Psychiatric Association (APA) recommended, in addition to the well-validated cognitive and behavioral therapies (CBT) and Cognitive Psychotherapy (CP), also panic-focused psychodynamic psychotherapy (PFPP), supportive therapy (ST), and Eye Movement Desensitization and Reprocessing (EMDR). The 2014 update⁵ to the British National Institute for Health and Care Excellence (NICE) guidelines confirmed the primacy of CBT, but also opened to new "unlicensed" therapeutic proposals, like computer-assisted cognitive-behavioral therapy (CCBT), mindfulness based cognitive therapy (MBCT), and metacognitive therapy (MT).

Nevertheless, it is not yet clear whether certain psychological therapies can be considered superior to others. This topic is crucial because the therapeutic strategy for PD requires a rich and differentiated range of cost-effective therapies to reduce both its socioeconomic and clinical impacts.

In this context, we studied Hypnotic Psychotherapy (HP), an innovative hypnotic practice promoted by Erickson's school^{6,7}, as a candidate for PD treat-

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ment. Hypnosis is recognized as a scientific discipline, able to adapt its therapeutic format to both clinical and experimental needs. HP has been found effective in many anecdotal case reports, alone or as hypnotically augmented CBT, in smoking cessation and posttraumatic stress disorder, anxiety, depression, and psychosomatic condition. However, no systematic studies have been made to ascertain its empirical efficacy in psychiatric disorders, although strongly recommended by the International Society of Hypnosis⁸.

In this article, we present our analysis: 1) to verify the efficacy and tolerability of HP in the short- and long-term management of outpatients with PD; 2) to apply evaluations with the same scales used in CP studies; 3) to replicate in the Italian population the standardized studies conducted in the international population; 4) to compare the impact of HP and CP in PD.

Materials and methods

General sample characteristics. The *inclusion criteria* were: 1) diagnosis of panic disorder, with or without agoraphobia, according to the DSM-IV criteria; 2) patients suffering from at least one panic attack a week, situational or unexpected, during the three weeks preceding the treatment. The *exclusion criteria* were adopted: 1) diagnosis of schizophrenia, depressive and bipolar disorder, alcohol and drug abuse, somatoform disorder, personality disorder; 2) diagnosis of generalized anxiety, obsessive-compulsive disorder, post-traumatic stress disorder; 3) presence of untreated or chronic disease and medical therapies that may cause panic disorder. The study is based on scores obtained from the clinical self-evaluation scales routinely used during therapy; however, the patients were informed on the use of these data for research and all gave their consent for research participation. No integrated therapy was considered.

Treatment characteristics. 21 PD outpatients, sequentially enrolled on an open naturalistic clinical trial, followed an original HP protocol of 10 weekly individual sessions, according to neo-Ericksonian HP practice⁹. Each patient entered a first 'standardized phase' (five sessions on basic clinical targets: working alliance, trance by direct and indirect hypnotic induction, focus on recent and early stressful life events, eliciting social and personal skills), followed by a second 'personalized phase' (five sessions on specific personal needs and resources: neuro-linguistic techniques and metaphorical approach with direct and indirect trance induction to cope with pathological patterns through an unconscious emotive-cognitive reprocessing). All patients were drug free

18 PD outpatients, enrolled in a controlled, non-randomized clinical trial¹⁰, received 10 weekly sessions, according to Andrews's guidelines for PD treatment¹¹, following a CP protocol, textbook supported, with standardized sessions (psycho-education focus, relaxation training, behavior and cognitive techniques, problem-solving techniques, conscious cognitive-emotional reprocessing of dysfunctional thoughts and beliefs). All patients were drug free.

Evaluation method

In accordance with empirically supported treatments guidelines¹², HP and CP used the same rating scales and timing of evaluation: at first contact before treatment (baseline assessment), at the end of treatment (treatment assessment) and at the end of a 12-month follow-up period (follow-up assessment). Data were analyzed statistically using the Chi square test with Yates correction and Student's t test.

Patients monitored their own daily panic attack frequency, duration and intensity, and phobic avoidance: this information was recorded on a weekly log. These panic logs were reviewed weekly at each session by the therapist to ensure accuracy of reporting. Moreover, the patients were assessed using patient self-reporting scales, Panic Attack and Anticipatory Anxiety Scale (PAAAS) by Sheehan and Phobia Scale (PS) by Marks & Sheehan for clinical symptomatology, Sheehan Disability Scale (DS) for quality of life.

The HP and CP impact on PD was evaluated as: 1) *treatment response*: $\geq 50\%$ reduction in the score of patient self-reporting symptomatology and of the quality of life scales compared to pretreatment baseline scores (*good response condition or responder patient*); 2) *remission*: absence of panic attacks (*panic free condition or remitted patient*).

The reappearance of panic attacks and/or the need for a psychotherapist or medical help (i.e., administration *ex novo* of medication, extra session of the psychological therapy in the follow-up period) were considered *relapse* in the first 6 months and *recurrence* of disease in the following 6 months.

A voluntary interruption of therapy is considered treatment dropout. The *tolerability* is evaluated as: 1) presence or absence of side effects, assessed by psychiatrist; 2) severity of side effects, assessed by psychiatrist: 1 = mild, no danger, no treatment; 2 = does not significantly interfere with patient's life; 3 = significantly interferes with patient's life; 4 = serious, counteracts the therapeutic effect and requires specific treatment.

The baseline socio-demographic and clinical characteristics of completer patients, compared between HP and CP samples, were well matched for gender, age average and range, marital status, co-diagnosis of agoraphobia, time since diagnosis, family history for psychiatric diseases, age of onset, severity of anxiety rated with Hamilton Anxious Rating Scale by psychiatrist.

Results

Hypnotic psychotherapy alone

Two of 21 enrolled patients leave treatment (dropout rate: 9%). Table I shows the HP response in the 19 completers at the baseline (T0), at the end of treatment (T1) and at the end of 12-month follow-up (F12).

Compared to baseline, the average number of weekly panic attacks evaluated with PAAAS decreases with high statistical significance, respectively, at the end of treatment

(T0 = 10 vs T1 = 2; Student's t paired = 4.6; $p < 0.0002$) and at the end of 12-month follow-up (T0 = 10 vs F12 = 0.39; Student's t paired = 5.1; $p < 0.0001$). Compared to baseline, the average weekly PS score also decreases significantly at end of treatment (T0 = 7 vs T1 = 4.3; Student's t paired = 2.3; $p < 0.02$) and at end of 12-month follow-up (T0 = 7 vs F12 = 3; Student's t paired = 3.4; $p < 0.002$). Moreover, the average weekly DS score decreases significantly from baseline to end of treatment (T0 = 17 vs T1 = 8; Student's t paired = 3.4; $p < 0.002$) and to end of 12-month follow-up (T0 = 17 vs F12 = 6.5; Student's t paired = 2.9; $p < 0.009$).

Comparisons between HP and CP

Clinical response at the end of treatment. Table II shows no statistical differences between the different groups for responder rate in the PAAAS, PS and DS scores (Chi square Test, p ns). By contrast, the panic free condition rate is higher in CP sample (94%) than that in HP sample (47%) with statistically significant difference (CP vs HP: Chi square test = 7.1, $p < 0.01$).

Dropout and tolerability. Table III shows similar low profiles rates for both HP and CP in dropout number and side effect presence.

Clinical response at the end of 12-month follow-up. Table IV shows no changes of statistical relevance can be

found in the comparison between HP and CP samples at 12-month follow-up. The PAAAS response rate and the positive impact on phobic behaviors and quality of life were similar in both treatments. By contrast, although the panic free condition index was statistically similar between HP and CP (HP 89% vs CP 59%: Chi square test = 3, p ns), their profile of change was different for specific therapy. In HP sample, the panic free condition was found in 9 of 19 patients (47%) after treatment, increasing with statistical significance to 17 of 19 (89%) through the follow-up period (Chi square test = 5.9, $p = 0.01$). In CP sample, the number of panic free patients decreased long term from 16 of 17 patients (94%) until 10 of 17 patients (59%) without statistical significance (Chi square test = 4, p ns) and maintaining a good response profile compared with CP baseline assessment.

Discussion

The study, the first in Italian literature to our knowledge, shows HP is able to adapt its therapeutic format to the needs of clinical research with good efficacy and tolerability. Using MEDLINE and PSYCHINFO, we searched systematic reviews and meta-analyses of EBM hypnosis validation efficacy published over the last 15 years. We found only one meta-analysis showing HP as EBM effec-

Table I. Response to hypnotic psychotherapy in 19 PD completers.

Variables	Baseline T0 average	Treatment T1 average	t paired T0 vs T1	Follow-up F12 average	t paired T0 vs F12
PAAAS score	10	2	$p < 0.0002$	0.39	$p < 0.0001$
PS score	7	4.3	$p < 0.02$	3	$p < 0.002$
DS score	17	8	$p < 0.002$	6.5	$p < 0.009$

Table II. Comparison between Hypnotic Psychotherapy (HP) and Cognitive Psychotherapy (CP) at the end of acute therapy of 36 DP patients.

Variables	Treatment CP	Treatment HP	Statistical significance CP vs HP
Completers	17	19	
Panic free	16 (94%)	9 (47%)	$p < 0.01$
PAAAS responder	17 (100%)	15 (79%)	p NS
PS responders	7 (41%)	8 (42%)	p NS
DS responders	7 (41%)	10 (52%)	p NS

Table III. Tolerability at the end of panic disorder treatment of 36 completers.

Treatment	Patients without side effects	Patients with side effects No. (%)	Severity of side effects 1-2 No. cases	Severity of side effects 3-4 No. cases
CP	15	2 (12)	2	1
HP	17	2 (10)	2	0
TOT	32	4		

Treatment	Completers	Dropouts
CP	17	1 (5%)
HP	19	2 (9%)

Table IV. Comparison between Hypnotic Psychotherapy (HP) and Cognitive Psychotherapy (CP) at the end of 12-months in 36 DP patients.

Variables	Treatment	Treatment	Statistical significance CP vs HP
	CP	HP	
Completers	17	19	
Panic free	10 (59%)	17 (89%)	p NS
PAAAS responders	16 (94%)	19 (100%)	p NS
PS responders	10 (59%)	13 (72%)	p NS
DS responders	12 (70%)	14 (72%)	p NS

tive and safe treatment for irritable bowel syndrome¹³, but there is no evidence of direct controlled studies comparing HP with drugs and/or other psychological therapies in PD. Adopting the empirically supported treatment (EST) criteria of the American Psychological Association¹², we therefore decided to compare the results on PD of our HP sample with those achieved by CP, as standard of EBM validated treatment commonly recommended in international and Italian guidelines.

First, we used a previous study of CP versus pharmacotherapy¹⁰ as separate control group database to compare HP effectiveness with that of CP. Then, we compared our results with those from the literature of other controlled CP studies compatible with our experimental evaluative design.

Although our findings have limitations in terms of sample size, experimental planning (patients not randomized, no blind evaluations, comparison between two separate open trials) and statistical evaluation (no multivariate statistical analysis), they nonetheless offer a basis for remarks useful in the therapeutic practice.

Quantitatively, our HP protocol, the first used in Italian literature to our knowledge, compared to baseline evaluation, shows a statistically significant reduction in the average number of weekly panic attacks and phobic complications, with an improvement of patient's living quality, at the end of both treatment and follow-up evaluations.

HP maintains and reinforces the good clinical response, progressively improving the panic free condition rate from 47% present after treatment to 89% at follow-up, while CP achieves long-term panic attacks remission in 59% of cases, but loses one third of its acute remission rate (94%). Acute HP remission rate is similar only to that of CP (53%) reported by Black¹⁴, but is substantially lower than those (87%, 88%, 70%) reported, respectively, by Klosko¹⁵, Clark¹⁶ and Sharp¹⁷ in their CP samples, in line with that (94%) of our CP group.

HP dropout rate (9%; one of two patients suffers from pregnancy complications) is slightly higher than that of our CP group (5%; one patient leaves therapy for extra-clinical reasons) and that of CP (6%) reported by Clark (18), but consistently lower than those of CP (16%, 30% and 36%) reported, respectively, by Klosko¹⁵, Sharp¹⁷, and Black¹⁴. Additionally, analyzing a variable often overlooked in clinical studies, HP and CP also produce undesired side effects in our patients, respectively in 10% (2 cases only mild: one for persistent nightmares and insomnia, one for nervousness and muscular tension) and 12% (2 cases for

somatic anxious reaction in homework which in one case creates a serious dissociative status). These percentages show HP, like CP, as a treatment well tolerated and recommendable in patients with high clinical history for hypersensitivity to drug side effects and for counter-indications to drugs.

Interestingly, HP brings 89% of patients to panic free condition at follow-up in line with that of CP (85%) in Clark's sample¹⁶, but superior to that (54%) of the CP Sharp's sample¹⁷, and exactly equal to that (59%) of our CP sample.

In general, the clinical cost-benefit of our HP 10-session protocol follows faithfully that of CP 8-12 session protocol, supported in CP meta-analysis studies in terms of EBM effectiveness in 78% of PD treated cases^{18,19} and long term stability of results²⁰.

The high rate of PD relapse and recurrences^{1,2} is a well-known problem that needs effective long-term strategies, pharmacological and psychological, for prevention of the disease and its complications. Our results seem to confirm general evidence that a residual PD process, active but hidden below the perceived symptomatological threshold after the end of treatment, could produce long-term relapses or recurrences of PD².

In contrast to widespread preconceptions, hypnosis is not authoritarian, passive and centered around the therapist, but a resource- and solution-oriented method in which the focus is on the patient's own potential. Waking suggestions in ordinary communications, restructuring of cognitive-affective patterns and of emotionally stressful events or sensations are the specific keys with which HP opens the door for reintegration of non-accessible (dissociated) feelings, often closed or resistant to change with problem-solving and cognitive mindful techniques.

Qualitatively, first, HP, like CP, has shown a similar ability to elicit affective, emotive and social resources in treated patients, to reprocess negative beliefs, and to implement new adaptive psychosocial skills to cope with stressful life events improving short term the impact of PD.

Second, our findings may indicate the hypothesis that the different patterns of long-term response among the treatments support specific PD subgroups in terms of resistance to change and/or to treatment. This may justify a range of prognoses and of profiles of recurrence rates to different treatments.

HP is able to focus on unconscious emotive memory stored after the impact of old stressful or traumatic experiences^{21,22} which create altered states of consciousness dissociated

from cognitive elaboration, but which flood from the past into the cognitive and emotive functions in the present moment⁷. HP works directly on the unconscious mind, without the need for conscious and rational learning. Thanks to this specific mechanism of action, unlike those of drugs and CP, HP could be more effective for management of patient subgroups with high resistance to treatment due to a posttraumatic and dissociative processes history. Our results could be a starting point for further investigations. This finding may contribute to enrich the field of empirically validated psychological treatments recommendable in national and international Guidelines as alternative strategies to the traditional management of PD²³.

Conclusions

In general, the efficacy-tolerability rate comparisons between HP and CP trials support some general and practical evaluations. Alone, HP shows a long maintenance of PD remitted condition without need of extra support health plans. On the other hand, integrated with another validated therapy, HP could meet clinical indications in the therapeutic plan of specific subgroups, like patients with a high level of resistance to change, with PD recurrence history after an effective CP acute treatment, and with no tolerance to drug side effects.

Pending confirmation from large samples and multivariate statistical analysis, our study, the first experimentally based in Italian literature to our knowledge, seems to indicate HP as a new interesting alternative treatment in the practice guidelines for PD therapy.

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Take home messages for psychiatric care

- Hypnosis is not authoritarian, passive and centered around the therapist, but a resource- and solution-oriented method in which the focus is on the patient's own potential
- Hypnotic psychotherapy, a new hypnotic practice promoted by Erickson's school, is able to adapt its therapeutic format to the needs of panic disorder clinical research with short-term good efficacy and tolerability. Long term, the hypnotic psychotherapy maintains and reinforces the good clinical response and remission outcomes
- Alone or integrated with other panic disorder therapies, like drugs and cognitive psychotherapy, hypnotic psychotherapy could be proposed in acute and long-term treatment of outpatients, with specific indication in cases resistant either to change or to the other evidence based medicine validated treatments

References

- 1 Mavissakalian MR, Prien RF. *Long-term treatments of anxiety disorders*. APA Press. Inc. 1996.
- 2 Palazzo L, Biondi M. *Il problema delle ricadute nel Disturbo di Panico dopo il termine di un trattamento*. Rivista Italiana di Psichiatria 2004;39:1-20.
- 3 Sackett DL Richardson WS, Rosenberg W, et al. *Evidence-Based Medicine*. New York: Churchill Livingstone 1997.
- 4 American Psychiatric Association. *Practice Guidelines for the treatment of patients with Panic Disorders*. Second Edition. APA 2010.
- 5 National Institute for Health and Care Excellence. *Clinical guidelines, Panic Disorder. Recognition and management*. 2014. www.nice.org.uk/guidance/cg113
- 6 Yapko DM. *Trancework: an introduction to the practice of clinical hypnosis*. New York: Brunner-Routledge 2003 (*Lavorare con l'ipnosi. Un'introduzione alla pratica clinica*. Milano: Franco Angeli 2011).
- 7 AMISI. *Hypnosis, hypnotic psychotherapy and 'neoericksonian' principles: a theoretical didactic manifesto, update*. ESH Newsletter 2016;2:14.
- 8 Alladin A, Sabatini L, Amundson JK. *Evidence-based practice in clinical hypnosis*. Int J Clin Exp Hypn 2007;55:115-30.
- 9 Calzeroni A, Mosconi GP. *Psicoterapia Ipnotica: l'approccio neoericksoniano per la cura del DAP*. In: Rovetto F, ed. *Panico*. Roma: Il Pensiero Scientifico Editore 2003.
- 10 Calzeroni A, Cammarano M, Sileoni A, et al. *Cognitive psychotherapy, pharmacotherapy and their integration for panic disorder: an acute and 12-months follow-up study*. Italian Journal for Psychiatry and Behavioural Sciences 2004;14:79-88.
- 11 Andrews G, Crino R, Hunt MG, et al. *The treatment of Anxiety Disorders*. New York: Cambridge University Press 1994. (*Il trattamento dei disturbi d'ansia*. Torino: Centro Scientifico 2003).
- 12 Chambless DL, Baker MJ, Baucom DH, et al. *Update on empirically validated therapies, II*. The Clinical Psychologist 1998;51:3-16.
- 13 Schaefer R, Klose P, Moser G, et al. *Efficacy, tolerability, and safety of hypnosis in adult irritable bowel syndrome: systematic review and meta-analysis*. Psychosom Med 2014;76:389-98.
- 14 Black DW, Wesner R, Bowers W, et al. *A comparison of fluvoxamine, cognitive therapy, and placebo in the treatment of panic disorder*. Arch Gen Psychiatry 1993;50:44-50.
- 15 Klosko IS, Barlow DH, Tassinari RH, et al. *Comparison of alprazolam and cognitive-behaviour therapy for panic disorder*. J Couns Clin Psychol 1990;58:77-84.
- 16 Clark DM, Salkovskis PM, Hackmann A, et al. *A comparison of cognitive therapy, applied relaxation and imipramine in the treatment of panic disorder*. Brit J Psychiatry 1994;164:759-69.
- 17 Sharp MA, Kevin G, Power MA, et al. *Fluvoxamine, placebo and cognitive behavior therapy alone and in combination in the treatment of panic disorder and agoraphobia*. J Anxiety Disord 1996;10:219-42.
- 18 Caselli G, Manfredi C, Ruggiero GM, et al. *La terapia cognitivo-comportamentale dei disturbi d'ansia: una revisione degli studi d'efficacia*. Psicoterapia Cognitiva e Comportamentale, 2016, 22, 1, 81-101.
- 19 Ost LG. *Efficacy of the third wave of behavioral therapies: a systematic review and meta-analysis*. Behav Res Ther 2008;46:296-321.
- 20 Norton PJ, Price EP. *A meta-analytic review of cognitive-be-*

- havioral treatment outcome across the anxiety disorders. J Nerv Ment Dis 2007;195:521-31.*
- ²¹ Bukner R, Andrews-Hanna J, et al. *The brain's default network: anatomy, function and relevance to disease. Ann N Y Acad Sci 2008;1124.*
- ²² Schacter DL, Addis DR. *Neuroscience of constructive memory: remembering the past and imagining the future. Journal Philos Trans R Soc Lond B Biol Sci 2007;362(1481).*
- ²³ Pompili A, Furukawa TA, Imai H, et al. *Psychological therapies for panic disorder with or without agoraphobia in adults: a network meta-analysis. Cochrane Database Syst Rev, 2016;13:CD011004.*



A case of *folie à trois*: a multidimensional clinical experience

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Summary

The shared psychotic disorder (or *folies à deux* et *à trois*) is a quite uncommon pathology characterized by delusions shared among two or more subjects (usually close relatives). Even if it is well described in DSM 5 its diagnosis is difficult and a very detailed medical history is needed to detect it and treat it correctly. In this case report we present the case of three patients affected by *folies à trois*.

Key words: *folie à trois*, shared psychotic disorder, management

Introduction

The shared psychotic disorder (or *folies à deux* et *à trois*) is included in the "Schizophrenia spectrum and other psychotic disorders" section of the 5th edition of the *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)*¹. Lasègue e Falret defined it as a disorder characterized by delusional ideas transferred from one subject (*inducer*) to another (*induced*). The *inducer*, in particular, has usually a dominant role and is also the intellectual leader². Another important aspect that could facilitate the shared psychotic disorder, is the social isolation and the presence of non-bizarre delusions linked to true life events common to all the subjects who share symptoms^{3,4}. Moreover, cases of shared psychotic disorder are more common among relatives and that supports the hypothesis of a genetic vulnerability⁵.

Case report

As consequence of a warning from a psychiatrist of the Mental Health Service of Chieti, alerted by a family doctor, Mr. C.A. and Mrs. S.T were conducted to the Emergency Room of the Hospital "S.S. Annunziata" Chieti on the 24th June 2017. During the psychiatric consultation, Mrs. S.T. was inappropriate and incoherent, revealing persecutory delusions. She had no insight of disease. The score of the Positive and Negative Syndrome Scale (PANSS) was 126 (Fig. 1). Since the patient refused any medication, the psychiatrist requested the involuntary psychiatric treatment and she was therefore admitted at the psychiatry ward of the hospital "F. Renzetti" of Lanciano.

In the meanwhile, Mr. C.A. showed delusions (paranoid and damage delusion), depressed mood characterized by huge psychic pain, and low levels of personal care and self-hygiene. His PANSS score was 105. The score of the Hamilton Rating scale for Depression (HAM-D21items) was 37 (Fig. 1), confirming severe depression. The patient was admitted at the psychiatry ward of Chieti. The psychiatrist disposed that the patients should be admitted in different hospitals in order to separate them and facilitate the treatments. During the clinical interview, it emerged that they both lived with their only son, in a severe condition of social isolation due to the psychotic distress linked to the content of the delusions. They all shared the delusional idea that an

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Arabic ancestor of Mr. C.A. bought 2500 hectare of land and left to the heirs 40 kg of 8 carats gold. During the past months they had sued many times “mean and jealous people”, mostly neighbors, that, according to their belief, stole all their property. The family, because of the bills of the great amount of legal complaint, lived in poverty and had accumulated many debts.

Their son, F.A., a 45 years old man, needed psychiatric assessment as well, but he escaped the Emergency Room that day. The police found him two days later and conducted him back to the hospital. He underwent to an involuntary psychiatric treatment at the hospital of Giulianova, always to keep all members of family separated. The PANSS score of F.A. was 97 (Fig. 1). On the 18th of July Mrs. S.T. was moved to the department of psychiatry of Chieti since it was not possible to discharge here and let her go back home (the hygienic conditions of their house were poor and the social operators needed more time to adjust another accommodation). Furthermore, that was a good opportunity to carefully reunite the family in a controlled environment such as the hospital.

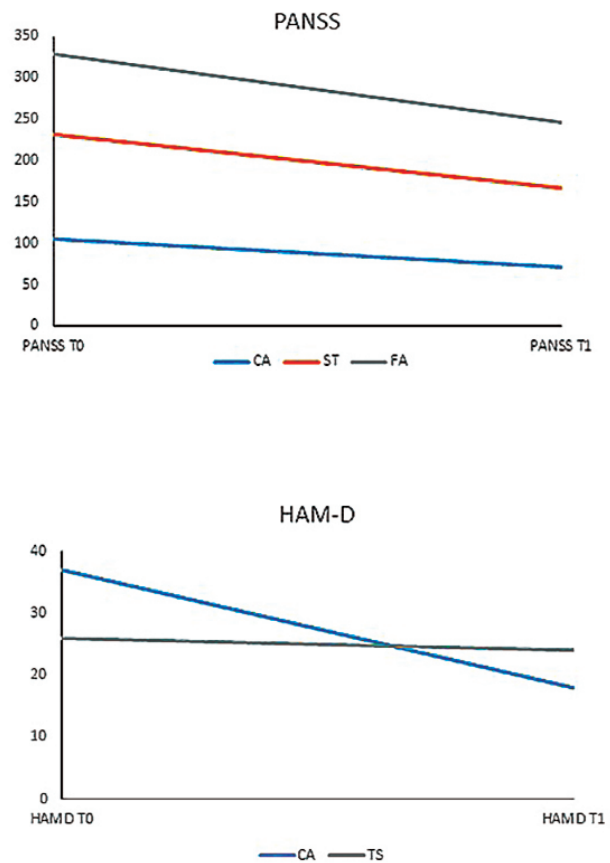
Mrs. S.T. was dismissed with her husband on the 28th July 2017 with psychopharmacological therapy with Haloperidol 3 mg/day, while her husband received a prescription of risperidone 2 mg/day and lorazepam 1mg/day. Their son was dismissed and transferred to a private facility for psychiatric disorders in order to stabilize the therapy composed by a long acting injection of Haloperidol decanoate 100 mg/20days, clonazepam 5 mg/day and risperidone 6 mg/day.

The day of discharge all patients showed a significant improvement of symptoms with an important reduction of delusions as confirmed by the PANSS scores (Fig. 1).

Discussion

The improvement of symptoms suggests that even though the pharmacological therapy is necessary, it is also important to obtain a detailed anamnesis to identify all the psychopathological elements that are fundamental to the diagnosis of the Lasègue Farlet syndrome¹. In fact, according to our opinion, the forced detachment of the inducer from the induced was crucial to interrupt the influence he had on her. In particular, even if some elements and some delusional ideas endured (as it is often observed by clinicians), those were less pervasive and, as consequence, even the mood improved.

All these elements seem to confirm that a valid tool to improve the psychopathology of patients affected by *folies à trois* (or shared psychotic disorder) could be the treatment in separated wards.



HAMD: Hamilton Depression Rating Scale; PANSS: Positive And Negative Schizophrenic Symptoms

Figure 1.

Psychometric evaluation before and after hospitalization.

References

- Vigo L, Ilzarbe D, Baeza I, et al. *Shared psychotic disorder in children and young people: a systematic review*. Eur Child Adolesc Psychiatry 2019;28:1555-66. <https://doi.org/10.1007/s00787-018-1236-7>
- Lazarus A. *Folie a deux in identical twins: interaction of nature and nurture*. Br J Psychiatry 1986;148:324-6.
- Shah K, Breitinger S, Avari J, et al. *Late-onset folie à deux in monozygotic twins*. Schizophr Res 2016. <https://doi.org/10.1016/j.schres.2016.10.038>
- Arnone D, Patel A, Tan GM-Y. *The nosological significance of Folie a Deux: a review of the literature*. Ann Gen Psychiatry 2006;5:11. <https://doi.org/10.1186/1744-859X-5-11>
- Lazarus A. *Folie a deux: psychosis by association or genetic determinism?* Compr Psychiatry 1985;26:129-35.