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The bidirectional influence of Borderline Personality Disorder and Life Events: a literature review

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List of Abbreviations

ADHD – Attention deficit and hyperactive disorder

BD – Bipolar Disorder

BDM – Biosocial Development Model

BPD – Borderline personality disorder

CBT – Cognitive behavioural therapy

DBT – Dialect behavioural therapy

DSM – Diagnostic and statistical manual of mental disorders

HP – Health problem

iBPD – Individuals with borderline personality disorder

ICD – International Classification of Diseases

LE – Life event

LTE-Q – List of Threatening Experiences Questionnaire

MBT – Mentalization-based therapy

MRI – Magnetic resonance imaging

NSSI - Non-suicidal self-injuries

PD – Personality disorder

RLCQ – Recent Life Changes Questionnaire

SAS-SR – Social Adjustment Scale Self-Report

SC – Shema therapy

SLE – Stressful life event

SSRI – Selective serotonin reuptake inhibitor

TFP – Transference-focused psychotherapy

Resumo

A perturbação da personalidade borderline é uma patologia psiquiátrica crónica caracterizada por instabilidade afetiva, impulsividade e dificuldade em relações interpessoais. A sua etiologia tem sido um importante foco de estudo e, nas últimas décadas, houve uma expansão no que toca à melhor compreensão e exploração dos diferentes fatores ambientais, genéticos e neurobiológicos. De facto, o papel de eventos de vida negativos, como adversidades na infância, está bem estabelecido como fator de risco para o seu desenvolvimento. No entanto, a evidência sobre a relação de eventos de vida negativos e a atividade da doença é escassa.

Os estudos têm demonstrado que a perturbação da personalidade borderline é fator de risco para situações de *stress* negativas e que estes indivíduos estão sujeitos a experienciarem um maior número de eventos de vida, principalmente quando relacionados com a sua psicopatologia – quebra de relações importantes e as consequências de ações impulsivas. Os eventos de vida são especialmente pertinentes no estudo desta perturbação da personalidade uma vez que a atividade da doença flutua ao longo do tempo e esta é, frequentemente, acompanhada por outras comorbilidades psiquiátricas, como depressão. Portanto, esta revisão pretende aumentar o conhecimento em relação a possíveis fatores precipitantes para recaídas sintomáticas, previsão de risco e decisões prognósticas.

Esta revisão da literatura médica visa explorar a relação do efeito dos eventos de vida na psicopatologia de indivíduos com perturbação da personalidade borderline. Para este trabalho, foram reunidos artigos através do motor de pesquisa do PubMed, com *"borderline personality disorder"* e *"life events"* como palavras-chave e a literatura relevante foi selecionada. Por fim, foi discutido o impacto desta pesquisa quanto à sua relevância na avaliação da relação do efeito de eventos de vida na perturbação da personalidade borderline.

Palavras chave: *borderline personality disorder*; *life events*

Abstract

Borderline personality disorder (BPD) is a chronic psychiatric disorder, characterized by affect instability, impulsivity, and interpersonal difficulties. The aetiology of BPD has been an important focus of studies on this disorder, and in the last decades, there has been a shift towards a better understanding of its multifactorial origin – environmental, genetic, and neurobiological. Indeed, the role of negative LEs, such as childhood adversity, has been well-established in the development of BPD, but research is lacking in addressing its impact on previously diagnosed adults.

Studies have shown that BPD is a risk factor for negative stressors and that a greater number of life events (LEs) occur, specifically related to their psychopathology - e.g., the break-up of important relationships and the effects of impulsive actions. LEs are especially pertinent in studying BPD considering BPD is often accompanied by psychiatric comorbidities such as depression and that its symptoms may fluctuate over time. Therefore, this review should increase understanding of possible triggers for symptoms relapse and risk forecasting and prognostic decisions.

This revision of medical literature aims to focus on the effect of LEs on individuals with borderline personality disorder (iBPD) and their influence on its trajectory. For this work, PubMed was used as the search engine and articles were gathered with “borderline personality disorder”, and “life events” as keywords. The relevant literature was selected, and the outcome of this research discussed in terms of its relevance on evaluating the impact of LEs on iBPD.

Key words: *borderline personality disorder*; *life events*

Index

Introduction

Defining a personality disorder (PD) has been a centuries-long psychiatric challenge. Since everyone has a personality, it is a fine line to define which quirks, peculiarities, reactions, and feelings are unhealthy, chronic or the source of major consequences not only for the individual but for others around them. Throughout history, there has been a consistent attempt to define what is a normal and abnormal personality. Abnormal personalities were first described with literary sketches, then clinical vignettes in psychiatric textbooks, and nowadays through lists of criteria (Stone, 2012). The diagnosis of a PD basis itself on the presence of an enduring and pervasive disturbance in how individuals experience and interpret themselves, others, and the world, which results in maladaptive patterns of cognition, emotional experience, emotional expression, and behaviour (Hall & Moran, 2019; World Health Organization, 2019).

In the early 20th century, psychiatric disorders were divided into two groups, the psychotic and the psychoneurotic. The term borderline emerged for those not fitting in either (Stone, 2012) and for experiencing a peculiar resistance to psychotherapy (Bozzatello et al., 2021). BPD was recognized as a personality disorder by the Diagnostic and Statistical Manual of Mental Disorders III (DSM-III) in 1980 through the analysis of patterns of symptoms (Stone, 2012). Ten years later was included in the International Classification of Diseases (ICD), as emotionally unstable personality disorder (Gunderson et al., 2018).

Borderline personality disorder (BPD) is a chronic psychiatric disorder, characterized by affect and behavioural dysregulation, interpersonal instability, and cognitive and self-disturbance. Its aetiology is multifactorial having genetic factors, neurobiological differences, and a multitude of environmental factors conditioning its development. BPD is the most frequently diagnosed personality disorder, with an estimated prevalence of 1 to 2.6% in the general population (Hall & Moran, 2019; Leichsenring et al., 2011). However, the difference between its reported prevalence in clinical settings (15%–25%) and the community (1.4%–5.9%) indicates that many

people with the disorder are undiagnosed and untreated (Gunderson, 2009; Leichsenring et al., 2011).

Life events (LEs) are defined as a social experience or change with a specific onset and course that has a psychological impact on the individual (Perkins, 1991).

The role of negative LEs, such as childhood adversity has been well-established in the development of BPD. Early exposure to traumatic events such as neglect and emotional, physical, or sexual abuse, combined with genetic and neurological factors, generates maladaptive patterns of affect, behaviour, and cognition. Once these mechanisms are established, they are further potentiated by negative LEs in later childhood and adolescence, leading to BPD psychopathology. (Hall & Moran, 2019; Porter et al., 2020; Winsper, 2018).

Research indicates that personality disorders are linked to negative LEs, such as trouble with the law, unemployment, and unstable interpersonal relationships (Timoney et al., 2017). In addition, individuals with PDs have a reduced ability to manage stressful LEs (Christopher Perry et al., 1992).

Additionally, individuals with borderline personality disorder (iBPD) are thought to create and put themselves into stressful environments. Indeed, studies have shown that BPD is a risk factor for negative stressors. Besides that, a greater number of life events (LEs), occur specifically related to their psychopathology - e.g., the break-up of important relationships and the effects of impulsive actions. (Jovev & Jackson, 2006; Labonte & Paris, 1993; Powers et al., 2013)

However, research is lacking in addressing LEs impact on previously diagnosed adults. LEs are especially pertinent in studying BPD considering its symptoms may fluctuate over time and BPD is often accompanied by psychiatric comorbidities such as depression. Therefore, this revision of medical literature aims to focus on the effect of LEs on individuals with borderline personality disorder (iBPD) and their influence on its trajectory, to possibly increase understanding of possible triggers for symptoms relapse, risk forecasting and prognostic decisions.

Background - Borderline Personality Disorder

Definition of BPD

A borderline personality disorder is a chronic psychiatric disorder characterized by persistent instability in affect regulation, impulse control, interpersonal relationships, self-image, and chronic feelings of emptiness (Hall & Moran, 2019; Leichsenring et al., 2011; Ruocco & Carcone, 2016).

In the DSM-V, BPD belongs to Cluster B of personality disorders, due to emotional and behavioural dysregulation. To establish the BPD diagnosis, by the DSM-V, we need five out of nine criteria as shown in table 1 (American Psychiatric Association, 2013).

Although all criteria weigh equally for the diagnosis, interpersonal dysfunction has been the core feature of BPD since the beginning of its description. Studies have shown that interpersonal dysfunction has the best-combined sensitivity and specificity for the diagnosis and has the strongest familiar aggregation (Bozzatello et al., 2021; Gunderson et al., 2018; Jeung & Herpertz, 2014a). On the other hand, suicidal tendency and self-injury are the most useful symptoms for a definitive diagnosis (Grilo et al., 2004). The chronic feelings of emptiness criteria has been associated with psychosocial morbidity (including the history of suicide attempts), hospitalization, global functional impairment, and association with other mental disorders (Thatcher et al., 2005), but shows the lowest item-total correlation and diagnostic efficiency among all BPD criteria (Rebok et al., 2015). Patients meeting up to five criteria on the DSM-V scale have been associated with more severe illnesses (Gunderson et al., 2018).

The new ICD-11 has an innovative approach to personality disorders using a five-domain dimensional-trait model. The clinician will first assess the patient with respect to the level of PD severity based on the degree of self and/or interpersonal dysfunction. Then, the clinician will rate the person concerning the five trait domains represented by negative affectivity, detachment, dissociality, disinhibition, and anankastia (or obsessionality), along with a borderline pattern qualifier. Research and clinicians expressed concerns relative to the new five-domain model, fearing the

abolishment of clinical knowledge collected over the years about BPD, especially regarding its treatment. In fact, the borderline label - now called borderline pattern, was the only PD label kept (Irwin & Malhi, 2019).

Table 1

Diagnostic Criteria for BPD, adapted from DSM-V and ICD-11 (American Psychiatric Association, 2013; World Health Organization, 2019)

Adapted from DSM-V Borderline Personality Disorder	Adapted from ICD-11 Borderline Pattern
Tremendous efforts to avoid, real or imagined, abandonment	Frantic efforts to avoid real or imagined abandonment
Unstable and intense interpersonal relationships that shift from extreme idealization to devaluation	A pattern of unstable and intense interpersonal relationships
Identity disturbance with intense self-image and self-perception instability	Identity disturbance with persistently unstable self-image or sense of self
Impulsivity in, at least, two potential self-destructive areas (sex, money, substance abuse, driving, binge eating)	Tendency to act rashly in states of high negative affect leading to potentially self-damaging behaviour
Recurrent suicidal thoughts or attempts or self-harming gestures	Recurrent episodes of self-harm
Affect instability due to mood hyperreactivity	Emotional instability due to marked reactivity of mood
Chronic feelings of emptiness	Chronic feelings of emptiness
Outbursts of intense and inappropriate anger	Inappropriate intense anger or difficulty controlling anger
Transient paranoid ideation or intense dissociate symptoms	Transient dissociative symptoms or psychotic-like features in situations of high affective arousal

Epidemiology

BPD is the most frequently diagnosed personality disorder, having an estimated prevalence of 1 to 2.6% in the general population (Hall & Moran, 2019). According to an American study that examined the results of the Wave 2 NESARC survey, with 34653 adults, BPD has a lifetime prevalence of 5.9% (Grant et al., 2009). However, the difference between its reported prevalence in clinical settings (15%–25%) and the community (1.4%–5.9%) indicates that many people with the disorder are undiagnosed and untreated (Gunderson, 2009).

Authors analysing The Wave 2 NESARC survey also found that BPD's prevalence is higher in individuals with low socioeconomic status and who are separated/divorced/widowed. It also found that the odds of having BPD were greater among respondents with a high school education or lower (Grant et al., 2009). Other studies have also reported that iBPD are more likely to live in urban cities (Stepp et al., 2016; Torgersen et al., 2001) and that unemployment is positively related to BPD (Lenzenweger et al., 2007).

Grant et al. (2009) also observed no differences between men (5.6%) and women (6.2%). Considering gender distribution there seems to be an idea that BPD is much more frequent in women, due to diagnostic and sampling inaccuracies (women in BPD are disproportionately represented in clinical settings) (Bozzatello et al., 2021; Hall & Moran, 2019).

The same study reported that the prevalence was higher in young adults and decreases with age, especially after 44 years (Grant et al., 2009).

Aetiology

The BPD aetiology is multifactorial. Recent theories propose a lifespan approach considering genetic factors, neurobiological differences, and a multitude of environmental factors conditioning the development of this disorder.

Genetic and Neurobiological factors

BPD is a moderate hereditary condition, being five times more likely in first-degree parents of individuals with BPD (American Psychiatric Association, 2013). Single-candidate genes have not been yet identified (Amad et al., 2014), but there is evidence that epigenetic mutations in genes related to stress and neurodevelopment have a role in the aetiology of BPD (Bassir Nia et al., 2018).

The serotoninergic system has been widely studied due to its role in impulsive aggression (Coccaro et al., 2015) and evidence suggests it is altered when compared with controls (Leichsenring et al., 2011; Ruocco & Carcone, 2016). Studies found: a higher binding potential for the 5-HT2A receptors in the left hippocampus; a lower serotonin trapping in the medial frontal gyrus, anterior cingulate gyrus, superior temporal gyrus, and corpus striatum in men with BPD; women showed a similar pattern of findings but in fewer brain regions; and a difference in presynaptic serotonin function (Soloff et al., 2014).

Interpersonal instability, being a core feature of BPD, led to various studies of the role of cortisol reactivity to stress, showing there is a hyper-suppression of cortisol in iBPD by the excess of negative feedback of the hypothalamic-pituitary-adrenocortical axis when compared with controls (D. J. Zimmerman & Choi-Kain, 2009).

Oxytocin regulation has also been implicated and some studies pointed to it being significantly reduced after social isolation in iBPD when compared with controls (Ruocco & Carcone, 2016).

Evidence through MRI studies has shown that there are volumetric differences in key neural regions of iBPD, leading to speculations about the integrity of the neural pathways that connect these regions (Ruocco & Carcone, 2016). The most consistent finding is the reduced volume in the amygdala and hippocampus (Nunes et al., 2009).

Environmental factors

One influential theory for the role of environmental factors is Linehan's biosocial model which considers BPD as an emotion dysregulation disorder that may arise when a child with an emotionally vulnerable temperament grows up in an invalidating environment (Hall & Moran, 2019; Winsper, 2018).

Further theories have risen to consider the BPD psychopathology in a lifespan approach, complementing Linehan's biosocial model (Winsper, 2018).

The Biosocial Development Model (BDM) adds impulsivity as an early trait vulnerability (Crowell et al., 2009). Shelby's Emotional Cascades Model complements BMD by proposing that emotion dysregulation is amplified and exacerbated by rumination in a positive feedback loop, causing individuals to resort to extreme behaviours as a distraction technique (Selby & Joiner, 2009).

Fonagy and colleagues' socially-oriented model of BPD proposes the lack of epistemic trust (such as the absence of non-verbal ostensive cues like eye contact, turn-taking, etc.) from the caregiver leads to a hypervigilant state, that later may manifest in over-interpretation and hyper mentalisation of the motives of others, originating a cycle of social dysfunction and mentalisation difficulties (Fonagy et al., 2017; Sharp et al., 2011).

Hughes and colleagues' developmental model of BPD proposes that successful co-regulation during infancy, e.g., via secure attachment relationships, strengthens the neural structures underpinning self-control. An over-reliance on self-regulation is supposed to deplete prefrontal cortex resources, subsequently potentiating ineffective and/or impulsive emotion regulation strategies (Coan & Sbarra, 2015; Hughes et al., 2012; Winsper et al., 2017).

So, it is pretty much established that environmental and familial risk factors, such as childhood trauma (e.g., neglect and emotional, physical, or sexual abuse), familial adversity, socioeconomic status, a history of psychopathology in the caregiver, as well as parental emotional under-involvement, play an important role in the development of BPD (Hall & Moran, 2019; Winsper, 2018). It is important to highlight the effect of social influences, like bullying and rejection by peers as important risk factors (Bozzatello et al., 2021).

Although trauma theories were extremely popular, they are oversimplistic, and severe abuse only occurs in a minority of iBPD (Paris, 2009). Trauma's role in the psychopathology of BPD depends more on its presence than on its intensity (Bozzatello, Rocca, & Bellino, 2020). However, as seen in the proposed models above, insecure attachment and early emotional invalidation from caregivers lead to the child's inability to process and control different emotional states, playing a significant role in emotional dysregulation and social cognition deficits (Hall & Moran, 2019; Porter et al., 2020; Winsper, 2018).

Once these maladaptive mechanisms are established, they are further potentiated by adverse life experiences, feeding into a positive feedback loop and by adolescence, the individual demonstrates a constellation of BPD precursor traits (Winsper, 2018).

Development of Borderline Personality Disorder

Like all personality disorders, BPD arises during adolescence or young adulthood (Sharp & Wall, 2018) and is typically associated with instability in interpersonal relationships (Hall & Moran, 2019).

However, before BPD onset, prodromic signs may be observed in early adolescence, such as internalizing (e.g., depression, anxiety, dissociative symptoms, suicidality) and externalizing psychopathology (e.g., conduct disorder, oppositional-defiant disorder, ADHD, impulsive-aggressive behaviour, self-injuries, and substance use disorder) (Stepp et al., 2013). Studies have shown a possible predominance of internalizing symptoms in women and externalizing symptoms in men (Bozzatello et al., 2021).

Adolescents with BPD are more likely to present for clinical care with more acute manifestations of the disorder (e.g., recurrent self-harm and suicidal behaviour, other impulsive and self-damaging behaviour, and inappropriate anger), (Gunderson et al., 2018; Lawrence et al., 2011). In clinical practice, the diagnosis, and consequently the treatment, of BPD in younger individuals are usually delayed due to underestimation of symptoms and underdiagnosis (Fonagy et al., 2015). Although the diagnosis of BPD in adolescents may not be consensual, it has been extensively performed in clinical practice, and it predicts adult dysfunction as well as adult BPD (Jeung & Herpertz, 2014a).

Young adults and older patients with BPD often seek help during an episode of another mental disorder, such as major depressive disorder, anxiety disorders, trauma-related disorders or substance use disorder. On other occasions, iBPD search for clinical care during a current crisis, interpersonal (often a relationship break-up) or of another nature (for example, job loss, school failure or a major life transition). In the most severe cases, patients can present after a suicide attempt or other impulsive and self-destructive behaviour (Bozzatello et al., 2021; Gunderson et al., 2018).

When these individuals seek psychiatric care, the diagnosis is made with five out of nine diagnostic criteria, so, theoretically, we have one hundred and fifty-one

combinations of iBPD, expressing patients with very heterogeneous clinical presentations (Rebok et al., 2015).

Furthermore, the time course of BPD is far more variable than traditionally assumed with periods of remission and relapses (Zanarini et al., 2007).

An Italian review of 171 records reported that affective and interpersonal features indicative of abandonment and dependency were the most prevalent and stable, whereas impulsive symptoms and interpersonal features indicative of treatment regressions were the least prevalent and consistent. With fewer features over time, personality disorders such as BPD become more correlated with each other and less distinct as individual disorders. By their 30s and 40s iBPD have greater stability in interpersonal relationships and vocational functioning (Bozzatello et al., 2021).

The term introduced by Schmideberg, in 1959, the *"stable instability"*, may well define the natural course of this disorder (Leichsenring et al., 2011).

Comorbidities

BPD is associated with several psychiatric comorbidities.

The Wave 2 NESARC survey described mood, anxiety, and substance use disorders as the most prevalent 12-month psychiatric diagnosis among iBPD, with a prevalence of 29.4%, 21.5% and 14.7%, respectively. On the other hand, the prevalence of BPD in individuals with a lifetime diagnosis of mood, anxiety and substance use disorders decreases to 17.2%, 14.8% and 9.5% respectively (Grant et al., 2009).

Additionally, iBPD may also suffer from eating disorders like bulimia nervosa and anorexia nervosa with an estimated prevalence of approximately 10% and 6%, respectively (Shah & Zanarini, 2018).

Indeed, longitudinal studies show that Axis I disorders are very common among BPD patients. Even though their prevalence tends to decrease gradually over time, it was still higher when compared to other PDs. Besides that, studies showed that when patients experienced BPD remission over time there was a substantial decrease in all comorbid Axis I disorders. Individuals with BPD who did not have remissions reported stable rates of Axis I comorbid disorders (Shah & Zanarini, 2018).

BPD influences and complicates the treatment of other psychiatric disorders, inducing a more chronic course. For example, the rate of remission of a major depressive disorder seems to be significantly reduced by the co-existence of BPD (Gunderson et al., 2004).

Furthermore, BPD may mimic depression, mania, or anxiety because of emotional dysregulation (Hall & Moran, 2019; Leichsenring et al., 2011).

When we talk about mood disorders, it's important to enhance that they have a confounding relationship with BPD. It is hard to define when they co-occur, and the prevalence differs in literature. M. Zimmerman & Morgan (2013) analysed 24 studies to assess the prevalence of BPD in patients with Bipolar Disorder and concluded that 20% of BPD patients had co-occurrent Bipolar Disorder, 10% of which had Bipolar Disorder I (BD-I) and the other 10% had Bipolar Disorder II (BD-II). Besides that, they

stated that 20% of BD-II patients had comorbid BPD but just 10% of patients with BD-I had comorbid BPD.

On the other hand, for the past twenty years, some authors defended that BPD belongs to the Bipolar Disorder spectrum due to the clinical overlap of symptomatology. This theory stands on the link between affect instability, emotional dysregulation, and hippomaniac episodes, seen in BD-II. BD-I is easier to distinguish since the maniac episodes are often accompanied by psychotic symptoms, increased goal-directed activities, and euphoric mood, rarely seen in iBPD.

Recent literature states that they are two separate and unique disorders. Firstly, affect instability and emotional dysregulation are chore features of BPD but this disorder has a lot more features that go beyond the mood sphere. Those are the key features that identify differences from Bipolar Disorders. Secondly, affect instability in BPD is usually triggered by interpersonal conflicts and mood shifts go from euthymia to anger, whereas in Bipolar Disorder they shift from depression to elation and are less reactive to environmental cues. Thirdly, the time frame of mood shifts plays a key role in the differential diagnosis between BPD and Bipolar Disorder. According to the DSM-V, a hippomaniac episode must last at least four days, unlike what is often observed in BPD patients, mood shifts occur in hours and don't last that long.

To sum up, misdiagnosis of BPD and BD-II is common due to their uncertain diagnostic boundaries and overlapping symptomology, which may only vary in intensity. (Massó Rodriguez et al., 2021; Paris & Black, 2015; M. Zimmerman & Morgan, 2013)

Besides psychiatric comorbidities, BPD is associated with a high prevalence of health problems. The relation between the psychopathology of BPD and health problems is suggested to be related to the role of interpersonal stressors and negative affect. Firstly, iBPD with emotional dysregulation takes a longer time to return to their basal status after a negative affect experience and it's theorized that the same happens for physical health symptoms. A study by Trull and colleagues, with 80 iBPD, suggested that, in the absence of remission, iBPD have a greater probability of any physical illness and chronic conditions, such as back pain and diabetes. This can partly

explain why the life expectancy of iBPD is shorter by at least 22 years (Hepp et al., 2020). We can also speculate that the higher probability of consummated suicide (8-10% higher, making it fifty times more likely than the general population) (Hall & Moran, 2019; Leichsenring et al., 2011) also plays a role in diminishing the life expectancy of iBPD.

Treatment

The first line of treatment for BPD is psychotherapy, unlike what is commonly seen in psychiatric settings. Indeed, four psychotherapeutic approaches were adapted for the treatment of BPD: Dialect Behavioural Therapy (DBT), Cognitive-Behavioural Therapy (CBT) and psychodynamic approaches like Mentalization-Based Therapy (MBT), Transference-Focused Psychotherapy (TFP) (Cristea A. et al., 2017). In combination with Schema Therapy (SC), these are the main therapeutic approaches used for the treatment of iBPD (Videler C. et al., 2019).

Research shows that a structured psychological approach has significant improvements among young people with borderline features or BPD (Chanen et al., 2020). However, trials of effectiveness are modest and clinical efficacy has not been analysed in long-term outcomes (Chanen et al., 2020; Cristea A. et al., 2017; Videler C. et al., 2019). On the other hand, psychotherapy seems to be superior to the treatment as usual for BPD related problems such as suicidality or parasuicidal behaviour (Cristea A. et al., 2017).

When talking about young individuals with BPD, generally, the focus of the treatment is BPD pathology and self-harm behaviours. In contrast, Chanen et al. (2020) showed that a strong focus on functional outcomes, especially social and vocational outcomes, is superior. Regarding age, it is important to mention that the majority of clinical trials with psychotherapy treatment were performed in individuals between 25 and 40 years old, neglecting the changes in BPD pathology across time (Videler C. et al., 2019).

A systematic review and meta-analyses on the efficacy of psychotherapies for BPD, done by Cristea A. et al. (2017), reported that most clinical trials focused primarily on DBT, and, secondly on psychodynamic approaches. These treatments showed significant clinical results and a minor difference between them. Nevertheless, studies regarding CBT were not superior to controls. They concluded that several types of psychotherapy are effective for relevant BPD symptoms like self-harm behaviours, suicide, excessive health care use, and general psychopathology but its effects are small and have some constraints regarding publication bias, particularly the follow-up.

Other types of psychological management, e.g., service model and family intervention may also be used, though their role is not established in treatment outcomes (Chanen et al., 2020).

In addition to this, pharmacotherapy is largely used in iBPD, with evidence showing that up to 96% of iBPD who seek treatment receive at least one psychotropic medication (Gartlehner et al., 2021). Conversely, recommendations about the use of pharmacotherapy in iBPD are controversial. Even though, there are several guidelines published for the treatment of BPD albeit no official indications for the use of medication (Bozzatello et al., 2020). Evidence is limited, with low-quality clinical trials, and, again, mostly with younger individuals (Bozzatello et al., 2020; Gartlehner et al., 2021; Videler C. et al., 2019).

Two systematic reviews and meta-analyses of the pharmacological treatments for BPD, performed by Bozzatello et al. (2020) and Gartlehner et al. (2021) found that most entities, recommend the use of off-label pharmacotherapy to treat specific symptoms of BPD, during periods of relapse and for a brief time. The three targeted symptomatic domains are affective dysregulation (including depressed mood, anxiety, anger, and mood liability), impulsive-behaviour instability and cognitive-perceptual symptoms. Even though the evidence is insufficient, the drugs studied in clinical trials were antidepressants, where SSRIs had a positive influence on affective instability and impulsivity. In addition, mood stabilizers, such as valproate, topiramate, and lamotrigine, were studied to treat impulsivity, anger, and affect instability. For the cognitive-perceptual symptoms, the drugs of choice are second-generation antipsychotics, e.g., olanzapine, although evidence shows they have a negligible effect in decreasing symptoms gravity but have a positive effect on general psychiatric symptoms.

Also, they reported that in recent years there has been a shift in drug preferences with mood stabilizers and second-generation antipsychotics replacing antidepressants.

On the other hand, some authors underline the importance of a combined approach with psychotherapy and pharmacotherapy, although data are still insufficient

to draw conclusions. To overcome this, most studies recommend the combined approach when there is a need to control certain BPD symptoms, especially in patients that are slow responders or do not respond to monotherapy (Bozzatello et al., 2020).

Objectives

This literature review aims to gather information about the bidirectional influence of BPD and LEs. We analyse if exacerbations of BPD have an impact on LEs by examining if evidence suggests that iBPD experience more negative LEs, if iBPD perceive LEs as more negative, as well as which BPD features have a bigger influence on generating LEs. Additionally, this research also focuses on the role of LEs in triggering BPD symptomatic relapse.

Research Questions

- What is the influence of BPD on LEs?
    - Do individuals with BPD experience more negative LEs?
    - Does BPD affect the perception of LEs?
    - Which BPD features have an impact on LEs?
- What is the influence of LEs on iBPD?
    - Do LEs play a role in triggering BPD symptomatic relapse?

Materials and Methods

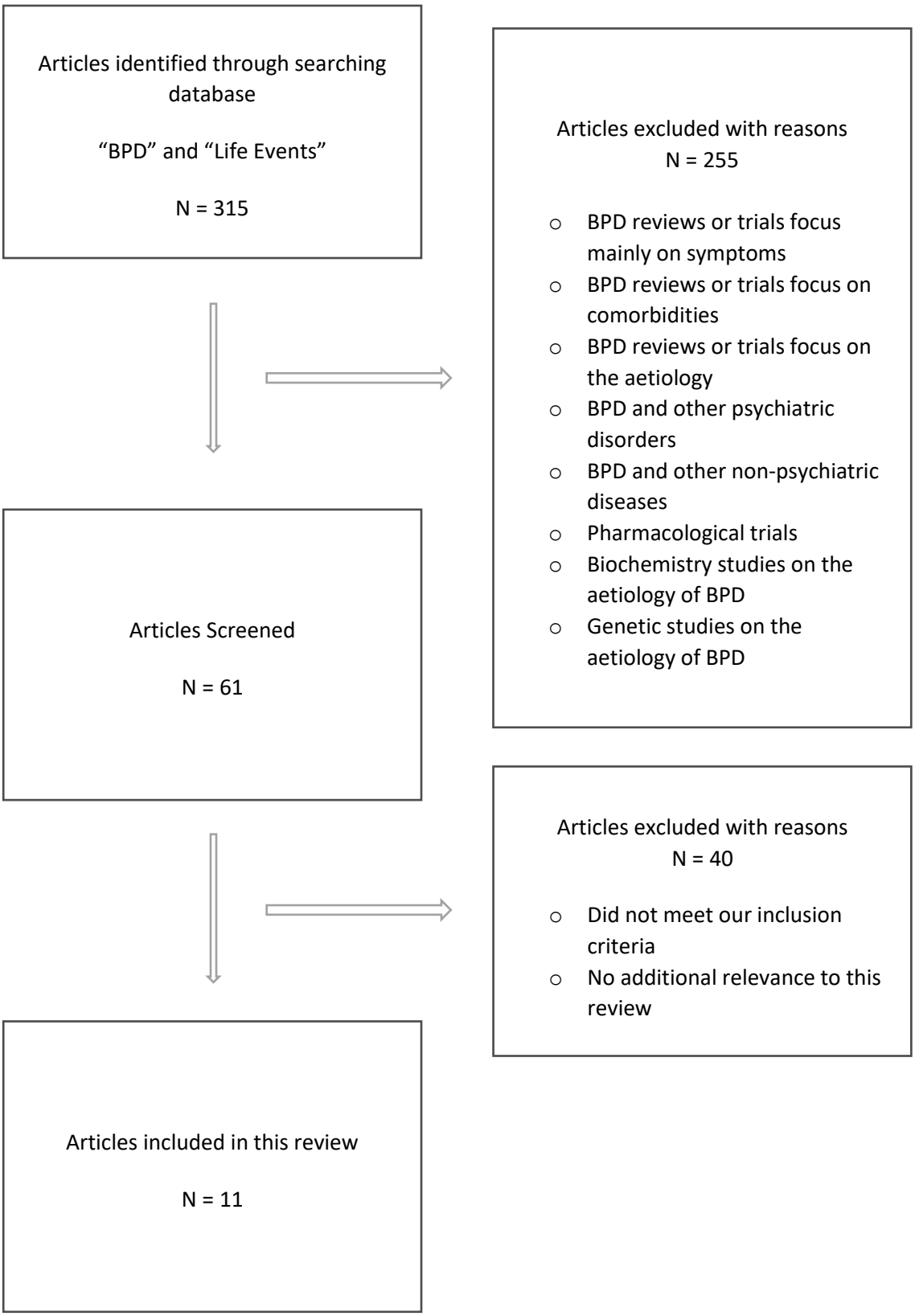
For this literature review, articles from various authors were gathered using PubMed as the search engine.

Initially, “Borderline Personality Disorder” was used as the main keyword and combined with “epidemiology”, “aetiology”, “comorbidities”, and “treatment” to gather information about the different topics of this review. The advanced search was used to narrow the information acquired and the relevant literature was selected.

Additionally, “Life Events” was grouped with “Borderline Personality Disorder”. This resulted in 315 articles from 1979 until 2022. We quickly understood that BPD is a PD of a lot of psychiatric interest, with an abundance of clinical research. However, studies on BPD and LEs were limited. Even though the first studies go back to the 1980s, only a few studies have been published in the meantime regarding this particular subject.

The article sample of our PubMed search was very heterogeneous, meaning different patient populations (e.g., Schizophrenia and BPD, Histrionic Personality Disorder, Axis I disorders), and different outcomes (e.g., randomized controlled trials for BPD pharmacotherapy). Firstly, the selection was based when the title suggested the focus of the study, the relationship of BPD with LEs. Secondly, articles regarding the influence LEs play in the aetiology of BPD during childhood and adolescence were excluded. Thirdly, due to the lack of studies, selection criteria such as the study design and details like the DSM edition, the method to determine personality pathology or features, and the questionnaires applied to measure LEs were taken out of the equation.

In the end, our inclusion criteria were papers written in English, with any publication date. Furthermore, we focused on primary research and published literature in the health field. The studies included were performed in adults (age >18 years) with BPD or BPD features, whose outcomes were related to the number of LEs experienced by iBPD, to the perception of LEs by iBPD, to features of BPD that could have an influence in certain LEs and to the role of LEs in BPD symptomatic exacerbations.


Articles identified through searching database
"BPD" and "Life Events"
N = 315
Articles excluded with reasons
N = 255
BPD reviews or trials focus mainly on symptoms
BPD reviews or trials focus on comorbidities
BPD reviews or trials focus on the aetiology
BPD and other psychiatric disorders
BPD and other non-psychiatric diseases
Pharmacological trials
Biochemistry studies on the aetiology of BPD
Genetic studies on the aetiology of BPD
Articles Screened
N = 61
Articles excluded with reasons
N = 40
Did not meet our inclusion criteria
No additional relevance to this review
Articles included in this review
N = 11

Discussion

There has been a significant shift towards a better understanding of BPD. Its aetiology is now seen as multifactorial, and its chronicity is being questioned.

Furthermore, personality keeps evolving and adult personality is not fixed. When talking about BPD, longitudinal studies showed that, between the ages of 20 and 40, iBPD had increased social skills, emotional stability, and decreased impulsivity. In other words, there seemed to be a consistent decline in BPD symptoms across adulthood (Bozzatello et al., 2021; Lilienfeld, 2005).

However, how individuals interpret their environment, memories and life events is influenced by personality traits and disorders (Lilienfeld, 2005). So, considering the main features of BPD, one can speculate that adverse LEs can play a role in its trajectory. For example, in triggering symptom exacerbations or being the repercussion of BPD psychopathology.

On the other hand, iBPD often have psychiatric comorbidities whose treatment is slowed down by co-occurring BPD. So, studying the relationship of BPD with LEs might bring some added value to these complex patients.

In addition to this, understanding how LEs influences BPD can contribute to a more emphatic behaviour from the health care community since iBPD are very present in the clinical context.

The influence of BPD on LEs

The impact that BPD psychopathology has on LEs has been widely discussed. Some studies established a relation between BPD and LEs by dividing LEs into dependent or unfaithful (directly related to BPD pathology – e.g., break up of a stable relationship, problems with law enforcement, losing a job) and independent or faithful events (e.g., serious illness or the death of a loved one).

The question whether the number of LEs experienced by iBPD is higher, when compared to certain populations, remains unanswered.

Gleason et al. (2012), in a community sample of 1234 participants between the age of 55 and 64, studied whether individuals with PDs and/or elevated levels of neuroticism experienced more LEs or reported more LEs, given the way LEs are usually assessed. They applied the List of Threatening Experiences Questionnaire (LTE-Q) and found that personality pathology was related to increased reports of stressful LEs. Additionally, individuals with elevated levels of neuroticism or with BPD symptoms, experienced more negative LEs, even in later adulthood. The research on the LEs impact on older iBPDs has great importance as there is a lack of studies on this population. A possible explanation could be that life itself is more uncertain, during early adulthood, which may lead to chronic instability, especially in the affect and impulse spheres. Besides that, changes in personality traits are accompanied by changes in BPD psychopathology, and features of this disorder decline over time (Bozzatello et al., 2021).

In contrast, Labonte & Paris (1993), performed a small sample study with 15 BPD patients and 29 controls (15 non-BPD patients from the crisis service, 14 non-BPD patients from the screening clinic), by applying the Life Events Survey. They concluded that patients with BPD when compared with controls (15 non-BPD patients from the crisis service, 14 non-BPD patients from the screening clinic), did not experience more LEs in the past 12 months.

Since literature is mostly focused on the frequency of LEs instead of the reaction to LEs and the coping mechanisms of iBPD, Jovev & Jackson (2006), evaluated the role of daily hassles and uplifts on psychosocial functioning according to its intensity. This study was performed in Australia, with 97 participants, of which 23 participants had BPD, 30 participants had an Axis I diagnosis, and 44 participants had other PDs. They found that iBPD experienced more LEs, in interpersonal relationships, personal health, and law domain, and experienced more daily hassles and fewer uplifts. Plus, they found that iBPD perceived daily hassles as more stressful considered fewer moments as uplifting and scored lower in coping effectiveness. A possible explanation for these findings is the intimate connection between affect instability and interpersonal stressors, which co-vary in the daily lives of iBPD (Hepp et al., 2018). Substantiating, studies that evaluated data from iBPD daily lives showed stronger

associations between momentary rejection and negative affect (Sadikaj et al., 2010), positive associations between rejection and aversive tension (Stiglmayr et al., 2008), as well as between rejection, disagreement, and negative affect (Chaudhury et al., 2017).

Additionally, a review, of three longitudinal studies, on the course and trajectory of PDs, by Lilienfeld (2005), stated that iBPD experience more negative LEs than patients with Axis II disorders and depression. Regardless, they also highlight that these findings are difficult to interpret since iBPD have important levels of negative emotionality, making them prone to focus selectively on the unpleasant features of one's life and to interpret LEs negatively.

Concerning LEs interpretation, in the study performed by Labonte & Paris (1993), they reported that iBPD did not perceive LEs as more negative. On the other hand, Gleason et al. (2012) concluded that people with higher borderline symptomatology were more likely to overreport LEs, especially with checklists. Furthermore, they emphasise the importance of distinguishing between the perception of and the actual experience of stressful LEs.

It is worth highlighting that the Labonte & Paris (1993), study had a relatively small sample when compared to the Gleason et al. (2012), study. Nevertheless, the Gleason et al. (2012), study did not specify the number of people with BPD or BPD features. On top of that, both the questionnaires and outcomes of the two studies were different.

On another topic, studies that have focused on specific BPD features and LEs mainly researched the impact of impulsivity and interpersonal relationships.

Traditional measures of impulsivity have been used to identify BPD symptom severity, diagnosis, and poor BPD treatment prognosis. In iBPD, impulsiveness is thought to be due to inattentiveness and a tendency toward action without anticipating consequences (Bornovalova et al., 2005). Labonte & Paris (1993), suggested that the consequences of impulsive actions may provide an additional source of negative LE for iBPD. Indeed, they concluded that LEs related to the

consequences of impulsive actions and the break-up of important relationships were significantly more common in iBPD.

In agreement with that, Powers et al. (2013), studied how symptoms of BPD could predict interpersonal, but not independent, stressful life events (SLEs) in a sample of 837 community adults with an average age of 60. For this research, they considered dependent, independent, and interpersonal LEs (e.g., breakups, serious problems with a close other). To assess for SLEs they applied the LTE-Q, 3 times, during 1.5 years at 6-month intervals. To control depressed mood, they applied the Beck Depression Inventory-II. Their research showed that, for dependent and independent LEs, unstable interpersonal relationships and impulsivity increased the risk for SLEs, even when the depressed mood was controlled. On the other hand, chronic feelings of emptiness decrease the risk, possibly because of the effect of social isolation on decreasing the chances of SLEs.

Indeed, iBPD with severe interpersonal dysfunction, have a low capacity to form satisfying and stable romantic relationships, and to achieve success and livelihood in their professional engagement (Jeung & Herpertz, 2014). These studies show that features like affective instability and difficulties in interpersonal relationships, remain pathogenic even in later adulthood. Moreover, even though impulsivity tends to attenuate with age, it shows that when present, it has an impact on the life of iBPD.

Kelly et al. (2000), studied the interaction of LE and BPD in suicide attempter status. They hypothesized that individuals with high levels of recent LE and low levels of social adjustment had a higher probability of suicide. They applied the Recent Life Changes Questionnaire (RLCQ) and the Social Adjustment Scale-Self Report (SAS-SR) in a sample of 80 subjects (34 individuals with major depression, 24 with BPD, and 22 with comorbid BPD and major depression). Despite the fact that depression is one of the most widely proposed risks factors for suicidal ideation (Bachmann, 2018), their research revealed that individuals with BPD and comorbid BPD and major depression had more suicide attempts than individuals with major depression only. In addition to

that, they reported that LEs experienced by the suicide attempters where more frequently related to family and economic struggles.

On this subject, Weyrauch et al. (2001), studied how SLEs, and impulsiveness played a role in triggering suicide attempts in a sample of 99 patients hospitalized for inpatient medical treatment of significant morbidity after attempting suicide. In all cases, there were reports of interpersonal loss and disruption in the year preceding the attempt, and 77% of the sample had an acute interpersonal conflict 1 to 7 days before the episode. However, they documented that, when three or more losses occurred in the preceding year, a decrease in the impulsivity of the suicide attempt was observed. The impulsiveness linked to the present suicide attempt increased when compared with a prior attempt. Similarly, so did the efforts to avoid discovery and the amount of communication about the attempt. These finding reflect a possible increase in the ambivalence towards subjects who had former suicide attempts. After all, impulsiveness is not fixed and may vary from one suicide attempt to another in response to different types of LEs. This evidence is consistent with the Jovev & Jackson (2006), study, that reported that LEs related to relationships and crime/legal matters were associated with an imminent risk of suicide attempts in the 2 months following the event.

Once again, these studies show that LEs related to BPD psychopathology such as interpersonal difficulties have a central role in suicide attempts. The association between suicidal ideation and BPD features may be explained by the negative interpersonal cognitions identified by the Interpersonal Theory of Suicide (Balzen et al., 2022). These include perceived burdensomeness, which is the feeling that one is a liability on others, and is often accompanied by self-derogating cognitions, and thwarted belongingness, that can be defined by the absence of reciprocal relationships and a sense of disconnection from others (van Orden et al., 2012). Furthermore, perceived burdensomeness and thwarted belongingness could be a variation of the cognitive symptoms of depression (Stewart et al., 2017), which gives a possible explanation for the results of the study performed by Kelly et al. (2000).

Furthermore, Kelly et al. (2000), found that social adjustment may act as a buffer against the stress caused by LE on iBPD. And so, low social adjustment in the immediate family and lower overall social adjustment were predictive of suicide attempter classifications, regardless of diagnosis. Therefore, individuals low on social adjustment are at the highest risk for attempting suicide.

Another study, performed by Blasco-Fontecilla et al. (2010), also researched the relation of suicide and LEs in subjects with PDs in a sample of 981 subjects, in which 466 had attempted suicide. Regarding BPD, they reported that a change in eating habits could trigger a suicide attempt with only a modest clinical significance after adjusting for concurrent Axis I diagnosis association. Even though eating disorders are relatively frequent in iBPD, this research still showed a modest clinical significance after adjusting for Axis I comorbidities which may be explained by the identity disturbance seen in iBPD. Assuming a change in eating habits for something that is unhealthy and may potentially change the body figure of iBPD, one can wonder if it doesn't increase self-image instability and therefore a symptomatic cascade that may trigger a suicide attempt.

Along with that, they did not find an association between LEs and BPD in suicide attempters independent of mood disorders, probably because subjects with repetitive self-harm behaviour were excluded. Non-suicidal self-injuries (NSSI) are very prevalent in iBPD, and despite the common features, they differ from suicide attempts by the lack of systematic suicidal intentions (Reichl & Kaess, 2021). However, they tend to be inter-related. Individuals with repeated NSSI have a higher risk of future suicide attempts within clinical and population-based sample, and this relation seems to be bigger in iBPD (Griep & MacKinnon, 2020).

The influence of LEs on BPD

iBPD are thought to live in *stable instability* and Conway et al. (2018), proposed that the shifting environmental conditions are responsible, at least in part, for fluctuations in symptom presentation over time. They performed a prospective,

longitudinal study that assessed 1630 community adults, 3 times, over a 5-year interval, by applying the LTE-Q. They hypothesized that life stress would be associated with future increases in borderline pathology and expected that borderline pathology would influence exposure to serious dependent, but not independent, stressors. They concluded that borderline pathology prospectively predicted rates of dependent SLEs beyond continuity in exposure to life stress. Additionally, they highlighted that stress does harm the physical health and social adjustment of individuals who exhibit symptoms of the disorder in later life.

In agreement with that, Powers et al. (2013), suggested that though the frequency and type of LEs change during BPD's course, the risk of negative interpersonal functioning persists. Consistent with those findings, Jovev & Jackson (2006), documented that iBPD have more hospitalizations, more substance-use problems, and more suicide attempts which indicates higher levels of impaired function. This shows that traits of BPD remain less stable and more chronic than what is expected for a personality disorder (Leichsenring et al., 2011). Although, it must be said, Jovev & Jackson (2006), also reported that levels of psychosocial function in iBPD did not change with the increased number of LEs, whereas in the non-BPD group (people with Axis I diagnosis and other PDs) the opposite was observed, confirming, once again, the *stable instability* these individuals live in. Which they explained by the fact that iBPD are distressed regardless of LEs, unlike the non-BPD group that gets distressed about the LEs.

Consistent with Conway et al. (2018), Christopher Perry et al. (1992) established that dependent events were more pathogenic than independent ones. They performed a prospective longitudinal study of iBPD where they investigated the temporal relationship between LEs and the exacerbation or recurrence of depression. They concluded that the exacerbations of depressive symptoms and both nonacute and acute major depressive episodes occurred at higher rates within the 8 weeks following the event. In these 8-weeks they also found that BPD predicted depression recurrence rates after interpersonal events, especially the dependent ones. Besides that, subjects with more SLEs had higher rates of depression, showing that the link between stress and depression is greatest for acute onset major depressive episodes.

Contrastingly, they did not find a statistically significant relationship between interpersonal LEs and higher rates of depression, even though they were consistently associated.

Limitations

The relationship between BPD and LEs has been a topic of interest for the past 30 years. However, some issues are still under debate, which may lead to limitations when studying PDs. For example, understanding what defines and how to classify a personality disorder is still in question. Additionally, patients' clinical heterogeneity leads to difficulties in classifying BPD subtypes. There are no universal sub-classifications, and some authors use subtypes, others, symptoms phenotype, and others don't even specify. Making it difficult to understand how LEs have an impact on certain subpopulations of BPD.

Regarding our study, we observed that most studies are not comparable because they used different methodologies. These included, different exclusion criteria and control groups; different questionaries were applied to evaluate LEs; some with further clinical assessments to avoid overreporting; LEs measured were divided or not, into dependent or independent; and the way LEs affect BPD used distinct outcomes. Studies whose outcomes focus on BPD symptomatology are mostly related to impulsivity and suicide, features whose psychopathology tends to decrease with age. However, all bring some added value to our clinical knowledge and eventually may impact our clinical practice.

Conclusion

Summing up, the relation between psychiatric diseases and the effects of LEs is interactive and reciprocal.

Regarding iBPD, they have important levels of negative emotionality, making them prone to focus selectively on the unpleasant features of one's life and to interpret LEs negatively. However, some studies do suggest that iBPD experience more negative LEs, even though they tend to overreport them.

In addition, the pathogenicity of LEs depends on whether the subject had an influence in causing it. In other words, negative LEs experienced by iBPD are associated with greater exposure to interpersonal relationships, the consequences of impulsive actions and difficulty in coping with those stressors. Accordingly, in iBPD, the risk of suicide, exacerbation of depressive symptoms, and non-acute or acute major depressive episodes, is higher in the two months following a dependent LE, especially events related to interpersonal conflicts.

Nevertheless, the levels of psychosocial function in iBPD do not change with the increased number of LEs, unlike the compared non-BPD control group, reflecting the so-called, *stable instability*.

So, we may speculate that stressful environmental conditions shape the temporal trajectory of BPD. Nevertheless, we can't forget that iBPD can also have a role in creating these conditions.

Recommendations

The number of studies on BPD published has increased strikingly since the eighties. Additionally, in this century, the research agenda has expanded with clinical and investigational medicine.

However, some issues regarding a better understanding of BPD still deserve some reflection. First, considering the epidemiology of BPD, every study researches its prevalence according to the gender binary. There is a considerable research gap related to the diagnosis, treatment, and psychiatric health care in gender minority individuals (such as transgender and gender diverse people) with or without BPD. Second, since BPD is a disorder with different modifiers throughout life, diagnostic criteria could be either age-specific or age-neutral.

Likewise, more studies are needed regarding the treatment of BPD since treatment trials (psycho and pharmacological therapy) have included just young individuals and data on long-term efficacy is still missing. Also, clinical recommendations on pharmacological treatment are still very low evidence-based.

Even though evidence shows us important links between BPD and LEs, there are still questions that may need more clinical investigation. It could be helpful to understand if BPD features like self-harming behaviour in young patients have a relation with certain LEs such as school failure or family problems. Along with that, it would also be interesting to understand the effect of negative LEs on self-image. Do comorbid psychiatric diseases like eating disorders exacerbate? On the topic of comorbid diseases, do iBPD with substance use disorder relapse after certain LEs?

Besides that, there's a need for information on the effect of psychotherapy or pharmacological treatment for BPD on LEs. Studies on the effect of LEs comparing BPD patients who are receiving, or not, treatment could bring valuable information. Does psychotherapy diminish interpersonal dysfunction and consequently dependent LEs? Do drugs that act on affect instability and emotional regulation influence LEs dependent on impulsivity or related to interpersonal stressors?

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