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LA DISREGOLAZIONE EMOTIVA NEI GIOVANI: PROSPETTIVE E MODELLI DI INTERVENTO

PFA21.CPD125

Terapia farmacologica dei disturbi di personalità

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National Education Alliance for Borderline Personality Disorder
NEA-BPD
P. O. Box 974, Rye, New York 10580

PREVALENCE

- About 2% of the general population
- About 10% among individuals seen in outpatient mental health clinics
- About 20% among psychiatric inpatients
- It ranges from 30% to 60% among clinical populations with Personality Disorders

Treatment in Psychiatry

Borderline Personality Disorder and Suicidality

Prevalence of Suicidality in Borderline Personality Disorder

- Borderline personality disorders are estimated to be present in more than 30% of individuals who die by suicide, about 40% of individuals who make suicide attempts, and about 50% of psychiatric outpatients who die by suicide.

- In clinical populations, the rate of suicide of patients with borderline personality disorder is estimated to be between 8% and 10%, a rate far greater than that in the general population.

Oldham J, Am. J. Psychiatry 163:1, Jan 2006

New onsets of substance use disorders in borderline personality disorder over 7 years of follow-ups: findings from the Collaborative Longitudinal Personality Disorders Study

Table 1 Frequency and percentage of co-occurrence of current and lifetime substance use disorder (SUD) in patients with personality disorder at baseline.

	BPD (n = 175)	*OPD (n = 396)*	
SUD	*n (%)*	*n (%)*	*P*
Alcohol use disorder	91 (52.0)	152 (38.4)	$\chi^2 = 9.20$, df = 1, $P = 0.002$
Alcohol Abuse	30 (17.1)	52 (13.1)	$\chi^2 = 1.59$, df = 1, n.s.
• Current alcohol abuse	6 (3.4)	7 (1.8)	$\chi^2 = 1.51$, df = 1, n.s.
• Lifetime alcohol abuse	24 (13.7)	45 (11.4)	$\chi^2 = 0.63$, df = 1, n.s.
Alcohol Dependence	61 (34.9)	100 (25.3)	$\chi^2 = 5.53$, df = 1, $P = 0.013$
Drug use disorder	96 (54.9)	121 (30.6)	$\chi^2 = 30.42$, df = 1, $P < 0.0001$
Drug Abuse	18 (10.3)	29 (7.3)	$\chi^2 = 1.41$, df = 1, n.s.
• Current drug abuse	4 (2.3)	6 (1.5)	$\chi^2 = 0.42$, df = 1, n.s.
• Lifetime drug abuse	14 (8.0)	23 (5.8)	$\chi^2 = 0.96$, df = 1, n.s.
Drug Dependence	78 (44.6)	92 (23.2)	$\chi^2 = 26.43$, df = 1, $P < 0.0001$

BPD, borderline personality disorder; OPD, other personality disorder.

Walter M et al. (2009). Addiction 104: 97-103

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Predictors of self-mutilation in patients with borderline personality disorder: A 10-year follow-up study

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Table 2

Multivariate predictors of self-mutilation among borderline patients over 10 years of prospective follow-up.

	Odds Ratio	SE	z-score	p	95% Confidence interval
Gender[a]	2.63	0.81	3.13	0.002	1.44, 4.81
Mean DAS cognition score (10 point increments)	1.35	0.07	5.47	<0.001	1.21, 1.50
Mean DES score (10 point increments)	1.19	0.06	3.27	0.001	1.07, 1.33
Major depression	1.68	0.23	3.73	<0.001	1.28, 2.21
Childhood history of sexual abuse[a]	1.63	0.37	2.15	0.031	1.04, 2.53
Adult sexual assault	1.87	0.46	2.57	0.010	1.16, 3.02
Time	0.23	0.05	−7.45	<0.001	0.15, 0.33

[a] Baseline predictors; all others are time-varying.

(DAS= Dysphoric Affect Scale; DES= Dissociative Experience Scale

GUIDELINES

Borderline and antisocial personality disorders: summary of NICE guidance

Tim Kendall,[1,2,3] Stephen Pilling,[4,5,6] Peter Tyrer,[7,8] Conor Duggan,[9,10] Rachel Burbeck,[4] Nicholas Meader,[1] Clare Taylor,[1] on behalf of the Guideline Development Groups

Recommendations for borderline personality disorder

The role of psychological treatment

- When providing psychological treatment, especially for people with multiple comorbidities or severe impairment (or both), include:
  - An explicit and integrated theoretical approach used by both the treatment team and the therapist, and shared with the service user
  - Structured care in accordance with this guideline
  - Provision for supervision by a therapist.
- Although the frequency of psychotherapy sessions should be adapted to the person's needs and context of living, consider twice weekly sessions.
- Do not use brief psychological interventions (of less than three months' duration) specifically for borderline personality disorder or for its individual symptoms outside a service that has the characteristics outlined above.

The role of drug treatment

- Do not use drug treatment specifically for borderline personality disorder or for the individual symptoms or behaviour associated with it.

Treatment Utilization by Patients With Personality Disorders

TABLE 3. Likelihood of Ever Having Received Psychotropic Medications for Patients With Schizotypal, Borderline, Avoidant, or Obsessive-Compulsive Personality Disorder, Relative to Comparison Patients With Major Depressive Disorder and With Controls for Demographic Variables[a] and Axis I Disorders

	Patients' Lifetime History of Medication Use						
	Frequency for Major Depressive Disorder	Schizotypal Personality Disorder (N=85)			Borderline Personality Disorder (N=173)		
			Likelihood Relative to Depression			Likelihood Relative to Depression	
Type of Medication	(%) (N=97)	Frequency (%)	Odds Ratio	95% CI	Frequency (%)	Odds Ratio	95% CI
Antianxiety	27	22	1.78	0.91–3.46	35	2.23**	1.23–4.01
Hypnotic	6	4	0.70	0.18–2.66	6	1.54	0.56–4.31
Mood stabilizer	10	12	2.04	0.89–4.71	27	6.22***	2.97–12.93
Antipsychotic	4	10	7.25***	2.34–22.19	10	10.47†	3.56–30.56
Antidepressant	60	52	1.36	0.70–2.61	61	2.10*	1.16–3.78

[a] Race, age, and gender. *p<0.05. **p<0.01. ***p<0.001. †p<0.0001.

Bender DS et al. Am J Psychiatry 158: 295-302

Why Patients With Severe Personality Disorders Are Overmedicated

[…] Although specific psychological treatments (BDT, MBT) are known to be efficacious, **they are not readily available. The reason is that therapy takes time and is expensive in human resources.** […] So, **the easiest choice is to focus on pharmacologic therapy for target symptoms rather than the personality disorder as a whole** […] **Faced with desperate patients, and with limited access to specialized psychotherapy, they do what they know how to do – they prescribe.**

The current situation, in which patients with severe personality disorders receive almost routine polypharmacy is unsatisfactory. **The only way this situation can change is to make specialized psychotherapy more readily available.** If it were, then psychiatrists would be slower to reach for their prescription pad and more likely to make referrals for psychological treatment. This problem requires a different kind of mental health system. […]

Paris J, 2015. J Clin Psychiatry.

State of the art

Pharmacological treatment of borderline personality disorder: a retrospective observational study at inpatient unit in Italy

ABSTRACT

Methods: Retrospective observational study evaluating 109 BPD inpatients from June 2011 to June 2013.

Results: There was evidence of an extensive use of drugs: benzodiazepines/hypnotics (85.2%), antipsychotics (78.7%), mood stabilizers (70.4%) and antidepressants (31.5%). Polypharmacy was common (83.5%). A longer length of stay in hospital was associated with the prescription of antipsychotic and/or antidepressant medication, while a shorter hospitalization was associated with the use of a mood stabilizer.

Conclusions: The rates of prescription of different classes of drugs reported in our sample and in similar 'naturalistic' studies highlight a heterogeneous pattern of prescriptions for BPD. Mood stabilizers showed a more favorable profile in terms in length of stay in hospital than antipsychotic and/or antidepressant. Our results reiterate the discrepancy between international recommendations and everyday clinical practice.

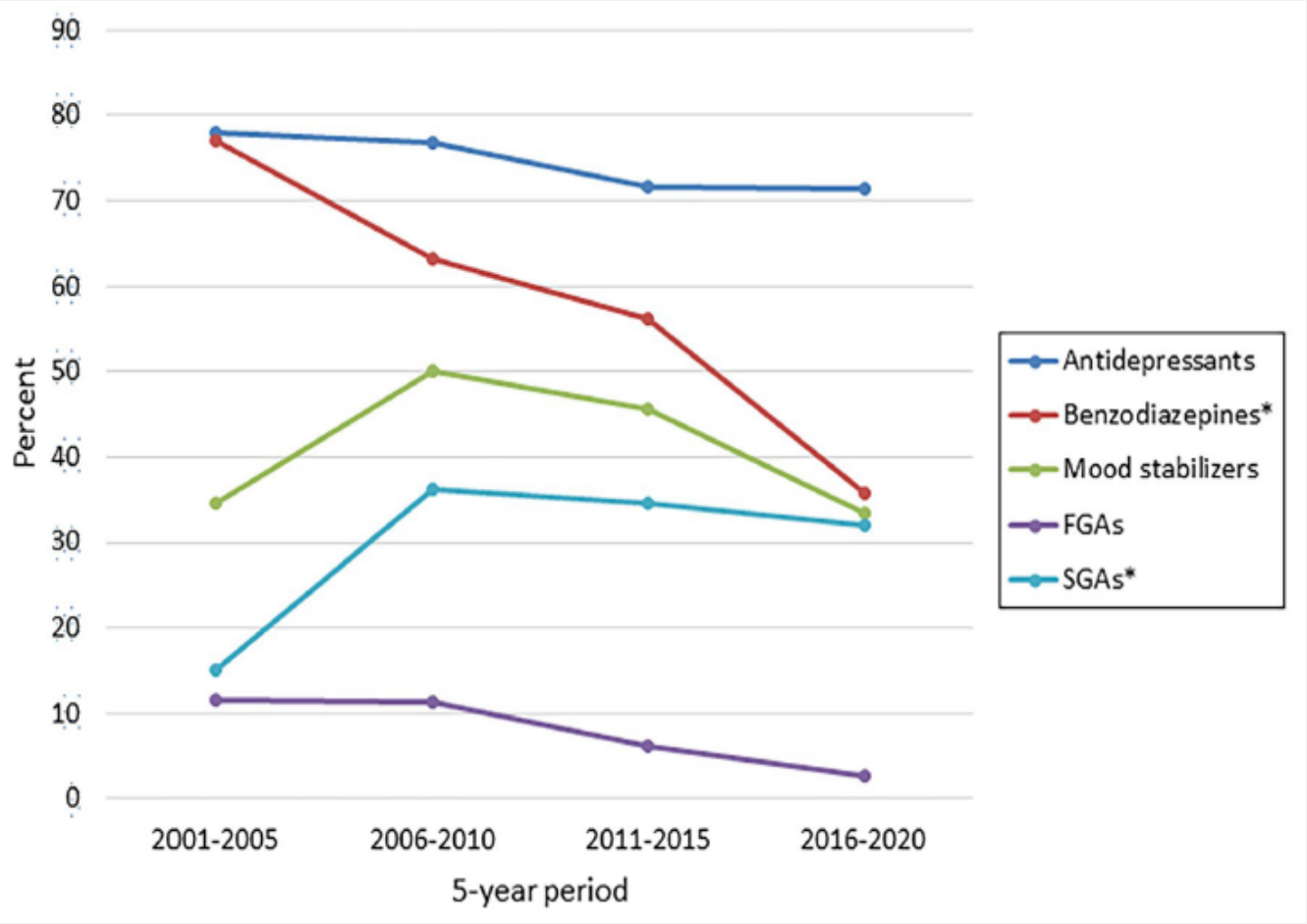
Paolini et al., 2017. INT J OF PSYCH IN CLIN PRACT

Twenty-Year Trends in the Psychopharmacological Treatment of Outpatients with Borderline Personality Disorder: A Cross-Sectional Naturalistic Study in Spain

Methods. Observational and cross-sectional study of all patients with a primary diagnosis of BPD (n = 620) consecutively admitted to a BPD outpatient program in Barcelona, Spain, from 2001 through 2020. For the analysis, prescription data were grouped into four 5-year periods. Logistic regression models were performed to identify sociodemographic and clinical variables associated with pharmacological prescription and polypharmacy.

Results. The percentage of patients receiving pharmacotherapy decreased over time. **Antidepressant prescription rates remained highly stable over time (74% of patients), while benzodiazepine use decreased significantly during the study period (from 77 to 36%) and SGA use increased from 15 to 32%. Psychiatric comorbidity was the main factor associated with pharmacological treatment and polypharmacy**, although a high percentage of patients without comorbidity were also taking medications.

Conclusions. **Over the past 20 years, the pharmacological treatment of BPD outpatients has undergone important changes, most notably the decrease in benzodiazepines and increase in SGAs**. The findings of this study demonstrate that pharmacotherapy is much more prevalent in patients with BPD than recommended in most clinical guidelines.



Pascual et al., 2021. CNS Drugs

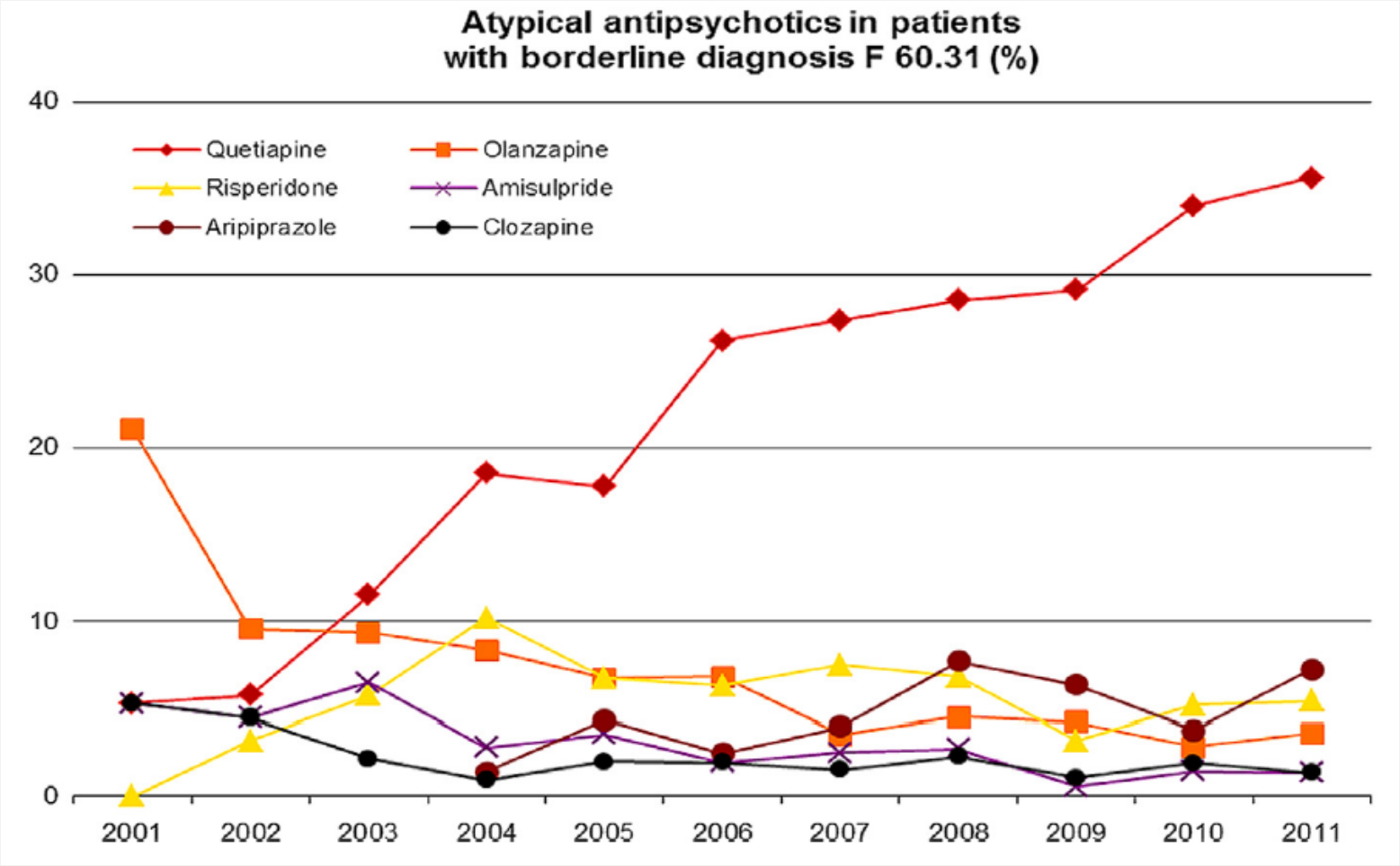
Psychopharmacological treatment of 2195 in-patients with Borderline personality disorder: A comparison with other psychiatric disorders

Abstract:

70% of all BPD patients were medicated with antipsychotics and/or antidepressants, 33% with anticonvulsants, 30% with benzodiazepines, and 4% with lithium; 90% received at least one, 80% ≥ 2, and 54% ≥ 3 psychotropic drugs concomitantly (mean: 2.8). Prescription rates for quetiapine, the single drug most often used in BPD (22%), increased significantly over time.

Sedative antipsychotics and anticonvulsants were prescribed more often in BPD than in the other diagnostic groups, with the exception of bipolar depression.

Contrary to the guidelines, about 90% of in-patients with BPD received psychotropic drugs. Polypharmacy was common, and antipsychotics with sedative profiles such as quetiapine and mood-stabilizing anticonvulsants such as valproate appear to be preferred.



Bridler et al., 2015. European Neuropsychopharmacology

Off-Label Use of Second-Generation Antipsychotics in Borderline Personality Disorder: A Survey of Italian Psychiatrists

Abstract

The guidelines for BPD treatment suggest non-pharmacological treatment as the first option, but SGAs are among the overprescribed medications. This study aimed to explore Italian psychiatrists' attitudes toward off-label use of SGAs in BPD. A randomly selected sample of Italian psychiatrists (n = 202) completed a questionnaire regarding off-label prescription of SGAs.

Most respondents reported the off-label use of SGAs. Among the reasons supporting the prescription of SGAs, the presence of strong published data was the most determining factor (51.5%).

The SGA olanzapine is considered the most appropriate, followed by quetiapine and aripiprazole.

Although off-label prescription of SGAs represents a common clinical practice in accordance with a worldwide trend, **the use of long-acting injection formulations was considered inappropriate by 69% of psychiatrists in our sample**.

Our results reiterate the discrepancy between everyday clinical practice and international recommendations and show how relevant the literature is in off-label drug prescription.

Aguglia et al., 2021 Journal of Personality Disorder

An historical perspective on pharmacotherapy in BPD

Pharmacotherapy for borderline personality disorder: Cochrane systematic review of randomised trials

Results Twenty-seven trials were included in which first- and secondgeneration antipsychotics, mood stabilisers, antidepressants and omega-3 fatty acids were tested. Most beneficial effects were found for the mood stabilisers topiramate, lamotrigine and valproate semisodium, and the second-generation antipsychotics aripiprazole and olanzapine. However, the robustness of findings is low, since they are based mostly on single, small studies. Selective serotonin reuptake inhibitors so far lack high-level evidence of effectiveness.

Conclusions The current evidence from randomised controlled trials suggests that drug treatment, especially with mood stabilisers and second-generation antipsychotics, may be effective for treating a number of core symptoms and associated psychopathology, but the evidence does not currently support effectiveness for overall severity of borderline personality disorder. Pharmacotherapy should therefore be targeted at specific symptoms.

Lieb et al., 2010. BJPysch

Table 1 Characteristics of included randomised comparisons

Study	Treatments	Mean dose
Bogenschutz 2004[18]	Olanzapine *v.* placebo	6.9 mg/day
De la Fuente 1994[19]	Carbamazepine *v.* placebo	Blood levels 6.4–7.1 μg/ml
EliLilly 2007a[22]	Olanzapine *v.* placebo	7.1 mg/day[a]
EliLilly 2007b[21]	Olanzapine *v.* placebo	6.7 mg/[a]
Frankenburg 2002[23]	Valproate semisodium *v.* placebo	850 mg/day
Goldberg 1986[23]	Thiothixene *v.* placebo	8.7 mg/day
Hallahan 2007[24]	Omega-3 fatty acids *v.* placebo	1.2 g/day of E-EPA + 0.9 g/day of DHA
Hollander 2001[25]	Valproate semisodium *v.* placebo	Mean blood valproate level 64.6 μg/ml
Leone 1982[26]	Loxapine Chlorpromazine *v.* placebo	14.4 mg/day 110 mg/day
Linehan 2008[27]	Olanzapine *v.* placebo	4.5 mg/day[b]
Loew 2006[28]	Topiramate *v.* placebo	200 mg/day
Montgomery 1979[30]	Flupentixol decanoate i.m. *v.* placebo	20 mg/4 weeks
Montgomery 1981[29]	Mianserin *v.* placebo	30 mg/day
Nickel 2004[31]	Topiramate *v.* placebo	250 mg/day
Nickel 2005[32]	Topiramate *v.*placebo	250 mg/day
Nickel 2006[33]	Aripiprazole *v.* placebo	15 mg/day
Pascual 2008[34]	Ziprasidone *v.* placebo	81 mg/day
Rinne 2002[35]	Fluvoxamine *v.* placebo	150 mg/day
Salzman 1995[36]	Fluoxetine *v.* placebo	40 mg/day
Simpson 2004[37]	Fluoxetine *v.* placebo	40 mg/day[b]
Soler 2005[38]	Olanzapine *v.* placebo	8.9 mg/day[b]
Soloff 1993[40]	Haloperidol Phenelzine sulfate *v.* placebo	3.9 mg/day 60.45 mg/day
Soloff 1989[39]	Haloperidol Amitriptyline *v.* placebo	4.8 mg/day 149.1 mg/day
Tritt 2005[41]	Lamotrigine *v.* placebo	200 mg/day
Zanarini 2001[42]	Olanzapine *v.* placebo	5.3 mg/day
Zanarini 2003[44]	Omega-3 fatty acids *v.* placebo	1 g/day of E-EPA
Zanarini 2004[43]	Olanzapine Fluoxetine Olanzapine + fluoxetine	3.3 mg/day 15.0 mg/day 3.2 mg/day olanzapine + 12.7 mg/day fluoxetine

Pharmacotherapy for Borderline Personality Disorder - Current Evidence and Recent Trends

Abstract

Drug treatment of patients with borderline personality disorder (BPD) is common but mostly not supported by evidence from high-quality research. This review summarizes the current evidence up to August 2014 and also aims to identify research trends in terms of ongoing randomized controlled trials (RCTs) as well as research gaps. **There is some evidence for beneficial effects by second-generation antipsychotics, mood stabilizers and omega-3 fatty acids, while the overall evidence base is still unsatisfying. The dominating role SSRI antidepressants usually play within the medical treatment of BPD patients is neither reflected nor supported by corresponding evidence. Any drug treatment of BPD patients should be planned and regularly evaluated against this background of evidence.** Research trends indicate increasing attention to alternative treatments such as dietary supplementation by omega-3 fatty acids or oxytocin.

Stoffers & Lieb, 2015. Curr Psychiatry Rep

ELSEVIER

Journal of Affective Disorders 111 (2008) 21–30

Journal of Affective Disorders

www.elsevier.com/locate/jad

Research report

Evidenced-based pharmacologic treatment of borderline personality disorder: A shift from SSRIs to anticonvulsants and atypical antipsychotics?

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Available online 4 March 2008

Abstract

Objective: The authors performed a review of double-blind, controlled studies of psychotropic drugs to evaluate the evidence base supporting their use in treatment of borderline personality disorder.
Methods: English language literature cited in Medline and published between 1970 and 2006 was searched using the following terms: *anticonvulsants*, *antidepressants*, *antipsychotics*, *anxiolytics*, *benzodiazepines*, *borderline personality disorder*, *lithium*, *medication*, *mood stabilizers*, *pharmacotherapy*, and *psychotropics*. Only reports of double-blind, randomized, controlled trials were included.
Results: Twenty eight double-blind, randomized, controlled trials were identified which included anticonvulsants, classical neuroleptics, the benzodiazepine alprazolam, lithium, monoamine oxidase inhibitors, the novel antipsychotic olanzapine, selective serotonin reuptake inhibitors, tricyclic antidepressants, and omega-3 fatty acids. All but three were placebo-controlled. With the exception of alprazolam and tricyclics, the data from these trials revealed evidence of improvements, although often circumscribed and variable. The novel antipsychotic olanzapine appeared to have the most empirical support for having a favorable effect on borderline personality disorder.
Conclusion: A growing body of data suggests that there are psychotropic agents which appear to be well tolerated, and which to varying degrees may be expected to ameliorate the domains of psychopathology associated with borderline personality disorder. The research literature, on which practice should be optimally based, appears to suggest a need for a shift from antidepressants to anticonvulsants and atypical antipsychotics.

Keywords: Borderline personality disorder; Controlled trials; Drugs

Is a symptom-based approach feasible for BPD?

REVIEW ARTICLE

Antipsychotics, Antidepressants, Anticonvulsants, and Placebo on the Symptom Dimensions of Borderline Personality Disorder

A Meta-Analysis of Randomized Controlled and Open-Label Trials

Antonio Vita, MD, PhD,† Luca De Peri, MD,* and Emilio Sacchetti, MD*†‡*

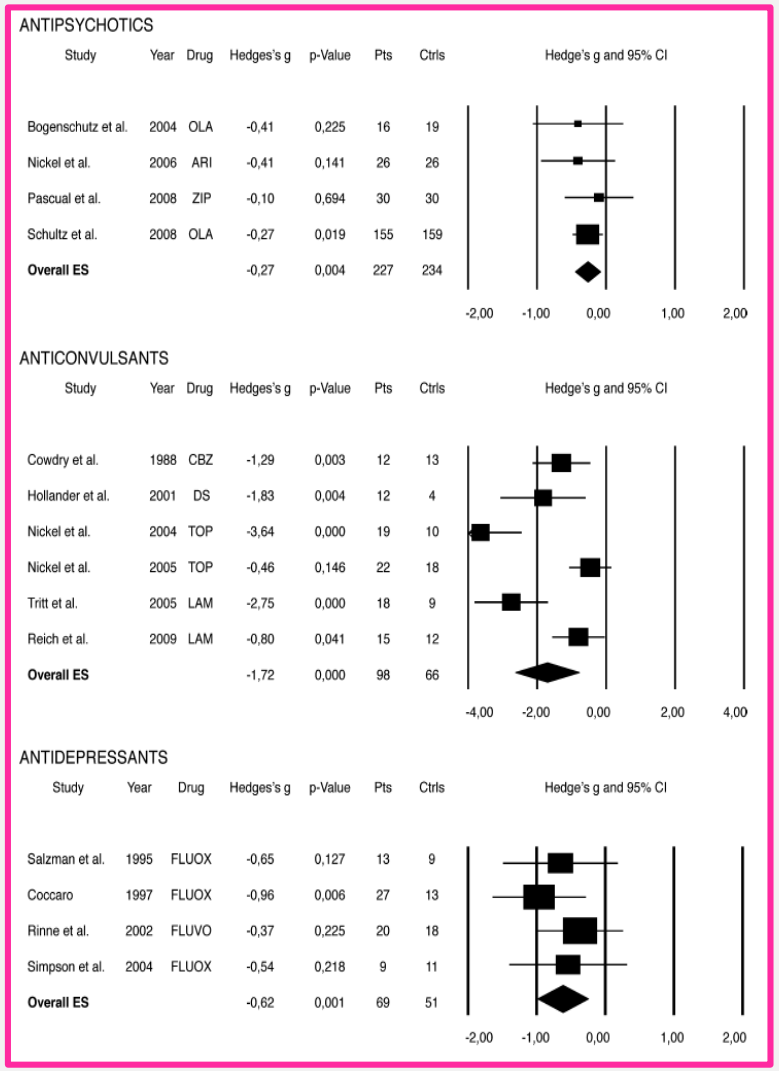
Abstract: The aim of this study was to quantitatively review randomized controlled trials (RCTs) and open-label trials analyzing the efficacy of antidepressants, mood stabilizers, and antipsychotics for the treatment of the core symptoms of borderline personality disorder (BPD). Using a similar meta-analytic approach, the efficacy of placebo on the same core symptoms of BPD was evaluated. The risk of discontinuation of each of the medication classes reported in the studies was also analyzed to establish the major causes of discontinuation. MEDLINE (1966 to June 2010) and EMBASE (1980 to June 2010) databases were systematically searched to identify relevant RCTs and open studies. The primary outcome was improvement in the specific core symptoms of the disorder: affective dysregulation, impulsive-behavioral dyscontrol, and cognitive-perceptual symptoms. Evidence from RCTs and open studies suggests that drug treatment, especially with mood stabilizers and antipsychotics, may be effective for treating affective dysregulation and impulsive-behavioral dyscontrol. Antipsychotics were also effective in reducing cognitive-perceptual symptoms. Antidepressants failed to show efficacy in treating BPD symptom dimensions other than affective dysregulation. Our analyses of the placebo arm of RCTs showed a significant improvement of symptomatology in these patients also. There were no significant differences in overall dropout rates between patients on medications and those on placebo. In conclusion, the efficacy of pharmacological treatment on the symptom dimensions of BPD has been shown by various independent meta-analyses, with a positive effect of drug treatment on the core symptoms of BPD and some documentable differences in terms of efficacy between different drug classes in each of the symptom domains.

Key Words: borderline personality disorder, antidepressants, antipsychotics, anticonvulsants, placebo, meta-analysis

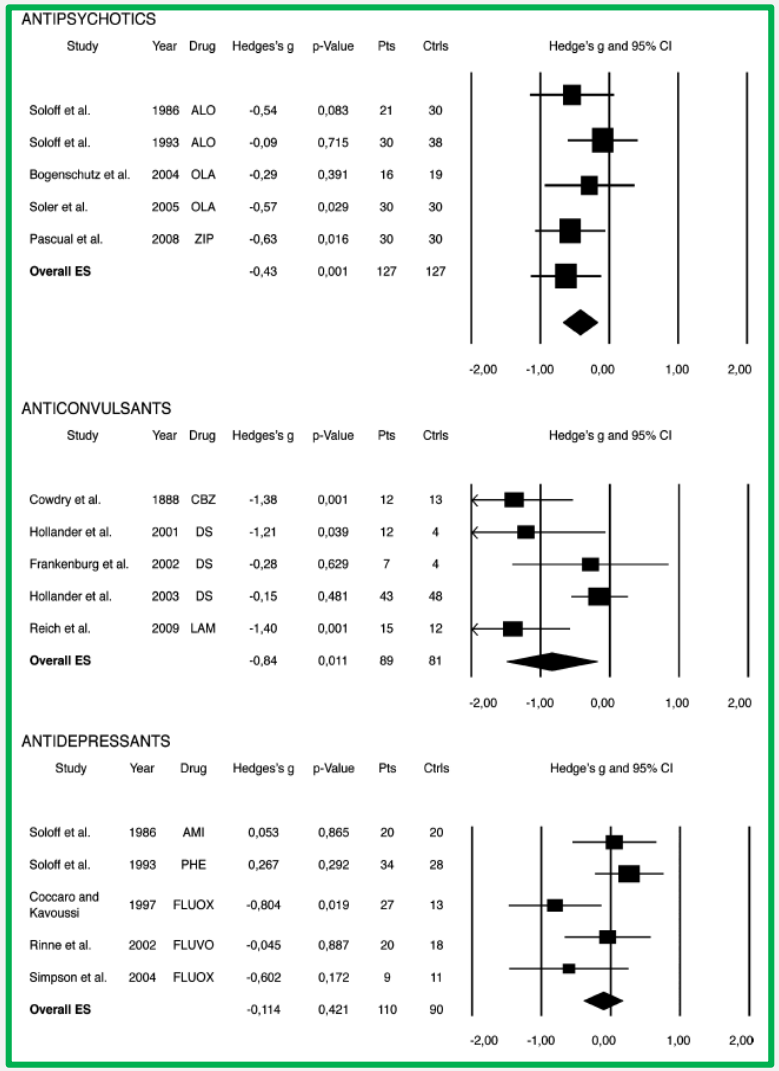
(*J Clin Psychopharmacol* 2011;31: 613–624)

Antipsychotics, Antidepressants, Anticonvulsants, and Placebo on the Symptom Dimensions of Borderline Personality Disorder. A Meta-Analysis of Randomized Controlled and Open-Label Trials

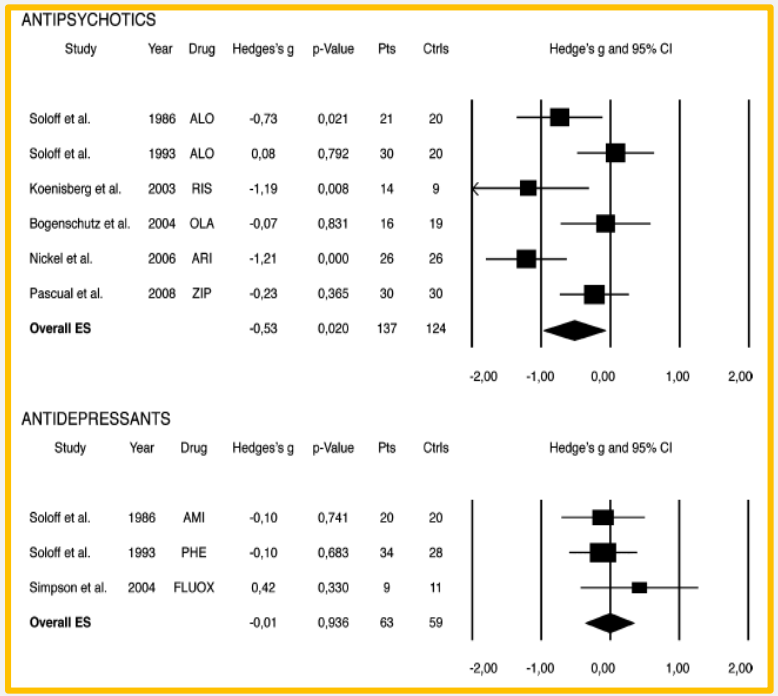
Affective dysregulation



Impulsive-behavioral dyscontrol



Cognitive-perceptual



Vita et al., 2011. J Clin Psychopharmacol

Impulsivity and its Therapeutic Management in Borderline Personality Disorder: a Systematic Review

Treatment	Source	Méthod	Participants	Scales	Interventions	Results
Fluvoxamine	Rinne et al, 2002 [14]	RCT 6 weeks double bind then single bind	38 female patients, median age 29.2 years with comorbidities: dysthymic disorder, depressive disorder, post-traumatic stress disorder, generalized anxiety disorders	BDPSI-impulsivity	Fluvoxamine (150 mg/d) $N=20$ vs placebo $N=18$	Not significant
Amitryptiline	Soloff et al, 1989 [22]	RCT 5 weeks	90 patients (68 women and 22 men), mean age 25.1 years, exclusions: schizophrenia, mania, chronic diseases, dual diagnostic presence (schizotypic / borderline)	Ward Scale of impulse actions patterns, BIS-11, STIC (self-evaluation)	Amitriptyline (149 mg/d after 3 weeks) $N=29$ vs placebo $N=28$	Not significant
Phenelzine	Soloff et al, 1993 [23]	RCT 5 weeks	108 patients (82 women and 26 men), mean age 26.7 years, exclusions: substance abuse and dependence, central nervous system disease, somatic diseases, mental retardation	Ward Scale of impulse actions patterns, BIS and STIC	Phenelzine sulfate up to 90 mg/d (mean 60,45 mg/d) $N=38$ vs placebo $N=34$	Not significant
Duloxetine	Bellino et al, 2010 [24]	Pilot study 12 weeks	18 patients, exclusion: dementia, cognitive disorder, psychotic disorder, schizophrenia, bipolar disorder, major depressive episode, substance abuse, psychotherapy in 3 months	BPDSI-impulsivity	duloxétine 60 mg/d	Significant $p=0.028$
Fluoxetine	Bellino et al, 2010 [25]	RCT 32 weeks	55 patients, exclusions: DSM-IVTR axis I and II disorder, cognitive impairment,	BPDSI impulsivity	fluoxétine 20 à 40 mg/d N=28 vs fluoxétine 20 à 40 mg/d +	Significant difference: fluoxetine + interpersonal> fluoxetine alone;

Mungo et al., 2020. Psychiatric Quarterly

Impulsivity and its Therapeutic Management in Borderline Personality Disorder: a Systematic Review

Treatment	Source	Méthod	Participants	Scales	Interventions	Results
Topiramate	Nickel et al, 2004 and 2005 [17, 29]	RCT 8 weeks	31 women (1st study) and 44 men (2nd study): suicidal ideation, alcohol and substance abuse, major depressive episode, schizophrenia, bipolar disorder, psychotherapy, pregnancy, somatic disease	STAXI-anger out	topiramate 250 mg/d N1 = 21 N2 = 22 vs placebo N1 = 10 N2 = 22	Significant difference SMD −3,36 (−4,44; −2,27)
Lamotrigine	Reich et al, 2009 [16]	RCT 12 weeks	27 patients (24 women and 3 men), mean age 31.2 years, exclusions: bipolar disorder, psychotic disorder, substance dependence, suicidal ideation, pregnancy, psychotherapy	ZAN BPD- impulsivity	Lamotrigine 25 à 225 mg (mean 106.7 mg/d) *N* = 15 vs placebo N = 12	Significant difference $p = 0.001$
Lamotrigine	Tritt et al, 2005 [30]	RCT 8 weeks	27 women, exclusions: bipolar disorder, major depressive episode, alcohol and substance abuse, schizophrenia, psychotherapy, suicidal ideation, pregnancy and somatic illness	STAXI anger out	Lamotrigine 200 mg/d N = 18 vs placebo *N* = 9	Significant difference SMD −1,62 (−2,54;-0,69)
Lamotrigine	Crawford et al, 2018 [31]	RCT 52 weeks	276 patients (208 women and 70 men), exclusions: bipolar disorder, psychotic disorder, mood stabilizer treatment, history of renal or hepatic impairment, cognitive impairment, pregnancy or breastfeeding	ZAN-BPD	Lamotrigine 200 mg/d (up to 400 mg / day for women on oral contraception) *N* = 137 vs placebo *N* = 1396	Not significant p = 0,824
Oxcarbazepine	Bellino et al, 2005 [32]	Pilot study 12 weeks	17 patients, 4 of whom left	BPDSI-impulsivity	Oxcarbazepine 1200 à 1500 mg/d	Significant difference p = 0,0005

Mungo et al., 2020. Psychiatric Quarterly

Impulsivity and its Therapeutic Management in Borderline Personality Disorder: a Systematic Review

Antipsychotics

Treatment	Source	Méthod	Participants	Scales	Interventions	Results
Flupentixol	Kutcher et al, 1995 [33]	Pilot study 6 weeks	13 patients (2 men and 11 women), 14 to 22 years (mean age: 17.2 years)	Ward scale of impulsivity	Flupentixol 3 mg/d	Significant p = 0.001
Quetiapine	Adityanjee et al, 2008 [39]	Pilot study 8 weeks	9 patients	BIS	Quetiapine 286.1 mg/d	Significant $p = 0.0021$
Quetiapine	Villeneuve et al, 2005 [42]	Pilot study 12 weeks	23 patients	BIS	Quetiapine 175 to 400 mg (mean 251 mg/d)	Significant $p = 0.0015$
Quetiapine	Bellino et al, 2006 [40]	Pilot study 12 weeks	14 patients	BIS-11 and BPDSI-impulsivity	quetiapine 200 à 400 mg/d (mean 309.9 mg/d)	Significant difference
Quetiapine	Van Den Eynde et al, 2008 [41]	Pilto study 12 weeks	41 patients (34 women and 7 men), mean age 27 years	BIS and STAXI	quetiapine 100 à 800 mg/d	Significant difference: BIS $p < 0{,}0001$, STAXI $p < 0.0001$
Quetiapine long acting	Black et al, 2014 [43]	RCT 8 weeks	95 patients aged 18 to 45, mean age 30.1 years excluded: Post-traumatic stress disorder, Obsessive-compulsive disorder, Major depressive episode, panic disorder, psychotic disorder, neurological disorder, cognitive disorder and substance dependence	ZAN-BPD- impulsivity and BIS	Quetiapine XR 150 mg/d $N = 33$ vs quetiapine XR 300 mg/d N = 33 vs placebo N = 29	Not significant
Paliperidone	Bellino et al, 2011 [47]	Pilot study 12 weeks	18 patients (5 men and 13 women), mean age 24.3 years, exclusion: psychotic disorder, bipolar disorder, major depressive episode, cognitive disorders, substance abuse and alcohol, dementia, treatment, pregnancy, hyperprolactinaemia	BIS-11 and BPDSI-impulsivity	paliperidone 3 à 6 mg/d, 4 left the study	Significant before-and-after difference in BIS-11 $p = 0.005$ and BPDSI-impulsivity $p = 0.001$
Aripiprazole	Nickel et al, 2006 [44]	RCT 8 weeks	52 patients (43 women and 9 men), mean age 21.2 years, exclusions: schizophrenia, suicidal ideation, somatic diseases, pregnancy or pregnancy project, psychotherapy	STAXI anger-out	aripiprazole 15 mg/d $N = 26$ vs placebo N = 26	Significant difference $p < 0.001$
Olanzapine	Schulz et al., 1999 [38]	Pilot study 8 weeks	11 patients with dysthymia, exclusion: schizophrenia, bipolar disorder or schizoaffective disorder	BIS-11	Olanzapine 2.5 mg at 10 mg / d average 7.72 mg / d	Significant p = 0.032
Risperidone	Friedel et al, 2008 [45]	Pilot study 8 weeks	18 patients, exclusion: participation in a clinical trial, pregnancy, Axis I disorder except posttraumatic stress disorder, dysthymic disorder, generalized anxiety disorder and substance abuse and dependence in remission for 3 months), schizotypal or antisocial personality disorder. suicidal ideation. unstable somatic disease, treatment less than one month before except an antidepressant	BIS and BDRS-impulsivity	risperidone 0,25 mg à 2 mg (moean1,8 mg)	Significant difference: BIS $p < 0{,}01$ et BDRS impulsivity $p < 0.005$
Risperidone intramusculaire	Carrasco et al, 2012 [46]	Pilot study 6 months	49 patients (30 women and 19 men) aged 18 to 45 years (mean age 27 years), exclusions: substance dependence, schizophrenia, schizophreniform disorder, bipolar disorder, neurological disorder, unstable somatic disease, pregnancy and oral risperidone intolerance	Overt aggression scale	Risperidone: 37.5 mg IM injection repeated every 2 weeks, sometimes increased to 50 mg	Significant difference $p < 0{,}001$
Aripiprazole + sertraline	Bellino et al, 2008 [48]	Pilot study	21 patients, exclusion: schizophrenia, psychotic disorder, bipolar disorder, major depressive episode and substance abuse of less than 6 months	BIS and BPDSI impulsivity	addition of aripriprazole from 10 to 15 mg in patients with sertraline (100–200 mg / day)	Significant BIS p = 0,017 BPDSI impulsivity $p = 0{,}011$

Mungo et al., 2020. Psychiatric Quarterly

Impulsivity and its Therapeutic Management in Borderline Personality Disorder: a Systematic Review

Other molecules

Treatment	Source	Méthod	Participants	Scales	Interventions	Results
Omega 3	Bozzatello et al, 2013 [51]	RCT 12 weeks	34 patients (8 men and 26 women), mean age 25.2 years exclusions: dementia, cognitive disorder, psychotic disorder, schizophrenia, bipolar disorder, major depressive episode, substance abuse, taking medication or psychotherapy 2 months ago	BIS 11, MOAS and BPDSI-impulsivity	valproic acid (800 to 1300 mg / day) N = 16 vs omega 3 (EPA 1.2 g / day and DHA 0.8 g / day) + valproic acid (800 to 1300 mg / day) N = 18	Significant: BIS-11 $p = 0.031$and BPDSI-impulsivity $p = 0.031$ Not significant MOAS $p = 0.068$
Omega 3	Bozzatello et al,2018 [52]	follow up after 24 weeks of Bozzatello and al, 2013	34 patients (8 men and 26 women), mean age 25.2 years exclusions: dementia, cognitive disorder, psychotic disorder, schizophrenia, bipolar disorder, major depressive episode, substance abuse, taking medication or psychotherapy 2 months ago	BIS 11 and BPDSI-impulsivity	valproic acid (800 to 1300 mg / day) $N = 16$ vs omega 3 (EPA 1.2 g / day and DHA 0.8 g / day) + valproic acid (800 to 1300 mg / day) $N = 18$	Significant: BIS 11 p = 0.02 and BPDSI impulsivity $p = 0.032$
Omega 3	Zanarini et al, 2003 [50]	RCT 8 weeks	30 women, mean age 26.3 years, exclusions: bipolar disorder type 1 and 2, schizophrenia, schizoaffective disorder, major depressive episode	MOAS	omega 3 1 g/d N = 20 vs placebo N = 10	Significant difference $p < 0{,}0001$

Mungo et al., 2020. Psychiatric Quarterly

Benzodiazepine use and aggressive behaviour: A systematic review

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Abstract

Context: The relationship between benzodiazepine consumption and subsequent increases in aggressive behaviour in humans is not well understood.

Objectives: The current study aimed to identify, via a systematic review, whether there is an association between benzodiazepine consumption and aggressive responding in adults.

Method: A systematic review was conducted and reported in line with the PRISMA statement. English articles within MEDLINE, PsycARTICLES, PsycINFO, Academic Search Complete, and Psychology and Behavioural Sciences Collection databases were searched. Additional studies were identified by searching reference lists of reviewed articles. Only articles that explicitly investigated the relationship between benzodiazepine consumption and subsequent aggressive behaviour, or a lack thereof, in human adults were included.

Results: Forty-six studies met the inclusion criteria. It was not possible to conduct a meta-analysis due to the heterogeneity of study design and benzodiazepine type and dose. An association between benzodiazepine use and subsequent aggressive behaviour was found in the majority of the more rigorous studies, although there is a paucity of high-quality research with clinical or forensic populations. Diazepam and alprazolam have received the most attention. Dose-related findings are inconsistent: therapeutic doses may be more likely to be associated with aggressive responding when administered as a once-off, whereas higher doses may be more risky following repeated administration. Trait levels of anxiety and hostility may indicate a vulnerability to the experience of benzodiazepine-related aggression.

Conclusions: There appears to be a moderate association between some benzodiazepines and subsequent aggressive behaviour in humans. The circumstances under which aggressive responding may be more likely to follow benzodiazepine use remain unclear, although some evidence suggests dose and/or personality factors may influence this effect.

Current and emerging medications for borderline personality disorder: is pharmacotherapy alone enough? - Antidepressants

Study (year) [Ref.]	Interventional arm(s)	Comparison arm(s)	Sample	Treatment duration	Results
Salzamann et al. (1995) [28]	Fluoxetine (20–60 mg/day)	Placebo	27 BPD patients	12 weeks	Decrease in anger, improvement in global functioning. No effect on depression
Markovitz (1995) [29]	Fluoxetine (20–80 mg/day)	Placebo	17 BPD patients with concomitant affective and anxiety disorders	14 weeks	Decrease of all symptoms
Coccaro and Kavoussi (1997) [30]	Fluoxetine (20–60 mg/day)	Placebo	40 patients with PDs (33% BPD) and comorbidity with dysthymia, anxiety disorders or substance abuse	12 weeks	Improving of irritability, impulsive-aggression, and global functioning
Simpson et al. (2004) [31]	Fluoxetine (40 mg/day) + DBT	Placebo + DBT	25 female BPD patients	12 weeks	No effects
Zanarini et al. (2004) [32]	Fluoxetine (15 mg/day)	Fluoxetine (15 mg/day) + olanzapine (2.5 mg/day) and olanzapine (2.5 mg/day)	45 female BPD patients	8 weeks	Both the comparison arms resulted to be superior to fluoxetine monotherapy to decrease all symptoms
Rinne et al. (2002) [34]	Fluvoxamine (150–250 mg/day)	Placebo	38 female BPD patients, comorbidity with mood and anxiety disorders	6 weeks	Decrease of rapid mood shifts. No effects on aggression and impulsivity
Jariani et al. (2010) [35]	Sertraline (50–100 mg/day)	Olanzapine (5–10 mg/day)	120 BPD patients on methadone therapy	12 weeks	Sertraline > olanzapine in decreasing depression, hypersensitivity in interpersonal relationship, and obsessions. Olanzapine > sertraline in decreasing anxiety, aggression, paranoia, and self-harming Sertraline = olanzapine in decreasing Somatization symptoms
Markovitz et al. (1995) [36]	Venlafaxine				Effective in reducing somatic symptoms
Bellino et al. (2010) [37]	Duloxetine (60 mg/day)		18 BPD patients	12 weeks	Improvement of depressive symptoms, impulsivity, outbursts of anger, and affective instability

The overall use of antidepressants in BPD has decreased recently.

Prescription of these agents is recommended only for comorbid affective disorder.

No placebo-controlled trials on the efficacy of antidepressants in BPD have been performed since 2010.

The main results were that SSRIs positively impacted affective symptoms in BPD. Controlled trials of SNRIs are lacking, and there have been no new studies of new antidepressants (vortioxetine).

Bozzatello et al., 2020 Expert Opin Pharmacother

Current and emerging medications for borderline personality disorder: is pharmacotherapy alone enough? – Mood Stabilizers

Study (year) [Ref.]	Interventional arm(s)	Comparison arm(s)	Sample	Treatment duration	Results
Links et al. (1990) [39]	Lithium (986 mg/day)	Desipramine and placebo	17 BPD patients receiving concomitant psychotherapy	6 weeks	Lithium was superior to ecrease anger, irritability and self-mutilation. No effects on mood symptoms
De la Fuente and Lotstra (1994) [40]	Carbamazepine (plasma level)	Placebo	20 BPD outpatients	4.5 weeks	No effects
Hollander et al. (2001) [41]	Valproate sodium(plasma level)	Placebo	16 BPD patients	10 weeks	No effects (probably because of high drop-out rate)
Hollander et al. (2005) [42]	Valproate sodium (plasma level)	Placebo	96 cluster B PDs (52 BPD) with impulsive-aggression	12 weeks	Improvement of global symptopathology, impulsive-aggression, and irritability
Frankenburg and Zanarini (2002) [43]	Valproate sodium (plasma level)	Placebo	30 female BPD patients with comorbid bipolar II disorder	6 months	Improvement of interpersonal sensitivity, anger, hostility, and aggressiveness
Moen et al. (2012) [44]	Divalproex ER (plasma level)	Placebo	15 BPD patients after 4 weeks of "condensed" DBT	4 weeks	No differences between the two arms
Bellino et al. (2014) [45]	EPA and DHA with valproic acid (plasma level)	Valproic acid only (plasma level)	43 BPD outpatients	12 weeks	Combined therapy > single therapy for impulsivity, self-harm, and outbursts of anger
Nickel et al. (2004) [46]	Topiramate (50–250 mg/day)	Placebo	31 female BPD patients	8 weeks	Improvement of irritability and anger
Nickel et al. (2005) [47]	Topiramate (50–250 mg/day)	Placebo	42 male BPD patients	8 weeks	Improvement of irritability and anger
Loew et al. (2008) [51]	Topiramate (25–200 mg/day)	Placebo	56 female BPD patients with concomitant mood disorders	10 weeks	Improvement of somatization, interpersonal sensitivity, hostility and global functioning
Tritt et al. (2005) [52]	Lamotrigine (50–200 mg/day)	Placebo	24 female BPD patients	8 weeks	Improvement of anger
Reich et al. (2009) [53]	Lamotrigine (25–275 mg/day)	Placebo	28 BPD patients with major depression and anxiety disorders	12 weeks	Improvement of impulsivity and affective instability
Leiberich et al., (2008) [54]	Lamotrigine (50–200 mg/day)	Placebo	27 female BPD patients	18 months follow-up	Improvement of aggression in the long-term treatment
Crawford et al., (2015) [55]	Lamotrigine (25–400 mg/die)	Placebo	28 BPD patients	52 weeks	No effect in terms of symptomatic reliefs and cost-effectiveness balance.

Large-scale double-blind placebo trials should be conducted. Drug-drug comparison trials between different mood stabilizers would clarify their effects on symptom domains and establish whether there are significant differences in efficacy between the drugs.

Nonetheless, the available evidence suggests that valproate, topiramate, and lamotrigine are a therapeutic option in treating impulsivity, anger, and affective instability in BPD patients.

Bozzatello et al., 2020 Expert Opin Pharmacother

Study (year) [Ref.]	Interventional arm(s)	Comparison arm(s)	Sample	Treatment Duration	Results
Cornelius et al. (1993) [61]	Haloperidol (≤6 mg/day)	Placebo	54 BPD outpatients from Soloff et al. (1993) study	16 weeks	Improvement of hostility and impulsive-aggression
Soloff et al. (1993) [62]	Haloperidol (4 mg/day)	Phenelzine (60 mg/day) and placebo	108 BPD inpatients with concomitant major depression	5 weeks	Improvement of irritability
Szigety &Schultz (1998) [75]	Risperidone (2.5 mg/day)	Placebo	27 BPD patients	8 weeks	No difference with regard to global functioning. Risperidone > placebo in reducing psychoticism, paranoid ideas, phobic anxiety and interpersonal sensitivity
Zanarini and Frankenburg (2001) [78]	Olanzapine (5.33 mg/day)	Placebo	28 female BPD patients	6 months	Improvement of anger, interpersonal sensitiv, anxiety, paranoid ideation and global functioning
Bogenschutz and Numberg (2004) [79]	Olanzapine (5–10 mg/day)	Placebo	40 BPD outpatients	12 weeks	Improvement of anger and global symptoms
Schulz et al. (1998) [80]	Olanzapine (2.5–20 mg/day)	Placebo	314 BPD patients	12 weeks	No differences between two groups. Faster amelioration in olanzapine group.
Zanarini et al. (2011) [81]	Olanzapine low doses (2.5 mg/day) and moderate doses (5–10 mg/day)	Placebo	451 BPD outpatients	12 weeks	Olanzapine moderate doses > placebo in global symptoms
Soler et al. (2005) [82]	Olanzapine (5–20 mg/day) + DBT	Placebo + DBT	60 BPD patients	12 weeks	Improvement of anxiety, depression and impulsive-aggression
Linehan et al. (2008) [83]	Olanzapine (5 mg/day) + DBT	Placebo + DBT	24 female BPD patients	21 weeks	No differences of general symptoms. Faster decrease of irritability and aggression in olanzapine group
Jariani et al. (2010) [84]	Olanzapine (5–10 mg/day)	Sertraline (50–100 mg/day)	120 BPD patients on methadone maintenance therapy	12 weeks	Both drugs improving depression, anxiety, aggression, sensitivity in interpersonal relationships, obsessive symptoms, pessimistic behaviors and somatization disorders
Shafti and Shahveisi (2010) [85]	Olanzapine (7 mg/day)	Haloperidol (7 mg/day)	28 female BPD inpatients	8 weeks	No differences
Bozzatello et al. (2017) [86]	Olanzapine (5–10 mg/day)	Asenapine (5–10 mg/day)	51 BPD patients between 18 and 50 years	12 weeks	Asenapine > Olanzapine in treating affective instability Olanzapine > Asenapine in treating paranoid ideation and dissociation
Shafti and Kaviani (2015) [87]	Olanzapine (6.4 mg/day)	Aripiprazole (7 mg/day)	24 female BPD inpatients	8 weeks	Olanzapine > Aripiprazole on uncooperativeness and excitement Aripiprazole > Olanzapine on suspiciousness and unusual thought content
Nickel et al. (2006) [88]	Aripiprazole (15 mg/day)	Placebo	57 BPD patients	8 weeks	Improvement of depression, anxiety, anger, aggressiveness, paranoia and global functioning
Nickel et al. (2007) [89]	Aripiprazole (15 mg/day)	Placebo	52 BPD patients	18 months	Effective and relatively safe agent in the long-term treatment
Chanen et al. (2018) [92]	Aripiprazole (2–30 mg/day)	Placebo	154 BPD patients	12 weeks + 27-week follow-up	Improvement of general psychopathology, borderline personality pathology, social and occupational functioning
Black et al. (2014) [100]	Quetiapine low (150 mg/day) and moderate doses (300 mg/day)	Placebo	95 BPD patients (70.5% female)	8 weeks	Quetiapine low doses > placebo in all the outcomes measures (in particular affective instability, cognitive-perceptual symptoms and aggressiveness). Faster response in both the treatment groups
Lee et al. (2016) [101]	Quetiapine low (150 mg/day) and moderate doses (300 mg/day)	Placebo	95 BPD patients (70.5% female)	8 weeks	Improvement of all the outcomes measures with both quetiapine doses
Pascual et al. (2008) [104]	Ziprasidone (84 mg/day)	Placebo	60 BPD patients	12 weeks	No effects
Bellino et al. (2009) [91]	Sertraline (50–100 mg/day) + Aripiprazole (10–15 mg/day)	Open label trial	21 BPD patients between 18 and 50 years	12 weeks	Improvement of impulsivity and dissociation/paranoid ideation
Perrella et al. (2007) [97]	Quetiapine (400–800 mg/day)	Open label trial	29 BPD outpatients	12 weeks	Improvement of mood symptoms and aggression
Bellino et al. (2011) [76]	Paliperidone ER (3–6 mg/day)	Open label trial	18 BPD outpatients	12 weeks	Improvement of impulsive dyscontrol, anger, and cognitive-perceptual disturbances
Rocca et al. (2002) [71]	Risperidone (3.27 mg/day)	Open label trial	15 BPD outpatients	8 weeks	Improvement of depressive symptoms, energy and global functioning

New Antipsychotics in Treatment of Mood Instability and Cognitive Perceptual Symptoms in Borderline Personality Disorder

Haloperidol was associated with hostility, irritability, and impulsive-aggressive behaviors reduction in BPD, but no improvement in global severity. Haloperidol seems to be responsible of depressive symptoms during prolonged treatment.

FGAs can be administered to BPD patients during acute states with impulsive-aggressive behaviors and psychotic-like symptoms but evidence on efficacy is limited. Thus, low doses and for short periods are needed to reduce AEs.

SGAs are associated with fewer EPS, lower risk of tardive dyskinesia, and moderate effects on negative affectivity, disinhibition, and interpersonal dysfunction.

Olanzapine and **aripiprazole** are efficacious both in treating cognitive-perceptual symptoms and in decreasing mood instability and impulsive dyscontrol.

Quetiapine showed effects on a wide range of BPD symptoms, including impulsive-aggressive behaviors, anger, and affective instability but evidence is limited due to lack of RCT.

Clozapine is useful in reducing impulsivity, affective instability, self-mutilating behaviors, and cognitive-perceptual symptoms, reducing psychiatric admission but its use is limited due to AEs and possible non-adherence in BPD population.

Limited results are provided regarding other anipsychotics**.**

Bellino et al., 2012 Current Psychopharmacology

Current and emerging medications for borderline personality disorder: is pharmacotherapy alone enough? - Other psychotropic agents

Study (year) [Ref.]	Interventional arm(s)	Comparison arm(s)	Sample	Treatment Duration	Results
Philipsen et al. (2004) [110]	Naloxone (0,4 mg/day)	Placebo	9 BPD patients	15 min	No differences in dissociative symptoms
Schmahl et al. (2012) [111]	Naltrexone (50 or 200 mg/day)	Placebo	29 BPD patients	3 weeks	No differences in dissociative symptoms
Bertsch et al. (2013) [115]	Oxytocin (26 IU)	Placebo	40 female nonmedicated BPD patients	45 minutes	Improvement of social hypersensitivity, anger and aggressive behavior
Philipsen et al. (2004) [119]	Clonidine (75 µg/day)	Clonidine (150 µg/day)	14 female BPD patients	30,60 and 120 min	Decrease (maximum after 30–60 min) of all the symptoms with both doses of clonidine
Ziegenhorn et al. (2009) [120]	Clonidine (up to 0,3 mg/day)	Placebo	18 BPD patients, some of them with concomitant PTSD	6 weeks	Decrease of hyperarousal symptoms independently of PTSD comorbidity. Decrease of BPD specific and general symptoms mainly in the PTSD-positive subgroup
Zanarini and Frankenburg, (2003) [121]	EPA (1 g/day)	Placebo	30 female BPD patients	8 weeks	Improvement of Depressive symptoms and aggressive behaviors
Hallahan et al. (2007) [122]	EPA (1.2 g/day)+DHA (0,9 g/day)	Placebo	49 patients with self-harm behaviors (35 BPD)	12 weeks	Improvement of depression, suicidality and reaction to daily stress
Amminger et al. (2013) [123]	PUFAs (1,2 g/day)	Placebo	15 adolescent BPD patients with high risk of psychosis	12 weeks	Improvement of global functioning and schizophrenia-like symptoms
Bellino et al. (2014) [45]	EPA (1.2 g/day) + DHA (0,8 g/day) + valproate (800–1300 mg/day)	Valproate (800–1300 mg/day)	43 BPD outpatients	12 weeks	No differences with regard to global symptoms. Improvement of impulsivity, anger and self-mutilating conducts in omega-3 group
Bozzatello et al. (2018) [124]	EPA (1.2 g/day) + DHA (0,8 g/day) + valproate (800–1300 mg/day)	Valproate (800–1300 mg/day)	43 BPD outpatients	24 weeks follow-up	Combined therapy with omega-3 fatty acids showed long-lasting effects after discontinuation in terms of anger control.
Kulkarni et al. (2018) [126]	Memantine (20 mg/die)	Placebo	33 BPD outpatients	8 weeks	Memantine showed > improvement on aggression, disinhibition, irritability and depressed mood

- **Omega-3 fatty (Bellino et al, 2014) (Bozzatello et al., 2018)**: 3 placebo-controlled studies compared the efficacy of omega-3 fatty acids with placebo, and 1 RCT compared the association of omega-3 fatty acids and valproate with single valproate. The association of eicosapentaenoic acid and docosahexaenoic acid was found efficacious in treating depressive symptoms, aggressive behaviors, impulsivity, anger, and self-injury. One study evaluated long-term efficacy of these agents in BPD (6 months after discontinuation of omega-3 fatty acids with ongoing valproate) suggested a long-lasting effect in terms of anger control.

Bozzatello et al., 2020. Expert Opin Pharmacother

Current and emerging medications for borderline personality disorder: is pharmacotherapy alone enough? – Conclusions

[..] **A careful examination of trials published in recent years provides only limited evidence of the efficacy of some mood stabilizers (valproic acid), new generation antipsychotic (olanzapine and, to lesser degree, aripiprazole), and omega-3 fatty acids.**

The small number of controlled studies, the heterogeneity of the results, and the methodological shortcomings in methods impede reaching any reliable conclusion on the utility of these drugs in clinical practice. Even less is known about specific adverse effects in BPD. Therefore, we suggest using these psychotropic agents only when a comorbid condition is present, or an acute crisis has to be addressed [..]

[..] Low-quality evidence, divergent guidelines recommendations, and differences between experimental settings and realworld clinical practice contributed to confusion and contrasting findings.

At the moment, there is a generally low level of evidence to support the efficacy of psychotropic agents in BPD patients.

Bozzatello et al., 2020. Expert Opin Pharmacother

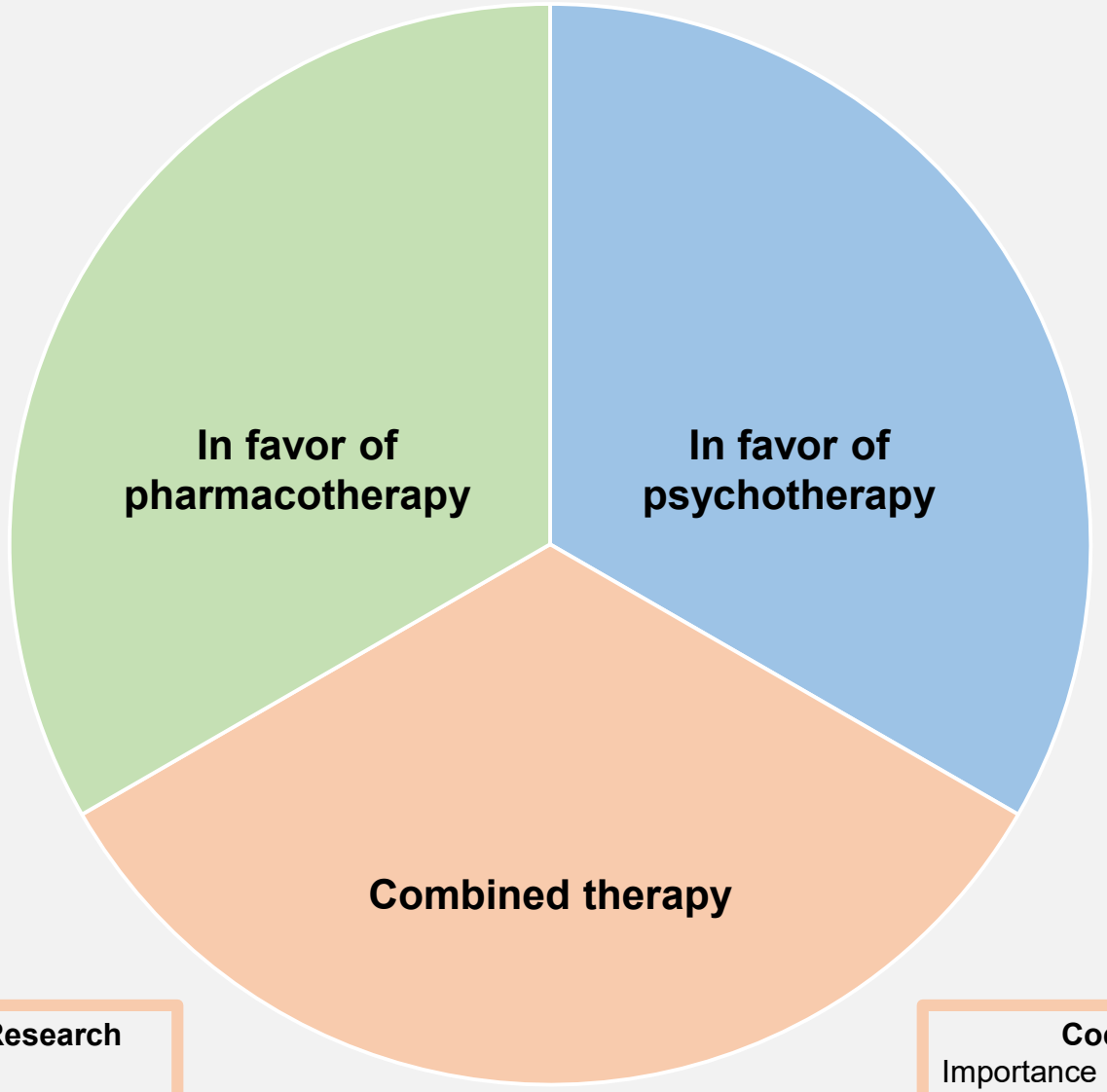
Drug treatment recommendations

Word Federation of Societies of Biological Psychiatry (2007)

Affective dysregulation, impulsivity, cognitive-perceptual symptoms and anger are main drug targets.
Pharmacological effects are increased when combined with psychosocial interventions.
Antidepressants and MS showed *Level B* evidence of efficacy (fair), SGAs showed *Level C* evidence (minimal).

APA guidelines (2001)

Targeting three main psychopatological domain (affective dysregulation, impulsivity, and cognitive-perceptual symptoms), pharmacotherapy is conceived as oriented at specific symptoms domain to treat stated symptoms during period of acute decompensation and trait vulnerabilities. Anyway, *«patients with BPD should be informed that there is no strong evidence base for the prescription of any drug»*



NICE guideline (2009)

Drug therapy is not recommended other than to treat comorbid mental disorder or to control specific acute symptoms during a crisis and with short-term prescription.

Australian National Health and Medical Research Council guidelines (2012)

Drug therapy is recognized as a second-line/adjunctive treatment whereas psychotherapy is confirmed as the first-line treatment.

Cochrane Review (Stoffer et al., 2015)

Importance to combine psychotherapy and medications.
Among drugs, some evidences on SGA, mood stabilizers and omega-3 fatty acids.
Data do not support the role of antidepressants.

Conclusions

Pharmacotherapy of borderline personality disorder: replacing confusion with prudent pragmatism

Prescribing psychotropic agents to patients with BPD is clearly off-label but […] the key issue here seems to be a dilemma about the appropriateness of alleviating the symptoms of BPD instead of treating BPD as a disorder.

symptom-based approach «has been criticized mainly on methodological grounds, but it has created an impression of a symptom-level precision in the pharmacological treatment of BPD, with clinician's key task being to match the specific medications with the specific BPD symptoms in each patient. Whether this is precision or pseudoprecision is debatable and an ongoing source of controversy and confusion.

The application of the targeted pharmacotherapy approach might have contributed to the polypharmacy in BPD, especially if interpreted to mean that different symptoms of BPD call for different medications».

However a targeted pharmacotherapy approach to BPD encourages clinicians to use medications for potentially medication-responsive BPD symptoms and it is not against good clinical practice more generally to choose a medication based on the predominant presenting symptoms.

In conclusion […] « **clinicians would do well to be both flexible and prudent about using medications for BPD**. Flexibility is needed when assessing the need for pharmacotherapy, so that medications are used when necessary but otherwise avoided. Prudence is required to maximize the benefits of pharmacotherapy and minimize its harm; **at present, this usually means a short-term administration of medication at times of crisis and exacerbation and frequent evaluation of a need to continue pharmacotherapy».**

Starcevic & Janca, 2019. Curr. Opin. Psych.