

Borderline personality - from psychoanalysis to epigenetics

Biological basis of attachment

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Abstract

In terms of object relations theory, borderline personality disorder (BPD) is characterized by a structural abnormality of identity, conflicting representations of self and others, and disorganization of attachment - a construct rooted in an individual's early experiences and central to the relationships established later in life. A special role in the formation of attachment style is attributed to the relationship with the caregiver and to difficult experiences or traumas from early developmental stages. These experiences not only provide the psychological basis for the development of an insecure attachment style, but also leave a biological mark in the body in the form of epigenetic modifications.

Although research on epigenetic modifications in BPD is scarce, a growing body of evidence supports the importance of oxytocin - the "social peptide" underlying attachment - in the etiology of BPD. We believe that the study of epigenetic modifications that affect the action of oxytocin in the BPD clinical population will provide a better understanding of the basis and process of development of the disorder, as well as provide a therapeutic direction to work effectively in the major areas of BPD.

Keywords: Borderline Personality Disorder, Epigenetics, Oxytocin

Introduction

Given its increasing prevalence, high suicide risk and frequent co-occurrence with symptoms of other disorders [1-4], borderline personality disorder (BPD) is now the subject of numerous scientific studies investigating its etiology and course, thus earning it the nickname "the personality of our time" [5]. In the DSM-5 classification, BPD is included in Cluster B personality disorders, whose common manifestations are exaggerated emotional expression, theatricality, and behavioral instability [6]. The criteria listed in the DSM-5 indicate the dual (structural and functional) nature of BPD symptoms - on the one hand, the disorder manifests itself in pathological personality traits, and on the other, in impaired personality functioning [7].

The impairment in personality functioning is observed primarily in the area of self-functioning, i.e., people with BPD do not have a coherent, integrated concept of self, and as a result of which their self-esteem, sense of identity, value system, or the goals they set also remain unstable [8]. The resulting lack of grounding prevents effective counteraction to the negative emotions experienced, does not allow for the development of an adequate sense of responsibility or self-criticism [9,10], and also leads to vulnerability to transient psychotic and depressive states [11].

Interpersonal functioning also remains affected by deficits - people with BPD show a reduced ability to recognize the feelings and needs of others while being significantly more sensitive and vulnerable to being hurt [9]. They perceive their loved ones through the prism of their own interpersonal needs, often changing their opinions of them dramatically - idealizing them to the extreme in one moment and accusing them of betrayal and neglect the next [12,13]. This inevitably affects the nature of intimate relationships, which are characterized by intensity and volatility, distrust and conflict, and excessive involvement that turns into withdrawal for fear of abandonment [13-15]. The experience of the described states reflects the cortical personality traits observed in BPD, such as negative emotionality, difficulty with impulse control, and a tendency toward oppositional behavior [16].

In addition, people with BPD often experience emotional intensity and lability out of proportion to events or circumstances, including feelings of anxiety and overwhelming separation anxiety [9,10]. High insecurity in a situation of loneliness leads to dependency and intolerance of the state [12], which in turn increases depression centered on the feelings of shame, being unhappy, miserable and worthless [9,10]. Limitations in emotional control lead

to significant impulsivity and a tendency to take risks aimed primarily for the immediate gratification of needs [17]. The described emotionality is stigmatized by persistent feelings of anger and irritation, even in response to seemingly minor stimuli [9,10].

Object relations theories versus structure and functioning of people with BPD

In order to better understand the symptoms that make up the clinical picture of the disorder and the underlying mechanisms, an attempt is made to place them in the context of psychological theories. Given the predominance of symptoms in the clinical picture of BPD in the area of the concept of self and the perception and patterns of interpersonal relationships, it seems appropriate to refer to the psychodynamic theory of object relations, which includes in its assumptions both the process of development of internalized representations of self and object and the emergence of the ego and superego.

In his work, Kernberg [18,19] distinguished three levels of personality organization - psychotic, borderline and neurotic. Although they do not correspond to personality disorders, later works by Kernberg [20] place them in the context of personality pathology, dividing borderline organization into higher-level borderline organization (including dependent, histrionic and avoidant personalities) and lower-level borderline organization (including paranoid, schizoid, schizotypal, borderline and antisocial personalities). According to the cited theory, the level of personality organization - and, at the same time, the depth of pathology - depends largely on the level of integration of mental structures, the expression of which is represented by the observed symptoms [21].

Abnormalities in the integration of positive and negative representations of self and object, and the relationships that link them, result in splitting - a mechanism by which people with BPD often oscillate between devaluation and idealization projected onto both the self and the external environment [12].

Splitting in BPD seems to be rooted in a fixation on the separation-individuation phase, in which there is an integration of the representation of the separate self from that of the mother [22], including the accompanying positive and negative affect [23]. The clear distinction between positive and negative representations is maintained as a mechanism to protect an object perceived as satisfying from the disappointment, anger, or hatred felt toward it [21]. Thus, the good object is protected from being hated outright [12], and the relationship with it is maintained.

According to Mahler's theory [22], the separation-individuation phase in normal development precedes the object constancy phase, in which the representation of the object - no longer valued only for the sake of the needs it satisfies, but also in spite of its negative aspects - is fixed in the child's psyche in such a way that it can function independently, while at the same time the internalized image of the caregiver is invoked, for example, for comfort. Without developed object constancy, a child in a separation situation fears that the caregiver is gone forever [12]. This pattern continues into later life. The expectation of rejection or unavailability of a significant other reinforces negative representations of the self as unlovable and of others as rejecting [24]. Thus, on the one hand, BPD patients are influenced by extremely positive and negative representations - they experience unstable emotional states, enter into chaotic relationships, engage in impulsive self-destructive behavior, and are often unable to understand the behavior of others [21]. On the other hand, they are accompanied by a constant, overwhelming fear of separation and abandonment [12], which characterizes all relationships with insecurity, uncertainty, instability, and the search for the satisfaction of one's own needs. As a result, BPD patients are unable to function in social interactions that require trust, cooperation, and gaining social acceptance [25].

Although the clinical picture of BPD consists of symptoms observed in multiple dimensions of functioning [26], they may in fact be rooted in the abnormal differentiation and integration of self and other images - positive and negative self and object representations. According to Kernberg's team [27], the emotional imbalance characteristic of BPD may be a symptom secondary to an unstable sense of self and conflicting object representations. This is because the internalization of object relations in early childhood provides the foundation not only for later evolving psychological structures, but also for unconscious conflicts [28]. The dyadic structures of self and object relations are a reflection of subjective developmental experiences rather than a reliable representation of them, but they serve an overarching function in organizing motivation and behavior in later stages of life [21]. Therefore, the lack of integration of the positive and negative aspects of early object relationships will set the tone for adult relationships, often giving them the intense, turbulent, and chaotic character inherent in BPD. Despite the emotional nature of the symptoms observed in this process, the concomitant activation of relevant cognitive content that justifies their occurrence is significant [21,29].

J. Bowlby's theory of attachment

The approaches discussed above create a picture of BPD conceived as a structural abnormality of identity with poor and contradictory representations of self and others and

accompanied by significant attachment disorganization [30]. The relationship with the object remains characterized by extremes, contradictions and a constant sense of threat of abandonment. These characteristics constitute the specific pattern of attachment described by Bowlby's concept of attachment [31]. As a construct that captures, on the one hand, a specific emotional bond with a caregiver (and later with others) and a motivational-behavioral system and, on the other hand, a mental representation of a specific relationship between self and figure (analogous to the object discussed earlier), attachment reveals the essence or core of BPD.

In seeking a framework for understanding personality disorders - their development and maintenance - Lyddon and Sherry (2001) describe insecure attachment styles specific to each diagnostic entity. The BPD-specific attachment style is characterized by instability and dynamic transitions between other insecure attachment styles [29]. In the absence of a stable attachment pattern, BPD patients may present as unstable, resentful, impulsive, highly emotional, helpless, or feeling an inner void when heavily influenced by external factors [29].

Depending on the concept adopted by researchers, BPD has been linked to a number of attachment styles - anxious, anxious-preoccupied, preoccupied, avoidant, dismissive. Regardless of the methodology employed, what appears to be significant in each of these cases is the insecure nature of the attachment [32-36].

It is worth mentioning that in a study conducted by Levy et al. (2005), individual attachment styles corresponded to different domains of BPD symptoms - the anxious style was associated with a lack of a stable sense of identity (at the trend level), the preoccupied style with fears and reactions to real or imagined abandonment, and the avoidant style with perceived anger.

Although insecure attachment style takes different forms, all of them are exacerbated in BPD patients compared to healthy controls [37]. Perhaps instability in BPD goes beyond emotionality and results in oscillation between insecure attachment states and corresponding symptoms. The apparent lack of a stable attachment pattern reflects multiple incompatible representations of the relationship with the object, formed as a result of conflicting early childhood experiences [38,39].

In contrast, in a study of a sample of adolescents, the object relationship representation in BPD not only included a more hostile image of the caregiver, but was also characterized by a greater degree of complexity than that of healthy peers and other clinical groups [40]. The authors suggest that representations in BPD may be distorted - shallow and one-dimensional,

overly complex, or relatively normal, with accompanying affect variability (e.g., low arousal is accompanied by normal representations) [40].

Sources of insecure attachment styles in BPD

The lack of a stable attachment pattern revealed by the disorganized attachment style helps to distinguish BPD not only from healthy controls, but also from other clinical groups [36,40,41]. Studies analyzing attachment in BPD have identified the following elements that characterize it: the unavailability of an attachment figure, withdrawal accompanied by anger, compulsive care-seeking [42], a lower sense of agency [43], excessive dependence accompanied by the presence of antisocial traits [44], sensitivity to abandonment and loneliness [45], and between 12 and 42 months of age, disorganization of attachment, maternal hostility, blurring of boundaries, family disruption (father's departure), family stress, and often unresolved experiences of loss or trauma [34]. This rationale suggests that BPD and its symptoms should be considered in the context of difficult experiences or trauma from early developmental stages.

According to Bowlby's theory, it is the first year of life that is crucial for the formation of the emotional bond between a child and its mother [46]. BPD traits have been linked to the insecure attachment style itself, as well as to other significant factors rooted in this period - the perception of the mother as uncaring [47] or the relationship with the parents [47,48].

The role of caregivers in the proper development of offspring is particularly important. Indeed, behavioral transmission between mother and offspring has been observed not only in humans but also in other primates [49], suggesting its primordial and natural nature. Both caregiving behaviors and prenatal experiences are important in this regard [50]; the mother's depressive or anxious mood affects the newborn, i.e., its development, stress response, and the expression of its genome [51].

The biological basis of attachment - the role of epigenetic mechanisms

The nature of biological embedding, which determines different trajectories of later development and is likely related to parenting style and early difficult experiences, is evident as early as the third month of life [52].

Its formation in the early stages of life occurs, among other things, through epigenetic mechanisms. They are an expression of the dynamic adaptation of the young organism to the conditions of the environment, involving changes in the expression of individual genes, without

disturbing the DNA sequence itself [53]. These changes have long-term effects on the somatic and mental aspects of health [54].

The term “epigenetics” was first used by C. H. Waddington at the end of the 1930s to describe a phenomenon related to the fact that phenotypic changes do not always go hand in hand with genotype changes, however, their importance in the etiology of mental disorders has been confirmed only in recent years [54].

Although epigenetic modifications are mainly studied as a result of an individual's experience [55, 56-57], recent findings suggest that they can be passed on to offspring through intergenerational transmission [58]. The modifications in question are manifested by three epigenetic mechanisms, namely, DNA methylation [58-61], miRNA (microRNA) expression [62-65], and modification of histone proteins [66-68]. Each of the three processes specified above, unlike genetic changes, do not involve changes in DNA sequence. These changes are affected to the largest extent by environmental factors [56]. Through their influence on transcription of genes they modify our phenotype [57].

Although epigenetic modifications associated with either the diagnosis or symptoms of BPD remain an area requiring further and more extensive research, to date researchers have been able to isolate several commonly observed changes. The most consistent findings relate to changes in methylation of two genes: the gene encoding the glucocorticoid receptor (NR3C1) (e.g., 69-72) and the gene encoding the brain-derived neurotrophic factor (BDNF) protein [73-76].

In the case of NR3C1, increased methylation of the gene has been associated not only with BPD symptoms in clinical populations [69,71,72,77], but also with childhood neglect and abuse experienced by patients [71,77]. The expression of the NR3C1 gene influences, among other things, the regulation of the HPA axis and the hormonal stress response, and its epigenetic changes are observed in cases of stress experienced early in life, including exposure to abuse or neglect by a caregiver [78-81]. In addition, studies conducted in a group with subclinical BPD symptoms revealed an association between the tendency to manifest BPD psychopathology and increased methylation of the gene encoding the glucocorticoid receptor. At the same time, an additive effect of childhood maltreatment and epigenetic modifications was found as predictors of BPD symptom development [82]. The importance of NR3C1 in the etiology of BPD is also underscored by studies in non-clinical populations. Even neonatal levels of NR3C1 methylation have been shown to be a key factor associated with later social-

emotional development in the newborn [83], also suggesting links between epigenetic mechanisms and early interpersonal relationships. Furthermore, in healthy adults, increased NR3C1 methylation has been associated with attachment avoidance, suggesting the potential importance of HPA axis activity and the regulatory role of social stress in shaping attachment style, with epigenetic modifications as its biomarkers [84].

In the case of BDNF, increased methylation of the gene and associated decreased BDNF protein production have been reported in BPD patients [75,76], with methylation levels correspondingly increasing with the intensity of early childhood maltreatment experiences [75]. Epigenetic modifications of BDNF are often associated with difficulties experienced early in life [85-87]. Studies using an animal model illustrate the role of BDNF not only for the earliest but also for later periods of development (mice raised in a rich and stimulating environment have not only better overall social competence, but also greater adult brain plasticity supported by BDNF) [88,89]. Meanwhile, BDNF expression in young rats appears to be influenced by negative experiences early in life, including maternal deprivation, which has been linked to BDNF protein levels [87], and aversive parenting, which has been associated with increased BDNF gene methylation [90]. It has also been observed that increased BDNF methylation can be passed from mother rats to their offspring [84]. Thus, the intergenerational transmission of parental behavior may occur not only at the behavioral level, but also at the biological level - leaving an epigenetic trail of negative experiences passed from mother to offspring [86].

Single studies have reported links between BPD and epigenetic methylation changes in other genes as well: APBA2 (1.08 fold), APBA3 (1.08 fold), GATA4 (1.1 fold), KCNQ1 (1.54 fold), MCF2 (1.10 fold), NINJ2 (1.17 fold), TAAR5 (1.05 fold) [91], 5-HT2A (1.24 fold), MAOA (1.05 fold), MAOB (1.08 fold), S-COMT [69], PRIMA1, or reduced rDNA methylation in the 51ETS region [91].

Also noteworthy are the studies by Arranz et al. [92], which consider gender differences in the context of BPD and epigenetic mechanisms, according to which lower methylation was observed on chromosome X (PQBP1, ZNF41, RPL10, cg07810091 and cg24395855) and chromosome 6 (TAP2), and the level of these changes depended on the intensity of childhood trauma experiences. Epigenetic modifications were significantly more frequent in the genes related to estrogen regulation, neurogenesis processes, and cell differentiation [92]. Although epigenetic modifications were a differentiating factor between the control group and the BPD group, similar differences were not found when childhood trauma was used as a criterion for

group separation [92]. These findings underscore the particular importance of early life stages for the emergence of epigenetic modifications.

Epigenetic modifications thus represent a biological trace of experience that can affect human functioning even after many years have passed. However, this biological nature does not seem to imply irreversibility. The dynamic adaptation of the body to changing environmental conditions is observed in the epigenetic changes that occur during the psychotherapy process. A reduction in BDNF methylation after a 4-week trial has been reported in BPD patients undergoing DBT therapy [75] and 12 psychotherapeutic interventions [76]. The results cited demonstrate not only the effect of the therapeutic methods used, measurable at the biological level, but also the potential for reversing epigenetic changes rooted in the earliest stages of life.

Further research directions - the role of oxytocin in bond formation

Studies of epigenetic modifications seem to confirm the fundamental importance of early experiences and the resulting attachment style for the later development of the BPD personality. Thus, attachment style is one of the predictors of BPD patients' response to therapy and the primary target of interventions [93]. As a disorder that underlies the functioning of the attachment and affiliation system, BPD may also be associated with alterations in the neuropeptides that regulate it, including oxytocin [94]. Oxytocin is a peptide neurohormone produced in the hypothalamus, and its activity is fundamental to the formation of social bonds; it is involved in the formation of bonds between mother and child [95], and its activity remains dependent on early experience, e.g., through reduced expression of the oxytocin receptor gene (OXTR) following early childhood trauma that persists into adulthood [96]. Despite the lack of studies in the BPD clinical group, epigenetic modifications of the OXTR gene have been implicated in neonatal emotion processing [97] and attachment style formation, including attachment avoidance in young adults [84, 98].

Significantly lower levels of oxytocin have been found in BPD patients compared to healthy individuals [99-102]. In addition, a disorganized attachment style is associated with lower oxytocin levels in BPD compared to a secure style [97]. While attachment style did not differentiate oxytocin levels in healthy individuals, oxytocin levels in BPD patients were significantly higher for the anxious-avoidant style compared to the anxious-preoccupied style [99]. In contrast, the OXTR gene polymorphism appears to predict an individual's susceptibility to adverse effects of the family environment [103,105]. When the A allele was present, the

severity of BPD symptoms was stronger with negative family conditions and weaker with positive ones, while the severity of symptoms for the recessive homozygote did not depend on the quality of family life [103]. Other studies reported that BPD patients carrying the A allele rated the level of emotional pain experienced as higher than others, indicating greater sensitivity to the effects of early childhood trauma and its impact on empathy manifested later in life [104].

Summary

The role of oxytocin in BPD centered on dysfunction in the area of attachment and bonding can be traced back to early experiences in the relationship with a caregiver that set the stage for the development of the disorder. Their biological footprints, in the form of epigenetic changes in the expression of certain genes, can also be seen in the expression of the oxytocin receptor gene (OXTR). Research focused on potential epigenetic changes in the action of oxytocin in BPD would be a direction of particular importance given its therapeutic potential. It has been observed that even a single intranasal administration of oxytocin in the BPD group can normalize some aspects of interpersonal dysfunction [105], increase emotional empathy and the approach motivation [106]. It also helps to regulate emotions [107], reduces social withdrawal and stress levels [108], and decreases sensitivity to complex social situations by regulating amygdala and insula activity [109]. Given the susceptibility of epigenetic modifications to therapeutic intervention, research on the mechanisms affecting oxytocin - the "social peptide" underlying attachment - may provide a therapeutic direction for effective work in key areas of BPD, such as the unstable, disorganized attachment pattern, the resulting involvement in unstable and intense relationships accompanied by a constant fear of abandonment, and inconsistent representations of self and others. At the same time, they can provide biological evidence for the efficacy of increasingly popular therapeutic approaches to working with personality disorders, such as schema therapy [110,111], providing a key to understanding both the basis of the pathology and the efficacy of specific interventions.

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