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Clinical Trials of Treatment for Personality Disorders

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Until recently, the treatment of patients with personality disorders was largely guided by clinical experience. However, in the past decade a series of important clinical trials, both of pharmacotherapy and psychotherapy, have been conducted. Almost all of this research deals with borderline personality disorder (BPD), a diagnosis that is common in clinical settings and that presents serious and worrisome challenges [1].

Personality disorders are chronic, but often improve with time [2–4]. In fact, the prognosis for many personality disorders (PDs) is better than for most serious Axis I disorders. Since it difficult to determine whether improvement is naturalistic or the result of any specific intervention, randomized controlled trials (RCTs) are crucial.

Another observation of importance for therapy is that depressed patients who also have PDs do not respond to the same treatment methods (whether pharmacological or psychotherapeutic) as those without PDs [5]. Some have challenged this conclusion in relation to antidepressants [6], but a recent meta-analysis supported it [7]. The implication is that if clinicians avoid making Axis II diagnoses, or only diagnose PD patients with comorbid Axis I conditions, they are likely to be disappointed with the results of drug treatment. Similarly, generic forms of psychotherapy may be less effective than methods specifically developed for PDs.

PSYCHOTHERAPIES

Dialectical Behavior Therapy

Dialectical behavior therapy (DBT) is an adaptation of cognitive behavioral therapy, but is an eclectic mix of methods common to several other approaches [8]. DBT is specifically designed to target the mood instability of BPD, but also addresses impulsive behaviors. It applies behavioral analysis to incidents leading to self-injury and overdoses, teaching patients alternative ways of handling dysphoric emotions. DBT emphasizes empathic responses to distress that

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provide "validation" for the inner experience of patients. The program consists of individual therapy, group psychoeducation, and telephone availability for "coaching."

DBT was the subject of one of the first randomized controlled trials of a psychotherapy designed for BPD [9]. The results, published in 1991, showed that it was clearly superior to "treatment as usual" (TAU, ie, outpatient therapy in the community). After a year, patients receiving DBT were less likely to make suicide gestures and spent less time in hospital. Although the gap narrowed at 1-year follow-up [10], patients treated with DBT continued to have a higher functional level than those who were not treated with DBT.

In the 1991 study, more than 90% of patients treated with DBT stayed in therapy for the full year. That was a remarkable finding in a patient population known for a lack of treatment compliance. The highly structured nature of DBT may be responsible. However, it should be noted that the patients in this study received free treatment, while the cohort in treatment as usual did not, and that replication studies in other centers have experienced higher rates of attrition [11–15]. But these studies also confirmed the efficacy of DBT, which is also effective in BPD patients with substance abuse [16].

The main limitation of the 1991 study was that it compared DBT to TAU, which tends to offer inconsistent follow-up. The advantage of DBT could have derived from its structure and consistency rather than from any specific form of intervention.

To address this problem, Linehan and colleagues [17], conducted a new clinical trial in which the comparison group was assigned to "treatment by community experts"–therapists in the Seattle area who identified themselves as interested in BPD, and whose fees were paid for by the research team. The results, published in 2006, found several outcomes that favored DBT: reductions in overdoses and subsequent hospitalizations within the first year of treatment. But this time there were no differences between the groups in the frequency of self-mutilation. Thus, DBT remained superior, even if its advantage was narrower.

While this research is highly encouraging, we need to determine whether its findings are generalizable to clinical settings. Selection biases affecting clinical research tend to produce samples of patients who are compliant. Since not every BPD patient will follow through with DBT, we do not know whether this treatment can be applied to all cases.

Another limitation concerns long-term efficacy. Linehan [8] had suggested that a full course of treatment could take several years, but tested only the first stage (in which parasuicidal behaviors were targeted and brought under control). We also do not know whether treated samples maintain their gains and continue to improve or whether they might relapse. Although the original cohort received therapy 15 years ago, there has been no follow up.

The largest problem for DBT is that it is resource-intensive and expensive. For this reason, more than a decade after its introduction, implementation of this treatment has been spotty. Where available, it can produce long waiting lists–not surprising for a treatment whose initial phase lasts a full year. It

remains to be seen whether DBT can be dismantled and streamlined for greater clinical impact, but one recent study suggests that it can [18].

Other Forms of Cognitive Therapy

Linehan [8] developed DBT because of her experience that standard cognitive behavioral therapy was not effective for this population. Nonetheless, CBT has been subjected to clinical trials in these patients. Results using a method developed by Beck (which focuses on correcting maladaptive cognitions) have been published, but the trial was open and uncontrolled [19]. In a large RCT, Tyrer and colleagues [20], found that manualized cognitive behavioral therapy was superior to treatment as usual for the treatment of recurrent deliberate self-harm in PD patients, but was less effective for those with a diagnosis of BPD.

Recently, an RCT by Davidson and colleagues [21–23] found standard CBT to be superior to treatment as usual for BPD. The average length of treatment was only 16 sessions, but CBT had a superior outcome. A report by Weinberg and colleagues [16] of a 12-week clinical trial, found that that this brief treatment was superior to TAU in that it rapidly reduced self-harm behavior in BPD. All these findings suggest that CBT for BPD need not require several years of treatment.

Schema-focused therapy, developed by Young [24], is a hybrid of CBT and psychodynamic therapy that focuses on maladaptive schema deriving from adverse experiences in childhood. A clinical trial [25] found that improvement was equivalent to a comparison group receiving transference-focused therapy (described later in this article).

The "STEPPS" program [26] is another cognitive method providing psychoeducation in a group format, designed to supplement standard therapy, and it has been subjected to a successful clinical trial.

In summary, cognitive therapy is a strong contender to be considered a standard treatment for BPD. A Cochrane review [27], applying its usual high standards of evidence, concluded that the data supporting this form of treatment are promising.

While cognitive therapy has been proposed for the treatment of other personality disorders [28], RCTs are rare and clinical guidelines unclear. For example, Emmelkamp and colleagues [29] examined the use of CBT in avoidant personality disorder, comparing it to brief dynamic therapy, yet neither method was superior to a waiting list control group.

Psychodynamic Therapies

Psychoanalysts have long been interested in treating personality disorders, but patients may not always do well with this approach. Thus, when BPD patients are offered open-ended psychodynamic therapy, most will drop out within a few months [30,31].

In the first formal study of dynamic therapy in BPD, Stevenson and Meares [32] reported improvement in 30 patients who received 2 years of a therapy based on self-psychology, and results remained stable after 5 years [33]. Since there was no control group and outcome was compared with untreated patients

on a waiting list (and to the overall course of the disorder), a replication was later performed [34]; however, it was not clear how representative these patients were of clinical populations.

Mentalization-based therapy (MBT) has been tested with an RCT [35], and the good results were stable on 18-month follow-up [36]. MBT is derived from attachment theory, and based on the idea that BPD patients need to taught to "mentalize" (ie, to stand outside their feelings and accurately observe emotions in self and others). MBT makes use of a number of cognitive methods, as acknowledged by Bateman and Fonagy [37,38]. For example, mentalization resembles the concept of "decentering," long applied by CBT [28]. Since the findings of the MBT trial were obtained to a day hospital, this milieu may have accounted for some of the improvement, and MBT is currently being tested in an outpatient setting [39].

Transference-focused psychotherapy (TFP) is a somewhat different psychodynamic method that aims to correct distortions in the patient's perception of significant others and of the therapist [40]. The method has been evaluated (in a comparison to DBT) in a randomized clinical trial, with results indicating approximately equivalent efficacy [41,42].

All these findings suggest that manualized dynamic therapies can also be successful for treating BPD, provided they are well structured. The most likely reason why past therapies have often failed may be that they relied on unstructured techniques, which leave patients adrift.

The findings also suggest that different forms of psychotherapy, based on different theories, can be effective.

Group Therapy

Groups have been used either as a primary therapy, or as an adjunct to other treatments. Only one controlled trial in BPD patients comparing long-term group to individual therapy has been published, with the finding that both methods achieved similar results [43].

Psychoeducation

A recent RCT [44] described the efficacy of brief psychoeducation for a mixed group of personality disorders. Education is also an essential element of DBT [8]. It is useful to explain Axis II diagnoses to patients and to encourage them to read and browse on the Internet to obtain more information.

Whereas the families of patients have been, in the past, blamed for the development of personality disorders, therapists have come to realize they are burdened by their children's psychopathology, and can be useful allies in treatment. Gunderson [45] developed a program for psychoeducation of family members, paralleling previous work on expressed emotion in schizophrenia, but has not published data on its effectiveness.

PHARMACOTHERAPIES

Almost all the research on drugs for PDs has been on BPD.

Neuroleptics

Low-dose neuroleptics have long been used for BPD, but have many side effects. Studies of haldoperidol show that patients tend to stop taking it, probably for this reason, and that short-term effects are not maintained on 6-month follow-up [46]. Three studies of olanzapine [47–49] found reductions in impulsivity in short-term clinical trials. One study [50] found that olanzapine added to efficacy in patients also receiving DBT. However, all of these reports used small samples. Moreover, clinical improvement did not translate into remission.

Specific Serotonin Reuptake Inhibitors

It is unusual today to see a patient with BPD who is not on an antidepressant. Yet this practice is not firmly based on controlled trials.

Specific serotonin reuptake inhibitors (SSRIs) have often been used for depressive symptoms in BPD. While one study [51] reported that SSRIs reduce mood swings in BPD, most [48,52,53] suggest that SSRIs are most effective in reducing anger and impulsive symptoms. High doses (eg, 60 to 80 mg of fluoxetine) may produce reductions of self-mutilation [54], but patients can have difficulty tolerating these levels.

Research has also examined MAO inhibitors [46,55] and tricyclic antidepressants [56] in BPD, but the side effects and potential lethality of these agents on overdose have not encouraged their use.

Like neuroleptics, antidepressants "take the edge off" symptoms of BPD, but do not lead to remission of a personality disorder.

Mood Stabilizers

BPD is associated with marked affective instability, and has sometimes been thought to lie in the bipolar spectrum [57]. One reason for doubting this reformulation is that studies on mood stabilizers in BPD have produced unconvincing results. The only controlled study of lithium in BPD [58] failed to demonstrate clinical efficacy, and few clinicians would wish to use a drug that is so dangerous on overdose. Carbamazepine can reduce impulsivity [55], but is also dangerous on overdose. Controlled trials of valproate [59–61] have shown only marginal efficacy in BPD, and the data suggest that while this drug reduces impulsive aggression, it is less useful for affective instability. The best results were obtained in a small-scale trial of valproate [62], but this sample was limited to patients who were comorbid for bipolar II disorder (ie, those with clear-cut hypomanic episodes), a very atypical group that may not even justify a BPD diagnosis. Lamotrigine [63] and topiramate [64,65] have also been studied in small clinical trials in BPD patients, with some effects in reducing anger and anxiety (but not depression).

In summary, mood stabilizers are more useful for impulsivity and aggression than for mood. As we have seen, the same effect can be obtained with SSRIs and low-dose neuroleptics. Although these agents are designated as "mood stabilizers," their effects do not seem to extend very well to PDs. Efficacy is better

documented in bipolar I and bipolar II; the emotional dysregulation in BPD patients may be an entirely different phenomenon [57].

Other Pharmacological Agents

Zanarini and Frankenburg [66], reported that omega-3 fatty acids were helpful for BPD symptoms (in a small sample of patients obtained by advertisement). Of course a single study is not sufficient evidence to recommend this agent for a clinical population.

Polypharmacy

A wide variety of pharmacological agents reduce impulsivity in personality disorders, but none have ever been shown to produce clinical remission. These drugs are of limited value because they were developed for other purposes, and are applied to Axis II diagnoses that probably have a different pathophysiology.

Patients receiving medication usually remain unstable–in mood, impulsive actions, and relationships. This sometimes leads to the prescription of additional agents, even if they have the same therapeutic effect (and limitations) as the original prescription. Thus, polypharmacy, a practice that is not evidence-based, is commonly applied to personality disorders, making it more likely that patients will suffer from side effects. Patients with BPD are often on four to five drugs, with at least one from each major group [67]. Unfortunately, algorithms for drug treatment in BPD, included in the American Psychiatric Association guidelines for the treatment of BPD [68], which are not based on RCT evidence, lead directly to this practice.

A recent Cochrane report [69] concluded that none of the clinical trials of drugs for BPD provides enough data to support their prescription. This being the case, it makes little sense to combine many drugs, none of which are specific to the disorder, when all of which do much the same thing.

SUMMARY

The treatment of patients with PDs is more hopeful than it was in the past. However, we have become overly dependent on pharmacological treatments, neglecting psychotherapies even when they are evidence-based. Yet there is much stronger evidence for the effectiveness of psychotherapy in PDs than for any pharmacological intervention.

The main reasons psychological therapies are not more widely used is their cost and the length of time they need to be used. But several types of therapy can be effective, and some recent evidence suggests that we may be able to provide these treatments in a briefer and more practical way [18].

Future research needs to answer other questions. First, since PDs are usually chronic, treatment research should move beyond short-term studies to examine long-term effects, and treatment effects need to be shown to be superior to naturalistic remission. Second, the effective factors common to all psychotherapies need to be more specifically identified. Third, we need to develop entirely new groups of drugs that specifically target the traits that underlie PDs.

References

[1] Lieb K, Zanarini MC, Schmahl C, et al. Borderline personality disorder. Lancet 2004;364(9432):453–61.
[2] Paris J. Personality disorders over time. Washington, DC: American Psychiatric Press; 2003.
[3] Skodol AE, Gunderson JG, Shea MT, et al. The collaborative longitudinal personality disorders study (CLPS) overview and implications. J Personal Disord 2005;19(5):487–504.
[4] Zanarini MC, Frankenburg FR, Hennen J, et al. The McLean study of adult development (MSAD): overview and implications of the first six years of prospective follow-up. J Personal Disord 2005;19:505–23.
[5] Shea MT, Pilkonis PA, Beckham E, et al. Personality disorders and treatment outcome in the NIMH treatment of depression collaborative research program. Am J Psychiatry 1990;147: 711–8.
[6] Mulder RT. Depression and personality disorder. Curr Psychiatry Rep 2004;6:51–7.
[7] Newton-Howes G, Tyrer P, Johnson T. Personality disorder and the outcome of depression: meta-analysis of published studies. Br J Psychiatry 2006;188:13–20.
[8] Linehan MM. Dialectical behavioral therapy of borderline personality disorder. New York: Guilford; 1993.
[9] Linehan MM, Armstrong HE, Suarez A, et al. Cognitive behavioral treatment of chronically parasuicidal borderline patients. Arch Gen Psychiatry 1991;48:1060–4.
[10] Linehan MM, Heard HL, Armstrong HE. Naturalistic follow-up of a behavioral treatment for chronically parasuicidal borderline patients. Arch Gen Psychiatry 1993;50:971–4.
[11] Koons CR, Robins CJ, Bishop GK, et al. Efficacy of dialectical behavior therapy with borderline women veterans: a randomized controlled trial. Behav Ther 2001;32:371–90.
[12] Verheul R, van den Bosch LMC, Maarten WJ, et al. Dialectical behaviour therapy for women with borderline personality disorder: 12-month, randomised clinical trial in The Netherlands. Br J Psychiatry 2003;182:135–40.
[13] Bohus M, Haaf B, Simms T, et al. Effectiveness of inpatient dialectical behavioral therapy for borderline personality disorder: a controlled trial. Behav Res Ther 2004;42:487–99.
[14] Simpson EB, Yen S, Costello E, et al. Combined dialectical behavior therapy and fluoxetine in the treatment of borderline personality disorder. J Clin Psychiatry 2004;65:379–85.
[15] Linehan MM, Schmidt H III, Dimeff LA, et al. Dialectical behavior therapy for patients with borderline personality disorder and drug-dependence. Am J Addict 1999;8:279–92.
[16] Weinberg I, Gunderson JG, Hennen J, et al. Manual assisted cognitive treatment for deliberate self-harm in borderline personality disorder patients. J Personal Disord 2006;20(5):482–92.
[17] Linehan MM, Comtois KA, Murray AM, et al. Two-year randomized controlled trial and follow-up of dialectical behavior therapy vs therapy by experts for suicidal behaviors and borderline personality disorder. Arch Gen Psychiatry 2006;63:757–66.
[18] Stanley B, Brodsky B, Nelson JD, Dulit R . Brief dialectical behavior therapy (DBT-B) for suicidal behavior and non-suicidal self injury. Arch Suicide Res 2007;11:337–41.
[19] Brown GK, Newman CF, Charlesworth SE, et al. An open clinical trial of cognitive therapy for borderline personality disorder. J Personal Disord 2004;18:257–71.
[20] Tyrer P, Thompson S, Schmidt U, et al. Randomized controlled trial of brief cognitive behaviour therapy versus treatment as usual in recurrent deliberate self-harm: the POPMACT study. Psychol Med 2003;33:969–76.
[21] Davidson K, Norrie J, Tyrer P, et al. The effectiveness of cognitive behavior therapy for borderline personality disorder: results from the borderline personality disorder study of cognitive therapy (BOSCOT) trial [comparative study]. J Personal Disord 2006;20(5):450–65.
[22] Davidson K, Tyrer P, Gumley A, et al. A randomized controlled trial of cognitive behavior therapy for borderline personality disorder: rationale for trial, method, and description of sample. J Personal Disord 2006;200(5):431–49.
[23] Palmer S, Davidson K, Tyrer P, et al. The cost-effectiveness of cognitive behavior therapy for borderline personality disorder: results from the BOSCOT trial. J Personal Disord 2006;20(5):466–81.

[24] Young JE. Cognitive therapy for personality disorders: a schema focused approach. 3rd edition. Sarasota (FL): Professional Resource Press; 1999.
[25] Giesen-Bloo J, van Dyck R, Spinhoven P, et al. Outpatient psychotherapy for borderline personality disorder: randomized trial of schema-focused therapy vs transference-focused psychotherapy. Arch Gen Psychiatry 2006;63(6):649–58.
[26] Blum N, St. John D, Pfohl B, et al. Systems Training for Emotional Predictability and Problem Solving (STEPPS) for outpatients with borderline personality disorder: a randomized controlled trial and 1-year follow-up. Am J Psychiatry 2008;165:468–78.
[27] Binks CA, Fenton M, McCarthy L, et al. Psychological therapies for people with borderline personality disorder. Cochrane Database Syst Rev 2006;(1):CD005652.
[28] Beck AT, Freeman A. Cognitive therapy of personality disorders. 2nd edition. New York: Guilford; 2002.
[29] Emmelkamp PM, Benner A, Kuipers A, et al. Comparison of brief dynamic and cognitive-behavioural therapies in avoidant personality disorder. Br J Psychiatry 2006;189:60–4.
[30] Gunderson JG, Frank AF, Ronningstam EF, et al. Early discontinuance of borderline patients from psychotherapy. J Nerv Ment Dis 1989;177:38–42.
[31] Skodol AE, Buckley P, Charles E. Is there a characteristic pattern in the treatment history of clinic outpatients with borderline personality? J Nerv Ment Dis 1983;171:405–10.
[32] Stevenson J, Meares R. An outcome study of psychotherapy for patients with borderline personality disorder. Am J Psychiatry 1992;149:358–62.
[33] Stevenson J, Meares R, D'Angelo R. Five-year outcome of outpatient psychotherapy with borderline patients. Psychol Med 2005;35:79–87.
[34] Korner A, Gerull F, Meares R, et al. Borderline personality disorder treated with the conversational model: a replication study. Compr Psychiatry 2006;47(5):406–11.
[35] Bateman A, Fonagy P. Effectiveness of partial hospitalization in the treatment of borderline personality disorder: a randomized controlled trial. Am J Psychiatry 1999;156:1563–9.
[36] Bateman A, Fonagy P. Treatment of borderline personality disorder with psychoanalytically oriented partial hospitalization: an 18-month follow-up. Am J Psychiatry 2001;158:36–42.
[37] Bateman A, Fonagy P. Psychotherapy for borderline personality disorder: mentalization based treatment. Oxford: Oxford University Press; 2004.
[38] Bateman A, Fonagy P. Mentalization-based treatment: a practical guide. New York: John Wiley; 2006.
[39] Fonagy P. An update of on BPD treatment evaluation research in England. Presented to the NIMH international think tank for the more effective treatment of borderline personality disorder. Lincthinum (MD); December 2004.
[40] Clarkin JF, Levy KN, Lenzenweger MF, et al. The personality disorders institute/borderline personality disorder research foundation randomized control trial for borderline personality disorder: rationale, methods, and patient characteristics. J Personal Disord 2004;18: 52–72.
[41] Clarkin JF, Levy KN, Lenzenweger MF, et al. Evaluating three treatments for borderline personality disorder: a multiwave study. Am J Psychiatry 2007;164:1–8.
[42] Levy KN, Clarkin JF, Yeomans FE, et al. The mechanisms of change in the treatment of borderline personality disorder with transference-focused psychotherapy. J Clin Psychol 2006;62(4):481–501.
[43] Munroe-Blum H, Marziali E. A controlled trial of short-term group treatment for borderline personality disorder. J Personal Disord 1995;9:190–8.
[44] Huband N, McMurran M, Evans C, et al. Social problem-solving plus psychoeducation for adults with personality disorder: pragmatic randomised controlled trial. Br J Psychiatry 2007;190:307–13.
[45] Gunderson JG. Borderline personality disorder: a clinical guide. Washington, DC: American Psychiatric Press; 2001.
[46] Soloff PH, Cornelius J, George A, et al. Efficacy of phenelzine and haloperidol in borderline personality disorder. Arch Gen Psychiatry 1993;50:377–85.

[47] Zanarini MC, Frankenburg FR. Olanzapine treatment of female borderline personality disorder patients: a double-blind, placebo-controlled pilot study. J Clin Psychiatry 2001;62: 849–54.
[48] Zanarini MC, Frankenburg FR, Parachini EA. A preliminary, randomized trial of fluoxetine, olanzapine, and the olanzapine-fluoxetine combination in women with borderline personality disorder. J Clin Psychiatry 2004;65:903–7.
[49] Bogenschutz MP, Nurnberg GH. Olanzapine versus placebo in the treatment of borderline personality disorder. J Clin Psychiatry 2004;65:104–9.
[50] Soler J, Pascual JC, Campins J, et al. Double-blind, placebo-controlled study of dialectical behavior therapy plus olanzapine for borderline personality disorder. Am J Psychiatry 2005;162:1221–4.
[51] Rinne T, van den Brink W, Wouters L, et al. SSRI treatment of borderline personality disorder: a randomized, placebo-controlled clinical trial for female patients with borderline personality disorder. Am J Psychiatry 2002;159:2048–54.
[52] Salzman C, Wolfson AN, Schatzberg A, et al. Effect of fluoxetine on anger in symptomatic volunteers with borderline personality disorder. J Clin Psychopharmacol 1995;15:23–9.
[53] Coccaro EF, Kavoussi RJ. Fluoxetine and impulsive aggressive behavior in personality-disordered subjects. Arch Gen Psychiatry 1997;54:1081–8.
[54] Markowitz PJ. Pharmacotherapy of impulsivity, aggression, and related disorders. In: Hollander EE, Stein DJ, editors. Impulsivity and Aggression. New York: John Wiley; 1995. p. 263–86.
[55] Cowdry RW, Gardner DL. Pharmacotherapy of borderline personality disorder: alprazolam, carbamazepine, trifluoperazine, and tranylcypromine. Arch Gen Psychiatry 1988;45:111–9.
[56] Soloff PH, George A, Nathan S, et al. Amitriptyline versus haloperidol in borderlines: final outcomes and predictors of response. J Clin Psychopharmacol 1989;9:238–46.
[57] Paris J, Gunderson JG, Weinberg I. The interface between borderline personality disorder and bipolar spectrum disorder. Compr Psychiatry 48:145–154.
[58] Links PS, Steiner M, Boiago I, et al. Lithium therapy for borderline patients: preliminary findings. J Personal Disord 1990;4:173–81.
[59] Hollander E, Tracy KA, Swann AC, et al. Divalproex in the treatment of impulsive aggression: efficacy in cluster B personality disorders. Neuropsychopharmacology 2003;28: 1186–97.
[60] Hollander E, Swann AC, Coccaro EF, et al. Impact of trait impulsivity and state aggression on divalproex versus placebo response in borderline personality disorder. Am J Psychiatry 2005;162:621–4.
[61] Kavoussi RJ, Coccaro EF. Divalproex sodium for impulsive aggressive behavior in patients with personality disorder. J Clin Psychiatry 1998;59:676–80.
[62] Frankenburg FR, Zanarini MC. Divalproex sodium treatment of women with borderline personality disorder and bipolar II disorder: a double-blind placebo-controlled pilot study. J Clin Psychiatry 2002;63:442–6.
[63] Tritt K, Nickel C, Lahmann C, et al. Lamotrigine treatment of aggression in female borderline-patients: a randomized, double-blind, placebo-controlled study. J Psychopharmacol 2005;19:287–91.
[64] Nickel MK, Nickel C, Mitterlehner FO, et al. Topiramate treatment of aggression in female borderline personality disorder patients: a double-blind, placebo-controlled study. J Clin Psychiatry 2004;65:1515–9.
[65] Loew TH, Nickel MK, Muehlbacher M, et al. Topiramate treatment for women with borderline personality disorder: a double-blind, placebo-controlled study. J Clin Psychopharmacol 2006;26:61–6.
[66] Zanarini MC, Frankenburg FR. Omega-3 fatty acid treatment of women with borderline personality disorder: a double-blind, placebo-controlled pilot study. Am J Psychiatry 2003;160:167–9.

[67] Zanarini MC, Frankenburg FR, Khera GS, et al. Treatment histories of borderline inpatients. Compr Psychiatry 2001;42:144–50.
[68] Oldham JM, Gabbard GO, Goin MK, et al. Practice guideline for the treatment of borderline personality disorder. Am J Psychiatry 2001;158(Suppl):1–52.
[69] Binks CA, Fenton M, McCarthy L, et al. Pharmacological interventions for people with borderline personality disorder. Cochrane Database Syst Rev 2006;(1):CD005653.