6 th Maudsley Mediterranean Forum

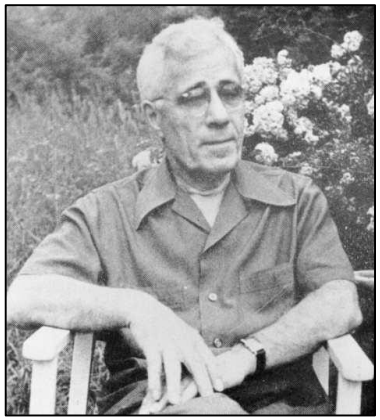
Palermo, 29 May 2019

UNIVERSITÀ DEGLI STUDI DI CATANIA
AZIENDA OSPEDALIERO UNIVERSITARIA
*«Policlinico – Vittorio Emanuele»*
CATTEDRA DI PSICHIATRIA

# Defining the borders between Borderline Personality disorder and Bipolar disorder

Ludovico Mineo
Eugenio Aguglia

# BORDERLINE PERSONALITY DISORDER: ORIGINS OF DIAGNOSIS



Adolph Stern
(1879-1958)

Adolph Stern recognized that a subgroup of his patients disregarded the usual boundaries of psychotherapy and did not fit into the existing classification system, a system concerned primarily with dividing psychoses from neuroses.

## BORDERLINE GROUP OF PATIENTS CORE SYMPTOMS

Narcissism, psychic bleeding, inordinate hypersensitivity, psychic and body rigidity, negative therapeutic reactions, what looks like constitutionally rooted feelings of inferiority (deeply imbedded in the personality of the patient), masochism, what can be described as a state of deep organic insecurity or anxiety, the use of projection mechanisms, difficulties in reality testing (particularly in personal relationships)

# FROM ORGANIZATION TO SYNDROME TO DISORDER

Otto Kernberg,
(1928 - )

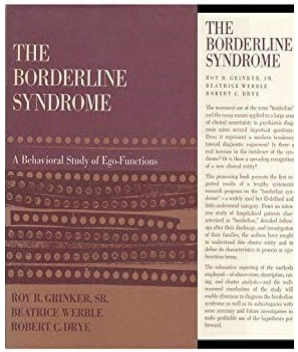
"not a transitory state fluctuating between neurosis and psychosis, but a stable personality organization "

Neurotic personality organization

Psychotic personality organization

## Borderline personality organization

Failed or weak identity formation, primitive defenses (namely, splitting and projective identification), and reality testing that transiently lapsed under stress.



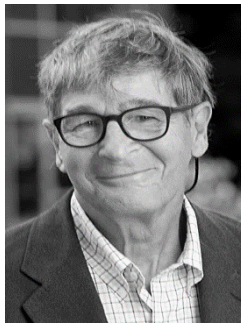

Roy R. Grinker, Sr.
(1900-1993)

## Borderline Syndrome

### Core Features

- Failures of self-identity
- Anaclitic relationships
- Depression based on loneliness
- Predominance of expressed anger.

# FROM ORGANIZATION TO SYNDROME TO DISORDER



John G. Gunderson,
(1942 - 2019)


**Discriminating Features of Borderline Patients**

BY JOHN G. GUNDERSON, M.D., AND JONATHAN E. KOLB, M.D.

*Am J Psychiatry 135:7, July 1978*

## CRITERIA FOR BORDERLINE PATIENTS

- **Low achievement**
- **Impulsivity**
- **Manipulative suicidal gestures**
- **Heightened affectivity**
- **Mild psychotic experiences**
- **High socialization (intolerance of being alone)**
- **Disturbed close relationships ( de-evaluation , manipulation, dependency)**

# DIAGNOSTIC CRITERIA DSM IV TR\DSM 5 FOR BORDERLINE PERSONALITY DISORDER



**Affective criteria**

- Inappropriate intense anger or difficulty controlling anger (eg, frequent displays of temper, constant anger, recurrent physical fights).
- Chronic feelings of emptiness.
- Affective instability that is due to marked reactivity of mood (eg, intense episodic dysphoria, irritability or anxiety usually lasting a few hours and only rarely more than a few days).

**Cognitive criteria**

- Transient, stress-related paranoid ideation or severe dissociative symptoms.
- Identity disturbance: notably and persistently unstable self-image or sense of self.

**Behavioral Criteria (forms of impulsivity)**

- Recurrent suicidal gestures, or threats or self-mutilating behaviour.
- Impulsivity in at least two areas that are potentially self-damaging (eg, spending, sex, substance misuse, reckless driving, binge eating).

**Interpersonal criteria**

- Frantic efforts to avoid real or imagined abandonment.
- A pattern of unstable and intense interpersonal relationships characterised by alternating between extremes of idealisation and devaluation.

DSM-V (American Psychiatric Association, 2013)

*"The typical clinical picture of borderline emerging from DSM-III and DSM-III-R describes an angry, depressed and impulsive patient, who, due to his mood instability,* ***can be considered not so much related to schizophrenia,*** *perhaps more so with* ***manic-depressive psychosis.*** *The features most typically considered close to schizophrenia (social isolation, suspiciousness, ideas of reference, inappropriateness, etc.) are in fact assigned to the diagnosis of schizotypical personality "*

"

# WHO IS A BPD PATIENT?

Amy Winehouse
1983 - 2003

Self-Injury
Shame
Volatile relationships
Substance abuse
Impulsive
Suicidal
Eating disorder
Excessive anger

A clinical definition of "borderline pathology" should be articulated on three differentiated levels, the clinical one, psychosocial and relational.

On the clinical level: "the borderline patient shows one chronic disease, "stable in its instability" that takes the form of a Personality disorder, characterized by unstable and atypical mood symptoms, anxiety symptoms, impulse dyscontrol, dissociative or micropsychotic phenomena, complicated by the use of substances or other addictive behaviours, often as form of selt-treatment

On the psychosocial level: “the borderline patient presents a problematic relationship compared to the concreteness of life, as shown by the partial or total incapacity to assume a role and a social and working identity, with consequent permanent project precariousness ”

On a relational level: "borderline patients present a particular form of ambivalent attachment to caregivers and partners, characterized by the" impossible triad ": inability to be alone, inability to maintain stable relationships, intolerance of separations. However, despite the precariousness and the high level of conflict between their relationships, sometimes these also show a paradoxical depth and duration ("Neither with you nor without you" )

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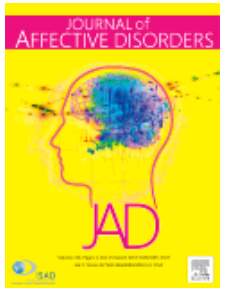
# Defining the borders between Borderline Personality disorder and Bipolar disorder

## BORDERLINE PERSONALITY DISORDER\BIPOLAR DISORDER COMORBIDITY:

## REALITY OR ARTIFICE?




# The prevalence and predictors of bipolar and borderline personality disorders comorbidity: Systematic review and meta-analysis

M. Fornaro [a,*], L. Orsolini [b,c,d], S. Marini [e], D. De Berardis [f], G. Perna [g], A. Valchera [d], L. Ganança [a,h], M. Solmi [i,j], N. Veronese [k], B. Stubbs [l,m]

M. Fornaro et al. / Journal of Affective Disorders 195 (2016) 105–118

42 papers (28 considering BPD in BD and 14 considering BD in BPD)

PREVALENCE OF BORDERLINE PERSONALITY DISORDER IN BIPOLAR DISORDERS:

26.1 % BDs

37,5 % Bd type II

**Higher comorbid BPD in BD were noted in BD II participants (37.7%, 95% CI 21.9–56.6, studies= 6) and North American studies (26.2%, 95% CI 18.7– 35.3, studies=11)**

PREVALENCE OF BIPOLAR DISORDER IN BORDERLINE PERSONALITY DISORDERS:

18.5% BDs

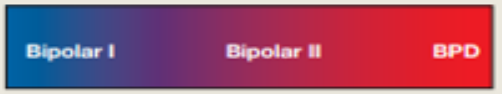
**BD mixed was evident in 19.89% (95% CI 12.23–30.67) of people with BPD, which was higher than BD I (15.30%, 95% CI 6.47–32.06) and BD II (12.65%, 95% CI 4.79–29.47)**

# BORDERLINE, BIPOLAR OR BOTH?

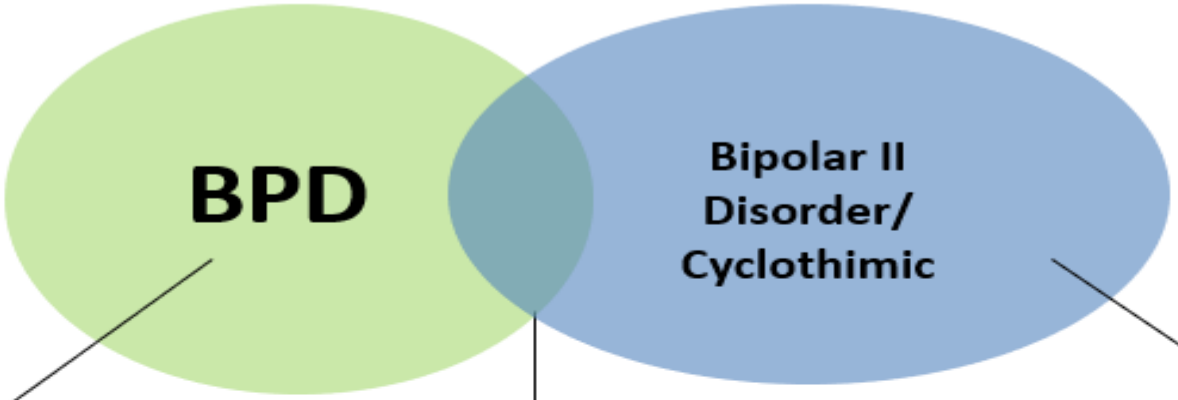
## MISDIAGNOSIS

Inability of current nosology to separate 2 distinct conditions


BPD exists on a spectrum with bipolar disorder




## OVERLAPPING SYMPTOMS




### Personality traits

Sensitivity to hostility and separations
"Badness self-image"
Identity disturbance
Chronic feeling of emptiness
Unstable relationships

### Overlapping characteristics

Impulsivity
Affective instability
Inappropriate anger
Recurrent suicidality and self-harm injuries
Psychotic traits

### Personality traits

Interpersonal insensitivity
Grandiose self image

# CRITICISMS TO THE BORDERLINE PERSONALITY DISORDER CONSTRUCT.


## Is BPD a personality disorder?

Studies conducted by well-known supporters of the conceptualization of BPD as a personality disorder have shown that **high rates of BPD patients undergo remission within the fourth decade of life**. Although this finding contradicts the very intrinsic definition of personality disorder, these same authors have not shown themselves opened to consider BPD as **a chronically fluctuating and relapsing affective disorder** , suggesting rather that the concept of personality disorder as life long disorder should be modified

## Definitional inadequacies of BPD

The operational construct of BPD has a low discriminatory validity. **BPD has an unwieldy heterogeneity, overlapping not only with personality disorders within its own erratic cluster, but also with the odd and anxious clusters**. Moreover BPD criteria, rather than restricting themselves to defining personality attributes, **mix traits, symptoms and behaviors** -- particularly of an affective nature, accounting for the significant overlap of BPD with affective and addictive disorder.

## Trivialization of Borderline personality organization

The operational construct of BPD has trivialized Kernberg's Borderline Personality Organization. **This latter is not a specific nosologic entity, but it describes a vulnerable psychic structure** that functions at a "stably unstable" level between the classic neuroses and psychoses, underpinning different personality dysfunctions .

Acta Psychiatrica Scandinavica

Acta Psychiatr Scand 2004: 110: 401–407

Editorial

# Demystifying borderline personality: critique of the concept and unorthodox reflections on its natural kinship with the bipolar spectrum

Hagop Akiskal

**BPD symptoms are primarily affective**: unstable, hostile, and labile moods - the unrelenting tension and irritability with superimposed paroxysms of rage – have been relegated by Gunderson and other authors into the characterologic realm. **Actually these are manifestations of a cyclothymic sensitive diathesis**

BPD patients are more likely to present a **higher familiarity for bipolar spectrum disorder than for schizophrenic spectrum**, **to have spontaneous and pharmacologic excursions into brief periods of elation**, **to receive an affective diagnosis at the follow up**

Beside the notion of hypomania as positive sunny euphoric traits and behaviour, there also exists **a more pervasive irritable-tempestuous side to bipolarity, the form most likely to arise from a cyclothymic baseline**, representing an unstable variant of bipolar II disorder that can be characterized as **"cyclothymic depression"**

The question of diagnostic overlap of BPD with other axis I disorders is **a fake issue**. Suffice it to say that such overlap pertains largely to anxiety, eating, addictive, and impulse control disorders, all of which **are well-known comorbid features of bipolar II**

"Psychoanalytic understanding and descriptive nosology are complimentary to one

Affective reconceptualization of borderline pathology may substantially reduce the therapists' countertransference because now the patient is viewed **as affectively ill, rather than "character flawed or sociopathic**


# Distinguishing bipolar disorder from borderline personality disorder: A study of current clinical practice

November 2015 Volume 30, Issue 8, Pages 965–974

K.E.A. Saunders, A.C. Bilderbeck, J. Price, G.M. Goodwin *

*University Department of Psychiatry, Warneford Hospital, Oxford, OX3 7JX, United Kingdom*

**A qualitative study exploring how British NHS psychiatrists are confronted with the differential diagnosis between BPD\BD in their practical experience.**

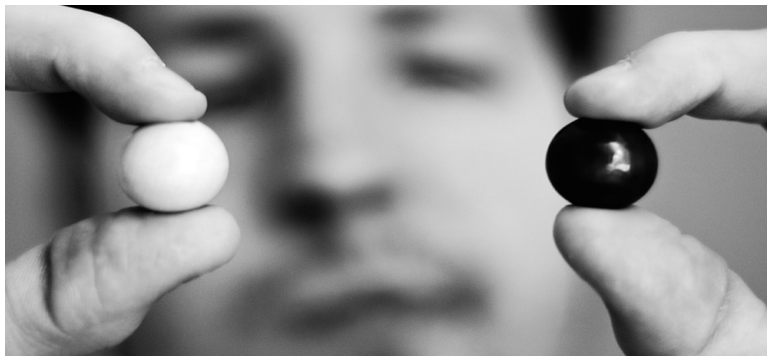
- **this differential diagnosis can be a source of disagreement amongst clinical staff;**

- **even if the majority of psychiatrists demonstrated a comprehensive understanding of the criteria recommended in DSM-IV-TR, many expressed the view that the diagnostic criteria did not necessarily assist diagnostic differentiation**

- **a quarter of respondents stated diagnostic criteria fail to correlate with the clinical phenomena in BPD and over a quarter of them (27%) expressed a preference for using an impressionistic approach rather than diagnostic criteria in diagnosing BPD**

# BORDERLINE PERSONALITY DISORDER VS BIPOLAR DISORDER: PHENOMENOLOGICAL DIFFERENCES

BORDERLINE PERSONALITY DISORDER



BIPOLAR SPECTRUM DISORDER

## Onset and longitudinal course

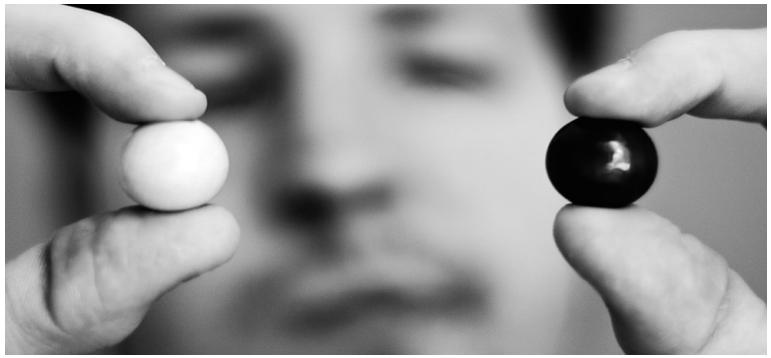
**Borderline personality disorder is generally partially structured by early adolescence**, **while onset of bipolar disorder generally occurs later (20 - 25 age)**

Long-term outcome studies in bipolar disorder and BPD seem to challenge the traditional Axis I/Axis II dichotomy, in which mood disorders are widely thought of as episodic and treatable, whereas personality disorders are considered life-long and treatment refractory. **Many cases of bipolar disorder assume a chronic course, with long-term morbidity and substantial inter-episode symptomatology**, **whereas multiyear follow-up studies of patients with BPD have found that most people eventually stop meeting threshold criteria for the disorder**

Bayes AJ, Parker GB. (2017). Clinical vs. DSM diagnosis of bipolar disorder, borderline personality disorder and their co-occurrence. Acta Psychiatr Scand;
Paris J. Differential diagnosis of bipolar disorder and borderline personality disorder. Bipolar Disord. 2017

# BORDERLINE PERSONALITY DISORDER VS BIPOLAR DISORDER: PHENOMENOLOGICAL DIFFERENCES

BORDERLINE PERSONALITY DISORDER



BIPOLAR SPECTRUM DISORDER

## Mood swings and emotional dysregulation

**In BPD, mood swings, usually of negative affect, are triggered by interpersonal stressors or perceived stressors, are transient, last from minutes to hours, and are highly dependent on the environment.**

**In bipolar disorder, mood swings are more spontaneous and of longer duration, especially for bipolar I disorder, and there are more extended periods of elation.**

Bayes AJ, Parker GB. (2017). Clinical vs. DSM diagnosis of bipolar disorder, borderline personality disorder and their co-occurrence. Acta Psychiatr Scand;
Paris J. Differential diagnosis of bipolar disorder and borderline personality disorder. Bipolar Disord. 2017

# BORDERLINE PERSONALITY DISORDER VS BIPOLAR DISORDER: PHENOMENOLOGICAL DIFFERENCES

BORDERLINE PERSONALITY DISORDER

BIPOLAR SPECTRUM DISORDER

## Affective-emotional content

**In distinguishing BPD from bipolar disorder II it is useful to look at different qualitative characteristics. In type II BD, there is generally a shift from euthymia to hyperthymia with an increase in energy, productivity that appears to be prominent with respect to anger and irritability. In the borderline a condition of real euthymia is generally absent, the euphoria is very rare.**

**In BD depressed mood in generally associated to the feeling of guilt, while in BPD to the feeling of emptiness.**

Bayes AJ, Parker GB. (2017). Clinical vs. DSM diagnosis of bipolar disorder, borderline personality disorder and their co-occurrence. Acta Psychiatr Scand;
Paris J. Differential diagnosis of bipolar disorder and borderline personality disorder. Bipolar Disord. 2017

# BORDERLINE PERSONALITY DISORDER VS BIPOLAR DISORDER: PHENOMENOLOGICAL DIFFERENCES

BORDERLINE PERSONALITY DISORDER

BIPOLAR SPECTRUM DISORDER

## Self-identity

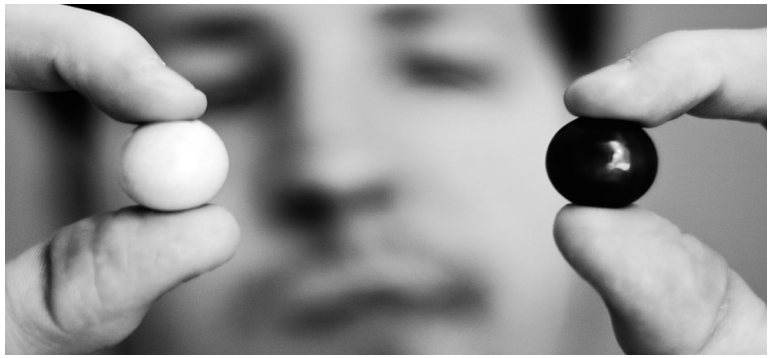
**Borderline patients present a stable disruption to their sense of Self with core elements as painful incoherence, a role absorption, inconsistency and lack of commitment.**

**Bipolar patients may present Self-deficits only when depressed and a grandiose self when hypomanic, with stability of Self-identity when euthymic.**

Bayes AJ, Parker GB. (2017). Clinical vs. DSM diagnosis of bipolar disorder, borderline personality disorder and their co-occurrence. Acta Psychiatr Scand;
Paris J. Differential diagnosis of bipolar disorder and borderline personality disorder. Bipolar Disord. 2017

# BORDERLINE PERSONALITY DISORDER VS BIPOLAR DISORDER: PHENOMENOLOGICAL DIFFERENCES

BORDERLINE PERSONALITY DISORDER



BIPOLAR SPECTRUM DISORDER

## Interpersonal relationships

By definition, **Borderline patients present a pattern of unstable and intense, turbulent interpersonal relationships. They are not able to see significant others as other than idealized, if gratifying, or devalued, if ungratifying.**

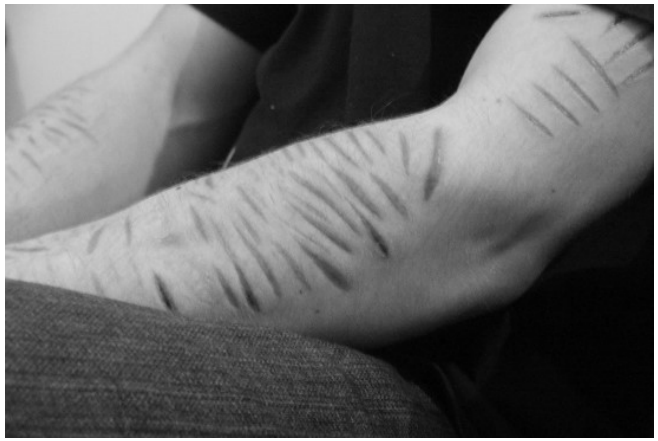
**Cases of pure bipolar symptomatology do not show severe pathology of object relations during periods of normal functioning, and even chronic bipolar patients, maintain the capacity for relationships in depth, stability in their relations with others**

Bayes AJ, Parker GB. (2017). Clinical vs. DSM diagnosis of bipolar disorder, borderline personality disorder and their co-occurrence. Acta Psychiatr Scand;
Paris J. Differential diagnosis of bipolar disorder and borderline personality disorder. Bipolar Disord. 2017

# BORDERLINE PERSONALITY DISORDER VS BIPOLAR DISORDER: PHENOMENOLOGICAL DIFFERENCES

BORDERLINE PERSONALITY DISORDER

BIPOLAR SPECTRUM DISORDER



## Parasucidal self-harm

**Borderline patients present a two- fold increased risk of non lethal self-mutilating acts (50–80% of cases) ,frequently repetitive (41% of patients have more than 50 self-mutilation acts)** compared to Bipolar patients.

## Sexual abuse

A key course feature that potentially could differentiate bipolar illness from borderline personality is a history of sexual abuse. **In most recent metanalysis, 50–76% of patients with borderline personality disorder had experienced sexual trauma in childhood. In contrast, sexual abuse occurs in less than 30% of bipolar subjects**

Bayes AJ, Parker GB. (2017). Clinical vs. DSM diagnosis of bipolar disorder, borderline personality disorder and their co-occurrence. Acta Psychiatr Scand;
Paris J. Differential diagnosis of bipolar disorder and borderline personality disorder. Bipolar Disord. 2017

# Misdiagnosis of bipolar disorder as borderline personality disorder and viceversa: implication for treatment

Psychotherapies (in particular DBT) are central to the treatment for borderline personality

While many BPD patients are on polypharmacy regimes, with 4–5 drugs drawn from each major class (including antidepressants), psychotropic medication induce marginal symptomatic benefits


Bipolar I and bipolar II disorder always require medical management.

Lithium and anticonvulsant mood stabilizers are the drugs with the strongest support for both types in clinical trials.

Antidepressants should be used with caution when there is a suspicion of bipolar diathesis as they are known to cause treatment refractoriness and may contribute to suicidality

Psychotherapies alone are not effective in bipolar patients

John H, Sharma V. Misdiagnosis of bipolar disorder as borderline personality disorder: clinical and economic consequences. World J Biol Psychiatry. 2009

6 th Maudsley Mediterranean Forum

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# Defining the borders between Borderline Personality disorder and Bipolar disorder

## BIPOLAR AND COMORBID BORDERLINE PERSONALITY DISORDER: OUR EXPERIENCE

# IMPULSIVITY AND AGGRESSIVENESS IN BIPOLAR AND BORDERLINE PERSONALITY DISORDER

## BPD

Stable core diagnostic feature

Prevalence of non planning impulsiveness over motor and attentional impulsiveness.

Preference for immediate gratification and discounting of delayed rewards underpins impulsive behaviors rather than emotional distress

Prospective predictor of suicidality and self-harm acts

Strict association with hostility


**Psychological mediator of aggressive behavior**

## Bip.Dis

Both trait and state feature: more episodic course than in BPD but inter-episode impulsivity observed in euthymia

IN BDII , episode-based impulsivity is more commonly associated with hypomanic rather depressive BP II mood states

General prevalence of “attentional impulsiveness”.
Motor impulsiveness generally linked to mood-related behavioral disinhibition

Prospective predictor of severity of suicide attempts

# Aggressiveness in DSM 5 criteria for Borderline Personality Disorder

Aggression against self

5. "**recurrent suicidal behavior, gestures, or threats, or self-mutilating behavior** "

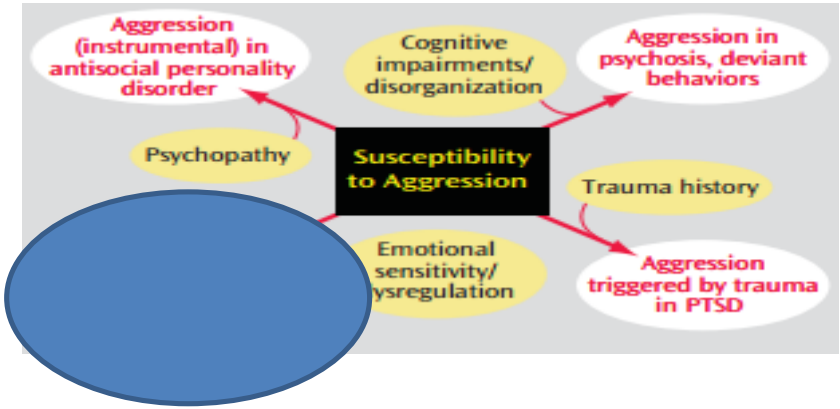
Aggression against others

8. " inappropriate, intense anger or difficulty controlling anger (e.g., frequent displays of temper, constant anger, **recurrent physical fights)** "

1st cause of hospitalization
9 % of patients die by suicide
58% have been involved occasionally or often' in physical fights as adults;
25% have used weapons against others

IMPULSIVE AGGRESSIVENESS

*Lack of behavioral inhibition and unconcern about consequences*
*Triggered by enviromental overstimulation and emotional distress*




Moore KE, Tull MT, Gratz KL. Borderline personality disorder symptoms and criminal justice system involvement: The roles of emotion-driven difficulties controlling impulsive behaviors and physical Aggression. Compr Psychiatry. 2017; Látalová K, Prasko J. Aggression in borderline personality disorder. Psychiatr Q. 2010 Sep;81(3):239-51

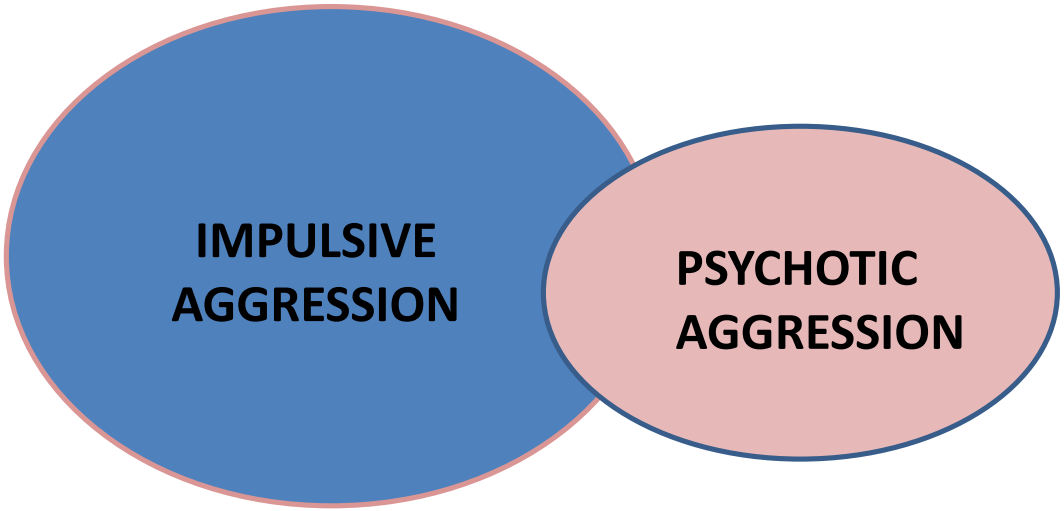
# IS BIPOLAR DISORDER SPECIFICALLY ASSOCIATED WITH AGGRESSION?

Lifetime Prevalence of "aggressive behaviours" in non-psychiatric sample: **0,66%**

Lifetime Prevalence of "aggressive behaviours" in Bipolar patients:

2,52% BDI  5,1 % BDII *

## (HIGHER THAN IN MDD, PTSD, PSYCHOTIC DISORDERS, PANIC DISORDER)




Higher levels of aggressiveness compared to healthy subjects even in euthymic phase

Strict correlation with impulsivity levels: aggressive acts are largely of the impulsive type

More likely occurring in acute phase, manic hypomanic episode than in depression

Current Psychotic symptoms increase risk of aggressive acts

*Pulay AJ, Dawson DA, Hasin DS, et al. Violent behavior and DSM-IV psychiatric disorders: results from the national epidemiologic survey on alcohol and related conditions. J Clin Psychiatry. 2008

Grunebaum et al., 2006; Najt et al., 2007; Látalová, 2009; Ballester et al., 2012

# EFFECTS OF BIPOLAR DISORDER\BPD COMORBIDITY

**Bipolar Disorder** + **Borderline Personality Disorder**

an earlier onset of BD (Goldberg et al., 2009; McDermid et al., 2015; Moor et al., 2012; Neves et al., 2009; Perugi et al., 2013)

Worse outcomes:
hospitalization (Colom et al., 2000), suicidal ideation and deliberate self-harm (Leverich et al., 2003), increased service utilization (Lembke et al., 2003), substance abuse (Kay et al., 2002), poor symptomatic outcome (George et al., 2003) and worse adherence and treatment response (Bieling et al., 2007; Colom et al., 2000)


Impulsivity and aggressiveness in bipolar disorder with co-morbid borderline personality disorder

Psychiatry Research 188 (2011) 40–44

Bernardo Carpiniello [a,*], Lorena Lai [a], Silvia Pirarba [a], Claudia Sardu [b], Federica Pinna [a]

## IMPULSIVITY (BIS-11 )

**BD/BPD patients showed significantly higher mean scores with respect to BD and BD/ OPD patients both on the Total Scale and the Attentional and Non- Planning subscales;** mean scores on the Motor subscale were significantly higher in BD/BPD patients with respect to BD but not BD/OPD patients.

## AGGRESSIVENESS (AQ)

**BD/BPD patients showed significantly higher mean scores for the Total Scale and on the Physical Aggression and Hostility subscales with respect to BD** but not BD/OPD patients; moreover, mean scores obtained by BD/BPD patients on the Verbal Aggressivity subscale were significantly higher than those in BD/OPD patients but not in BD patients.

# TREATMENT OF BP DISORDERS WITH COMORBID BORDERLINE PERSONALITY DISORDER: AN UNDERINVESTIGATED FIELD

## GUIDELINE RECOMMENDATION

BAP British Association for Psychopharmacology

**Evidence-based guidelines for treating bipolar disorder: Revised third edition recommendations from the British Association for Psychopharmacology**

*J Psychopharmacol.* 2016 June ; 30(6):

*"Although the place of pharmacotherapy for borderline symptoms is based on limited evidence, the* ***shared symptom of mood instability may be appropriately treated by medicines (e.g. lamotrigine, lithium, olanzapine, risperidone, aripiprazole and quetiapine)*** *and borderline symptoms improved"*

## AVAILABLE STUDIES

THE JOURNAL OF CLINICAL PSYCHIATRY

**Divalproex Sodium Treatment of Women With Borderline Personality Disorder and Bipolar II Disorder: A Double-Blind Placebo-Controlled Pilot Study**

Frances R. Frankenburg and Mary C. Zanarini

***Divalproex sodium*** *proved to be superior to placebo in diminishing interpersonal sensitivity, irritability and anger/hostility*

JOURNAL of AFFECTIVE DISORDERS

Journal of Affective Disorders 79 (2004) 297–303

Borderline personality disorder in patients with bipolar disorder and response to lamotrigine

Gilbert A. Preston*, Barrie K. Marchant, Fredrick W. Reimherr, Robert E. Strong, Dawson W. Hedges

**Lamotrigine was effective in reducing borderline dimensions in bipolar I patients** who qualified for a concomitant diagnosis of BPD after a retrospective evaluation

# MEDICATION STRATEGIES FOR BORDERLINE PERSONALITY DISORDER SYMPTOMS

Drugs should not be used as primary therapy for borderline personality disorder, because they have only modest and inconsistent effects

The time-limited use of drugs can be considered as an adjunct to psychological therapy, to manage specific symptoms.

Patients with BPD should be informed that there is no strong evidence base for the prescription of any drug'

Cautious prescription of drugs that could be lethal in overdose or associated with substance misuse, because of high suicide risk with prescribed drugs in people with borderline personality disorder

The use of drugs can be considered in acute crisis situations but should be withdrawn once the crisis is resolved


| Affective Dysregulation Symptoms | Impulsive Behavioural Symptoms | Cognitive Perceptual Symptoms |
|---|---|---|
| SSRI, SNRI | SSRI, SNRI | FGA |
| Antidepressants Tryciclics | Antidepressants Tryciclics | SGA |
| MAOI | FGA | |
| Benzodiazepines | SGA | |
| Mood Stabilizers Lithium Anticonvulsivants | Mood Stabilizers Lithium Anticonvulsivants | |
| Omega-3 fatty acids | Omega-3 fatty acids | |

Starcevic V, Janca A. Pharmacotherapy of borderline personality disorder: replacing confusion with prudent pragmatism. Curr Opin Psychiatry. 2018

# MANAGING IMPULSIVITY-AGGRESSIVENESS IN BORDERLINE PERSONALITY DISORDER: CURRENT EVIDENCES

THE COCHRANE COLLABORATION®

## IMPULSIVENESS, SELF MUTILATING BEHAVIOUR, SUICIDAL BEHAVIOUR

**First generation antipsychotics**

- Haloperidol → Significant effect on **reduction of anger**
- Flupentixole Decanoate → Large significant effect on reduction of **suicidial behaviour**

**Second generation antipsychotics**

- Olanzapine → Significant effect on **reduction of anger, unfavourable effect on suicidality and self mutilating behaviour**
- **Aripiprazole** → Large significant effect on **reduction of impulsivity and anger**; small significant effect on reduction of **self mutilating behaviour**
- Ziprasidone

**Mood stabilizers**

- **Lamotrigine** → Large significant effect on **reduction of impulsivity and anger**
- **Topiramate**
- Valproate → Large significant effect on **reduction of anger**, no effect on impulsivity and suicidality
- Carbamazepine
- Lithium

**Antidepressants**

- Fluoxetine
- Fluvoxamine
- Phenelzine Sulfate

**Omega-3 fatty acids** → Slight significant effect on **suicidal ideation**

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# Asenapine in the management of impulsivity and aggressiveness in bipolar disorder and comorbid borderline personality disorder: an open-label uncontrolled study

Andrea Aguglia[a,b], Ludovico Mineo[c], Alessandro Rodolico[c], Maria S. Signorelli[c] and Eugenio Aguglia[c]

**Borderline personality disorder (BPD) often co-occurres with bipolar disorder (BD). Impulsivity and aggressiveness represent core shared features and their pharmacological management is mainly based on mood stabilizers and antipsychotics, although scarce evidence is available for this context of comorbidity. The aim of the present study was to evaluate the role of Asenapine as an adjunctive drug for reducing aggressiveness and impulsivity in a sample of Italian BD type I outpatients with or without a comorbid BPD. This was an observational 12-week open-label uncontrolled clinical study carried out from April to October 2014 in two psychiatric clinics in Sicily. Each patient was treated with asenapine at two dose options, 5 mg (twice daily) or 10 mg (twice daily), and concomitant ongoing medications were not discontinued. We measured impulsivity using the Barratt Impulsiveness Scale (BIS) and aggressiveness using the Aggressive Questionnaire (AQ). For the analysis of our outcomes, patients were divided into two groups: with or without comorbid BPD. Adjunctive therapy was associated with a significant decrease of BIS and AQ overall scores in the entire bipolar sample. Yet, there was no significant difference in BIS and AQ reductions between subgroups. Using a regression model, we observed that concomitant BPD played a negative role on the Hostility subscale and overall AQ score variations; otherwise, borderline co-diagnosis was related positively to the reduction of physical aggression. According to our post-hoc analysis, global aggressiveness scores are less prone to decrease in patients with a dual diagnosis, whereas physical aggressiveness appears to be more responsive to the add-on therapy in patients with comorbidity. *Int Clin Psychopharmacol* 33:121–130** 

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**Keywords: aggression, asenapine, bipolar disorder, borderline personality disorder, impulsivity, pharmacologic management**

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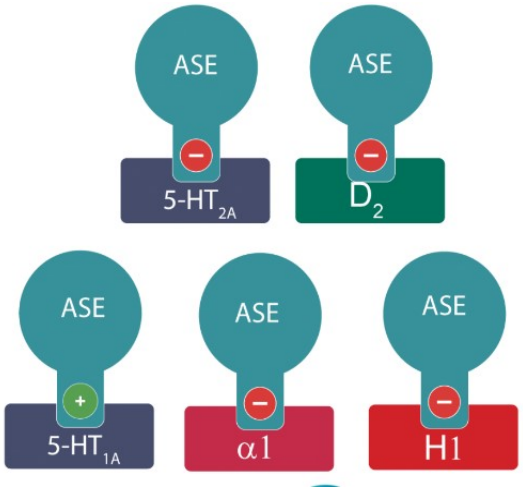
# ASENAPINE




The dopamine D4/D2 receptor antagonist affinity ratio as a predictor of anti-aggression medication efficacy

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Medical Hypotheses 80 (2013) 530–533

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Asenapine
Clozapine

D4\D2 >1

Anti-aggression effect separated from antipsychotic effect due to D2 activation associated with reduced D4 activity.

*In several RCT, clozapine has been shown to be superior to haloperidol, risperidone, and olanzapine in reducing aggression in psychotic patients*

Asenapine is unique among antipsychotics in its sublingual administration, necessitated by its poor GI absorption

The most common side effects are sedation, orthostatic hypotension and oral hypoesthesia.

Lower propensity to cause weight gain, prolactin elevation, or QTc prolongation compared to most atypical antipsychotics. EPS rate similar to other SGA

# *Asenapine in the management of impulsivity and aggressiveness in Bipolar Disorder and comorbid Borderline personality disorder: an open label uncontrolled study*

## STUDY PROCEDURE

**Observational, 12-weeks open-label uncontrolled clinical study,** carried out from April to October 2014

*Patients, aged between 18 and 65, with a previous diagnosis of Bipolar I Disorder in euthymic phase, with history of impulsive-aggressive behaviours, recruited into the A.O.U. Psichiatric Clinic "Policlinico Vittorio-Emanuele" of Catania*

EXCLUSION CRITERIA → *Neurological illness , a past or current schizophrenia spectrum disorder or other psychotic disorder; a past or current mental disorder due to a medical condition; current mental retardation or other significant neurocognitive disturbances; current severe physical illness; and concurrent alcohol and/or other substance abuse/dependence. Pregnant and sexually active women unwilling to use an effective means of contraception*

PSYCHOPATHOLOGICAL ASSESSMENT:

*Validation of BD type I diagnosis:* Structured Clinical Interview for DSM-IV (SCID- I)
Mood Disorder Questionnaire (MDQ)

BPD comorbidity: Structured Clinical Interview for DSM-IV Axis II Disorders (SCID-II)
Borderline Syndrome Index (BSI)

Levels of impulsiveness and aggressiveness (V0 and V1) : Italian version of the **Aggression Questionnaire (AQ)**
Italian version of the **Barratt Impulsiveness scale 11 ( BIS-11**)

PHARMACOLOGICAL INTERVENTION: 12 Weeks period administration of Asenapine at flexible dose of 5 mg (BID) or 10 mg (BID) in addition to current medication

# BASELINE DATA

| | BD only (*N* = 15) | BD and BPD (*N* = 35) | Total (*N* = 50) | *P* value (two-sided *t*-test) |
|---|---|---|---|---|
| SCID-II | | | | |
| Mean (SD) | 9.8 (1.82) | 10.6 (1.67) | 10.4 (1.74) | 0.137 |
| Median | 10 | 11 | 11 | |
| Minimum–maximum | 5–13 | 7–13 | 5–13 | |
| BSI | | | | |
| Mean (SD) | 16.2 (8.09) | 37.9 (7.08) | 31.4 (12.42) | <0.001* |
| Median | 20 | 40 | 33 | |
| Minimum–maximum | 4–25 | 26–50 | 4–50 | |
| MDQ [*n* (%)] | | | | |
| Negative | 6 (40.0) | 2 (5.7) | 8 (16.0) | 0.002* |
| Positive | 9 (60.0) | 33 (94.3) | 42 (84.0) | |
| AQ-PA | | | | |
| Mean (SD) | 23.7 (8.41) | 29.5 (6.49) | 27.8 (7.52) | 0.012* |
| Median | 23 | 32 | 30.5 | |
| Minimum–maximum | 13–36 | 14–43 | 13–43 | |
| AQ-VA | | | | |
| Mean (SD) | 17.3 (7.48) | 19.3 (3.83) | 18.7 (5.20) | 0.22 |
| Median | 19 | 20 | 20 | |
| Minimum–maximum | 5–28 | 10–28 | 5–28 | |
| AQ-A | | | | |
| Mean (SD) | 21.5 (5.77) | 25.6 (4.05) | 24.4 (4.94) | 0.007* |
| Median | 21 | 27 | 25.5 | |
| Minimum–maximum | 13–32 | 14–34 | 13–34 | |
| AQ-H | | | | |
| Mean (SD) | 21.2 (6.92) | 27.0 (5.16) | 25.3 (6.28) | 0.002* |
| Median | 20 | 28 | 25.5 | |
| Minimum–maximum | 8–31 | 18–35 | 8–35 | |
| AQ-total | | | | |
| Mean (SD) | 83.8 (22.23) | 101.4 (14.09) | 96.1 (18.58) | 0.001* |
| Median | 89 | 104 | 101 | |
| Minimum–maximum | 43–114 | 66–129 | 43–129 | |
| BIS | | | | |
| Mean (SD) | 67.2 (10.27) | 69.2 (11.45) | 68.6 (11.04) | 0.563 |
| Median | 64 | 71 | 69 | |
| Minimum–maximum | 56–92 | 44–84 | 44–92 | |

AQ-A, Aggression Questionnair-Anger; AQ-H, Aggression Questionnaire-Hostility; AQ-PA, Aggression Questionnaire-Physical Aggression; AQ-VA, Aggression Questionnaire-Verbal Aggression; BD, bipolar disorder; BIS, Barratt Impulsiveness scale; BPD, borderline peronality disorder; BSI, Brief Symptom Inventory; MDQ, Mood Disorder Questionnaire; SCID-II, Structured Clinical Interview for DSM-IV Axis II Disorders.
**P* value indicates significant.

## BORDERLINE PERSONALITY COMORBIDITY

**50 BD type 1 patients; 15 (30%) pure;**
**BDP comorbidity= 35 (70%);**

## IMPULSIVITY AND AGGRESSIVENESS LEVELS

BD/BPD : **significantly higher mean scores for the Total Scale of AQ and on Physical Aggression and Hostility subscales** in comparison to *pure* BD patients;
**Levels of impulsivity between the two groups were instead found similar although** a quantification of the three singular BIS subdimensions was not performed

# RESULTS

**Table 2 Impulsivity and aggression score variations: differences between BD and BD/BPD**

| | BD only ($N=15$) | BD and BPD ($N=35$) | $P$ value (two-sided $t$-test) |
|---|---|---|---|
| ΔAQ-PA | −7.1 (7.72) | −7.0 (4.02) | 0.962 |
| ΔAQ-VA | −5.9 (5.08) | −4.3 (3.99) | 0.287 |
| ΔAQ-A | −4.8 (4.16) | −6.8 (3.94) | 0.121 |
| ΔAQ-H | −7.2 (6.98) | −7.2 (5.55) | 1 |
| ΔAQ | −24.9 (16.57) | −25.3 (11.37) | 0.933 |
| ΔBIS | −15.7 (11.06) | −13.6 (11.47) | 0.544 |

AQ, Aggression Questionnaire; AQ-A, Aggression Questionnaire-Anger; AQ-H, Aggression Questionnaire-Hostility; AQ-PA, Aggression Questionnaire-Physical Aggression; AQ-VA, Aggression Questionnaire-Verbal Aggression; BD, bipolar disorder; BIS, Barratt Impulsiveness Scale; BPD, borderline peronality disorder.

We recorded a significant decrease for each sub-dimensions of Aggressiveness (Physical, Verbal, Anger, Hostility) and for impulsivity, regardless of concomitant BPD. However, after controlling for confounding baseline factors, **the magnitude of variations were influenced by BPD co-diagnosis.**

After 12 weeks of administration, Asenapine has been proven to be effective in reducing impulsiveness (BIS score) and aggressiveness levels (AQ scores) in the total sample and in both subgroups of patients (pure BD and BD\BPD)

**BPD**

\+ Positive correlation with Physical aggression score reduction

\− Negatively associat to total aggressiven and hostility score

?

Higher ability of Asenapine in targeting neural mechanism related to physical aggressiveness

## Side effects

No serious adverse effect was recorded and there was not any discontinuation of treatment. Nineteen (38%) patients reported increased somnolence\sedation, fourteen (28%) oral hypoestesia, ten (20%) dysgeusia, 8 (16%) patients sporadic dizziness. No movement disorder was spontaneously reported or detected after clinical evaluation with dedicated scales. At V1 we didn't find any significant weight variation, $t(49)= 0.884$, $p=0.381$, two tails.

# LIMITATIONS


Open-label study

Small simple size

Systematic clinical evaluation is missing

Role of concomitant medication was not analyzed and might affect asenapine response.

# CLOSING REMARKS

A deeper phenomenological analysis of psychopathological domains, including impulsivity and aggression, can facilitate the differential diagnosis

An accurate clinical definition of comorbidity between BD and BPD is extremely important as the two conditions require different therapeutic modalities

Misdiagnosis can deprive the patient of potentially effective treatment or conversely lead to unnecessary and improper pharmacological prescription.

Given the burden of impulsivity and aggressiveness in the morbidity and mortality associated with these disorders, in the pharmacotherapy approach, clinicians should consider drugs able to specifically target these dimensions without jeopardizing other treatment outcomes

# Thanks