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# Combined treatment of borderline personality disorder with interpersonal psychotherapy and pharmacotherapy: Predictors of response

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## ABSTRACT

Borderline personality disorder (BPD) is characterized by affective instability, impulsive behaviors, and disturbed interpersonal relationships. A previous study of our group found that combined therapy with interpersonal psychotherapy adapted to BPD (IPT-BPD) and fluoxetine was superior to single pharmacotherapy in BPD patients. The aim of the present study was to examine what clinical factors predicted response to combined therapy in patients evaluated in the previous efficacy study. The subgroup of 27 patients allocated to combined therapy was analyzed. Patients were treated for 32 weeks with fluoxetine 20–40 mg/day plus IPT-BPD. Patients were assessed at baseline and week 32 with an interview for demographic and clinical variables, CGI-S, HDRS, HARS, SOFAS, BPDSI, and SAT-P. Statistical analysis was performed with multiple regression. The difference of CGI-S score between baseline and week 32 ( $\Delta$ CGI-S) was the dependent variable. Factors significantly and independently related to  $\Delta$ CGI-S were the BPDSI total score and the items abandonment, affective instability, and identity. Patients with more severe BPD psychopathology and with a higher degree of core symptoms such as fear of abandonment, affective instability, and identity disturbance have a better chance to improve with combined therapy with fluoxetine and IPT-BPD.

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## 1. Introduction

Borderline personality disorder is a complex and severe mental disorder that is characterized by a pervasive pattern of instability of interpersonal relationships, self-image and emotions, and impulsive behaviors. It affects approximately 1–5% of the general population and as many as 25% of psychiatric outpatients (Gunderson and Ridolfi, 2001; Torgersen et al., 2001; Grant et al., 2008; Perroud et al., 2010). The long-standing impairment in functioning and personal distress are extensively documented in BPD. Patients affected by this disorder often require high treatment costs through broad use of psychiatric services (National Institute for Mental Health in England, 2003; Ansell et al., 2007), stemming in part from their instability in affect and interpersonal relationships.

In the last two decades a growing number of studies about psychotherapy of BPD have been performed and several treat-

ent models have shown some evidence of efficacy, including mentalization-based therapy (Bateman and Fonagy, 1999, 2008), dialectical behavior therapy (Linehan, 1993; Linehan et al., 1999, 2006; Verheul et al., 2003), cognitive therapy (Davidson et al., 2006), schema-focused therapy (Kelloff and Young, 2006; Giesen-Bloo et al., 2006), and systems training for emotional predictability and problem solving (STEPPS) (Blum et al., 2002). As for transference focused therapy (Clarkin et al., 2007; Yeomans et al., 2007), efficacy in BPD patients can be questioned as results of two controlled trials lead to divergent conclusions (Doering et al., 2010; Giesen-Bloo et al., 2006). A recent addition to these proposals is represented by interpersonal psychotherapy adapted to BPD (IPT-BPD), an intervention specifically designed for BPD patients to deal with problems in interpersonal contexts (Markowitz, 2005; Markowitz et al., 2006; Bellino et al., 2010).

The standard model of IPT for major depression was modified by Markowitz (2005) to address the peculiar characteristics and the complex psychopathology of patients with BPD. Authors conceptualized BPD as a mood-inflected chronic illness with recurrent outbursts of anger requiring prolonged duration of treatment up to 34 sessions over 8 months, and provided a more flexible setting to handle crises and improve compliance.

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This modified version of IPT (IPT-BPD) shows some relevant similarities with other effective psychotherapies, such as a clear treatment framework, attention to affect, focus on treatment relationship, active role of therapist, change-oriented interventions (Weinberg et al., 2011).

Combination of a specific psychotherapy for BPD patients with drug therapy, i.e. serotonergic antidepressants, is common in clinical practice and was recommended as first choice for patients with affective dysregulation and impulsive-behavioral dyscontrol by the American Psychiatric Association treatment guidelines (American Psychiatric Association, 2001; Oldham, 2005). Moreover, there is some evidence that psychotherapy may enhance pharmacotherapy effects (Herpertz et al., 2007; Lieb et al., 2010; Stoffers et al., 2010).

In a randomized controlled study (Bellino et al., 2010) we compared single pharmacotherapy with fluoxetine 20–40 mg/day and combined therapy with IPT-BPD plus fluoxetine at the same dose in a sample of BPD outpatients with no psychiatric comorbidity. Results highlighted that combined therapy with IPT-BPD was superior to fluoxetine monotherapy with respect to three of the core symptoms of BPD (interpersonal relationships, affective instability, and impulsivity), anxiety symptoms and subjective quality of life (subjective perception of psychological and social functioning). According to these initial results, combination of antidepressants and adapted IPT can be considered as a potentially useful intervention in this clinical population. Nevertheless, the combined approach requires a large investment of clinical and economical resources and it should be targeted on selected patients. The need to provide clear indications for combined therapy can be addressed by investigating clinical predictors of response to this treatment modality.

The aim of the present study was to examine what demographical and clinical characteristics predicted response to combined therapy with IPT-BPD in the sample of BPD patients assessed in our previous study of efficacy (Bellino et al., 2010). Our hypothesis is that the association of the two treatments has more chances to induce a clinical response in patients with specific BPD symptoms, independently of general psychopathology and symptoms of anxiety and depression.

## 2. Methods

The present study is a further evaluation of the same BPD patients already included in our previous investigation (Bellino et al., 2010). The subgroup of 27 patients randomly allocated to combined therapy with fluoxetine 20–40 mg/day plus IPT adapted to BPD was analyzed. Methods concerning trial design, selection and randomization of patients, and assessment instruments were the same.

Participants were enrolled from outpatients attending the Centre for Personality Disorder of Psychiatric Clinic, Department of Neuroscience, University of Turin, Italy, from January to December 2007. Consecutive outpatients who received a DSM-IV-TR diagnosis of BPD were included. Exclusion criteria were: a lifetime diagnosis of delirium, dementia, amnesic disorder, or other cognitive disorders; schizophrenia or other psychotic disorders; bipolar disorder; a concomitant diagnosis of any Axis I or II disorder. Diagnoses were made by an expert clinician and were confirmed using the Structured Clinical Interview for DSM-IV Axis I or II disorders (First et al., 1997a, 1997b). Patients of childbearing age were excluded if they were not using an adequate method of birth control according to the judgment of the clinician. Patients were also excluded if receiving psychotropic drugs in the last 2 months and (or) psychotherapy in the last 6 months. The study was approved by the Ethical Committee of our University Hospital. Written informed consent was obtained from all patients prior to their participation. Declaration of Helsinki guidelines were followed.

Patients analyzed in the present study were those treated with fluoxetine 20–40 mg/day associated with IPT-BPD. Psychotherapy was provided by a therapist who was not the psychiatrist prescribing medication and who had at least 5 years of experience practicing IPT. Sessions of psychotherapy were steadily supervised by a senior psychotherapist (S.B.) with particular attention to check for fidelity to the manual. Pharmacotherapy and psychotherapy were started at the same time and lasted 32 weeks. Thirty-four sessions of IPT-BPD were provided.

Patients were assessed at baseline and week 32 with the following instruments: a semi-structured interview for clinical and demographical characteristics; the severity item of the Clinical Global Impression scale (CGI-S) (Guy, 1976); the Hamilton scales for depressive and anxious symptoms (HDRS, HARS) (Hamilton, 1959, 1960); the Social and Occupational Functioning Assessment Scale (SOFAS) (Goldman et al., 1992); the Satisfaction Profile (SAT-P) (Majani and Callegari, 1998); and the Borderline Personality Disorder Severity Index (BPDSI) (Arntz et al., 2003).

The CGI is a clinician-rated instrument to make global assessment of illness and consists of three different measures: severity of illness, global improvement, and efficacy index (comparison between patient's baseline condition and a ratio of current therapeutic benefit and severity of side effects). In this study, we considered the first scale: severity of illness. It is a seven-point scale that requires the clinician to rate the severity of illness at the time of assessment: (1) normal, (2), borderline mentally ill, (3) mildly ill, (4) moderately ill, (5) markedly ill, (6) severely ill, and (7) extremely ill.

The HDRS is a clinician-rated scale that scores severity of 21 depressive symptoms in the last week. Items are variably scored 0–2, 0–3, or 0–4, with a total score ranging from 0 to 64. Higher scores indicate more severe symptoms of depression.

The HARS is a clinician-rated scale scoring severity of 14 symptoms of anxiety in the last week. Items are all scored 0–4, with a total score ranging from 0 to 56. Higher scores indicate more severe anxiety symptoms.

The SOFAS is a clinician-rated scale to measure a patient's impairment in social and occupational areas. It is independent of the psychiatric diagnosis and the severity of the patient's symptoms. The score is ranged between 0 and 100. Higher scores indicate a better functioning.

The SAT-P is a self-administered questionnaire consisting of 32 scales which provides a satisfaction profile in daily life and can be considered as an indicator of subjective quality of life. The SAT-P considers five different factors: "psychological functioning"; "physical functioning"; "work"; "sleep, food, and free time"; and "social functioning". The SAT-P asks the patient to evaluate his satisfaction in the last month for each of the 32 life aspects on a 10 cm analogical scale ranging from "extremely dissatisfied" to "extremely satisfied".

The BPDSI is a semi-structured clinical interview assessing frequency and severity of BPD related symptoms. The interview consists of eight items scored on 10-point frequency scales (0=never; 10=daily), including 'abandonment', 'interpersonal relationships', 'impulsivity', 'parasuicidal behavior', 'affective instability', 'emptiness', 'outbursts of anger', 'dissociation and paranoid ideation', and one item scored on a four-point severity scale, concerning 'identity'.

Response was measured as the change of CGI-S score during the trial period. A comprehensive review of literature was used to identify potential predictors of response. In our study the putative predictors were the following: demographic characteristics (age, gender, and marital status), clinical features (family psychiatric history, baseline global severity of symptoms – CGI-S, baseline severity of depressive and anxious symptoms – HDRS, HARS, baseline severity of BPD symptoms – BPDSI total score and single items), and measures of social functioning (SOFAS) and subjective quality of life (SAT-P five factors).

Statistical analysis was performed with analysis of variance for categorical variables (gender, marital status, previous hospitalization, and employment), with linear regression for continuous variables (age, education, baseline CGI-S, HDRS, HARS, SOFAS, BPDSI total score and single items, and SAT-P factors). Dependent variable was the difference of CGI-S score between baseline and week 32 ( $\Delta$ CGI-S). All variables that were found significant were included in a multiple regression analysis (stepwise backward). Significance level was  $P \leq 0.05$ .

## 3. Results

We analyzed data concerning the 27 patients allocated to the arm of combined therapy in our previous study (Bellino et al., 2010). Five drop-outs (18.5% of the initial sample) were due to non-compliance. Twenty-two patients completed the trial (81.5%).

The mean age of the sample was  $26.23 \pm 6.4$  years; the male to female ratio was 8 to 19. Twelve of the 27 patients (44.4%) were married; 16 subjects (59.26%) had a previous hospitalization; and 13 patients (48.15%) were employed. Table 1 reports other demographic and clinical characteristics of the participants.

The statistical analysis of outcome measures was performed on the 22 patients who completed the 32 weeks of treatment. Results of ANOVA calculated for categorical variables did not show any significant differences of mean  $\Delta$ CGI-S between groups. Continuous variables significantly related to  $\Delta$ CGI-S at the linear regression were: SOFAS ( $P=0.043$ ); BPDSI total score ( $P=0.001$ ) and BPDSI domains abandonment ( $P=0.001$ ), affective instability ( $P=0.030$ ), identity ( $P=0.001$ ), and paranoid ideation/dissociative symptoms ( $P=0.008$ ). At the multiple regression analysis, the

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