

## **The Neurobiological Aspects of Borderline Personality Disorder (Excerpt)**

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Borderline Personality Disorder (BPD) is the single most prevalent personality disorder (Lawson, 2000). In this paper, I first describe BPD, followed by some of the genetic, chemical and psychoneurobiological explanations of the condition. I then review various interventions, with an emphasis on long-term psychotherapy focusing on reparative right-brain communication (Schoore, 2003b).

### **Description of Condition**

According to the DSM-IV-TR, BPD is characterized by a pervasive instability of interpersonal relationships, self-image, and affects, together with marked impulsivity that begins by early adulthood and is present in multiple contexts (p. 725). It generally comprises the following symptoms:

1. Hypersensitivity to real or imagined abandonment.
2. Disturbances of self-identity.
3. Intense and unstable relationships
4. Alternating idealization and devaluation of themselves and others (black and white thinking).
5. Compulsive, risky, and sometimes self-destructive behaviors. (Cozolino, 2010, p.281)

BPD has also been described from a more subjective vantage, as “a pattern of fearful attachment (attachment-anxiety and relational avoidance), painful intolerance of aloneness, hypersensitivity to social environment, expectation of hostility from others, and greatly reduced positive memories of dyadic interactions” (Critchfield, Levy, Clarkin, & Kernberg, 2008; Gunderson & Lyons-Ruth, 2008, as cited in Fonagy, Luyten & Strathearn, 2011, p. 48). It is further

distinguished by “intense inner pain” (Zanarini & Frankenburg, 2007, as cited in Fonagy, et al., 2011, p. 48), an acute sense of shame (Levy, Edell, & McGlashan, 2007, as cited in Fonagy, et al., 2011, p. 48), and episodes of dissociation (Philipsen, richter, Schmahl, Peters, Rusch, Bohus, et al., 2004, as cited in Fonagy, et al., 2011, p. 48).

### **Neurobiological Aspects of BPD**

A paucity of brain research has been performed on individuals with BPD (Fonagy, Luyten & Strathearn, 2011, p.49; Cozolino, 2010, p. 283). Studies have found potential genetic factors (e.g., Dell’Osso, Berlin, Serati, & Altamura, 2010), chemical components (e.g., Holden, Pakula, & Mooney, 1997), and neurobiological elements. (e.g. Schore, 2003a,b). Schore’s psychoneurobiological theory (2003a,b) appears to be the most comprehensive.

#### **Genetic Factors.**

Genetic research of BPD is rudimentary, with few studies to date (Dell’Osso, Berlin, Serati, & Altamura, 2010). One heritability study suggests a 37% concordance between monozygotic twins compared to 7% in dizygotic twins (Torgersen, 1984, as cited in Dell’Osso, et al., 2010). A later study attributed 69% of the variance in BPD to genetic factors (Torgerson, 2000, as cited in Bandelow, Schmahl, Falkai & Wedekind, 2010). According to some theorists genes associated with BPD are linked to serotonin (Dell’Osso, et al., 2010; Bandelow, et al., 2010). Abnormalities have been reported in the 5-HTT, tryptophan hydroxylase, and 5-HT<sub>2A</sub> receptor gene of BPD patients, all of which are involved in neurotransmissions within the serotonin system (New, Goodman, Triebwasser, & Siever, 2008, as cited in Bandelow, et al, 2010, p. 624). However, these irregularities may have become phenotypic as a result of early bonding failures (Cozolino, 2010, Schore, 2003a,b).

### **Chemical/Hormonal Factors.**

Some research suggests that BPD results from a dysregulation of the endogenous opioid system (EOS) (Hughes, et al., 1975; Pert & Snyder, 1973, as cited in Bandelow, Schmahl, Falkai, & Wedekind, 2010; Holden, Pakula, & Mooney, 1997). Such dysregulation is said to be due to under-sensitive endorphin receptors, and/or inadequate levels of endogenous opioids (Bandelow, et al., 2010). This theory is limited by a dearth of studies measuring endorphins in BPD patients, but is based largely on the fact that the quintessential symptoms of BPD appear to be “desperate, albeit mostly unconscious, effort[s] to achieve higher opioid receptor occupancy or normal levels of endorphins in the shortest possible time” (Bandelow, 2010, p. 626).

Endogenous opioids are similar to morphine in their rewarding and addictive effects (van Ree, 1979, as cited in Bandelow, Schmahl, Falkai, & Wedekind, 2010). Although three classes of opioids comprise the EOS:  $\beta$ -endorphins, enkaphalins, and dynorphins (Dhawan, et al., 1996, as cited in Bandelow, et al., 2010),  $\beta$ -endorphin may be the most important (Bandelow, et al., 2010; Holden, Pakula, & Mooney, 1997). It is released during stress (Roth-Deri, et al., 2008, as cited in Bandelow, et al., 2010), and contributes to myriad positive sequelae, including: (1) analgesic effects in response to severe injury (Bandelow, et al., 2010), (2) euphoric experiences such as being in love, kissing or engaging in sexual activities (Esch & Stefano, 2005, as cited in Bandelow, 2010); (3) the placebo effect (Johansen, Brox, & Flaten, 2003, as cited in Bandelow, 2010); and (4) the “runner’s high” (sense of euphoria and reduced pain sensitivity in response to long-distance running) (Goldfarb & Jamurtas, 1997, as cited in Bandelow, 2010). Endogenous opioids are also believed to stimulate the release and transportation of dopamine to the nucleus accumbens, which is one of the “pleasure centers” in the brain. (De Vries & Sheppenber, 2002, as cited in Bandelow, 2010).

Although speculative, evidence suggests a connection between dysregulation of the EOS and certain stereotypical features of BPD, such as: intense separation distress, drug addiction and impulsivity, self-injurious behavior (SIB), and eating disorders. However, it is unclear from the literature whether the behaviors of BPD patients are aimed at increasing or decreasing endogenous opioids, since some authors suggest that the goal is to stimulate the EOS (Bandelow, et al, 2010), while others propose that elevated levels of  $\beta$ -endorphin promote anxiety and depression, which is alleviated through impulsiveness or SIB (Holden, et al, 1997). The following is a synopsis of the relationship between the EOS and various stereotypical BPD characteristics:

1. Fear of abandonment and interpersonal distress.  $\beta$ -endorphins play a dominant role in the formation of social bonds (Panksepp, Herman, Conner, Bishop, & Scott, 1978, as cited in Bandelow, 2010). Thus, separation distress may reflect endogenous endorphin withdrawal or other disruptions in opioid neurotransmission. Also, morphine (which mimics endogenous opioids) can relieve separation distress, suggesting a possible deficiency in endogenous opioid tone in BPD patients (Bandelow, et al., 2010).

2. Drug addiction and impulsivity. Approximately 75% of BPD patients experience substance abuse problems (Hatzitaskos, Soldatos, Kokkevi, & Stefanis, 1999, as cited in Bandelow, et al., 2010), and 45% of heroin addicts suffer from BPD (Darke, Ross, Williamson, & Teeson, 2005, as cited by Bandelow, et al., 2010). Numerous drugs of abuse, such as heroin, cocaine, amphetamines, alcohol, cannabis, and nicotine, increase dopamine levels in the nucleus accumbens (Nestler, 2005, as cited in Bandelow, 2010). Moreover, individuals with BPD favor drugs with immediate effects, such as crack and “speedballs” (heroin and cocaine combination) (Bandelow, et al., 2010). This preference may reflect a desperate need to stimulate the EOS. Similarly, other impulse control disorders, such as gambling addiction, kleptomania, and compulsive purchasing are common among

BPD patients, and also involve endorphin release (Brewer & Potenza, 2008, as cited in Bandelow, et al., 2010).

3. Self-injurious behavior. The vast majority of BPD patients engage in SIB (Herpertz, 1995, as cited in Bandelow, 2010). According to Holden, Pakula, and Mooney (1997), SIB provides swift relief from anxiety, anger and racing thoughts. BPD patients report feeling little or no pain during acts of SIB, and a compelling need to engage in it, both of which imply an elevation of  $\beta$ -endorphins (Holden, et al., 1997; Bandelow, et al., 2010).

4. Eating disorders. Both binge eating and excessive dieting can be attributed to attempts to stimulate the EOS (Holden, et al., 1997). Binge eating has been interpreted as a recalcitrant attempt to trigger the reward system and EOS (Bandelow, et al., 2010). Anorectic patients have elevated endogenous opioids (Marrazzi, Luby, Kinzie, Munjal, & Spector, 1997, as cited in Bandelow, et al., 2010), which is consistent with the auto-addiction opioid model of anorexia, pursuant to which endogenous opioids released during initial dieting reinforce starvation (Marrazi, et al., 1997, as cited in Bandelow, 2010).

### **Neurobiological Factors.**

Neuroimaging data reveal dysfunction in certain brain regions of BPD patients, predominantly the frontolimbic structures, which include the anterior cingulate cortex, orbitofrontal and dorsolateral prefrontal cortex, amygdala, and hippocampus (Dell'Osso, Berlin, Serati, & Altamura, 2010). In particular, the amygdala and orbitofrontal cortex seem to play pivotal roles in the processes that contribute to BPD (Schoe, 2003a,b).

Critical to Schoe's (2003a,b) theory, is the predominance of the right hemisphere in processing social-emotional data, facilitating attachment, regulating affect, and managing stress (2003a, p. 129). The right brain stores the individual's "internal working model" of relationships (pp.

108, 129), including traumatic, nonverbal, emotional memories (p. 125). It plays a greater role than the left in all areas of emotional processing because it contains deeper structural and functional connections to the limbic and autonomic nervous systems (p. 222). Evidence of this asymmetry includes the fact that the orbitofrontal system is enlarged in the right hemisphere (Falk, et al., 1990, as cited in Schore, 2003a, p. 222), and the right amygdala is preferentially activated by facial and auditory cues (p. 257).

The amygdala is the most primitive limbic regulatory structure (Schore, 2003a). It is the only limbic constituent on line at birth, and appraises only crude sensory information. It responds with a cascade of unregulated, autonomic fear reactions, including fight, flight, freeze, increased norepinephrine, respiration and fearful facial interpretation and expression (Cozolino, 2010; Schore, 2003a, p. 155, 293).

The orbitofrontal cortex is the brain's "central emotion-regulating system" (p. 272). It is considered the mechanism by which humans exercise cognitive control over immediate, instinctive reactions generated by the amygdala (p. 256). Its role is to "facilitate or inhibit the defense reactions of the amygdala (Timms, 1977), and thereby adaptively regulate amygdala-driven autonomic hyperarousal or hypoarousal" (Schore, 2003a p. 293). The neuronal connections that facilitate this dynamic are forged during the first two years of life. As Schore explains,

Over the course of postnatal development connections between the orbitofrontal cortex and amygdala increase (Bouwmeester, Wolterink, & van Ree, 2002), and this hierarchical organization allows this prefrontal system to take over amygdala functions (Rolls, 1996), and for the right frontotemporal cortex to maintain inhibitory control over intense emotional arousal (Kinsbourne & Bemporad, 1984). (p. 256)

This process is "experience-dependent" (Schore, 2003a, p. 125), in that dyadic interactions with the caregiver mediate the development of these connections by influencing the production of

stress-induced steroid hormones, such as corticosteroids, that are toxic to the infant brain (Schore, 2003a, p. 116). An attentive caregiver modulates infant affect, inhibiting the secretion of such hormones, thus, preserving the integrity of developing neurons. Chronic, severe attachment disruption during the first two years of life stimulates excessive stress hormone secretion, which induces over-pruning of the neurons connecting the amygdala to the orbitofrontal cortex. Thus, initial autonomic reactions in the amygdala become inhibited from transmitting to, and integrating with, the higher, more conscious processes in the orbitofrontal cortex (Schore, 2003a).

Individuals with these structural impairments typically suffer from a disorganized/disoriented attachment pattern, since they exhibit “fragile regulatory capacities, [that] even under moderate stress, . . . [are] vulnerable to disorganization and to affect shifts that are extremely discontinuous and labile” (Schore, p. 119). Schore (2003a) posits that borderline personality organization (in addition to PTSD and psychopathy) generally reflects this deficient right-hemispheric orbitofrontal and amygdala functioning.

## **Interventions**

### **Pharmacological Treatments.**

Pharmacological interventions for the treatment of BPD are scant (Holden, Pakula, & Mooney, 1997). BPD patients are typically first administered antidepressants, followed by a combination of antipsychotics, hypnotics, antihistamines, and mood stabilizers (Belino, Paradiso, & Bogetto, 2008, as cited in Bandelow, Schmahl, Falkai, & Wedekind, 2010). However, these medications generally provide only mild to moderate symptom relief. (Bandelow, et al.). In contrast, drugs of abuse seem to more effectively mitigate symptoms, which may be due in part to their stimulation of dopamine transmission (Bandelow, et al.), but only for brief periods and at the cost of inebriation and addiction.

According to the EOS theory, opioid antagonists, such as naltrexone, which block the rewarding effects of endorphins, may curb SIB and other impulsive behaviors. However, it has been shown to elevate opioid receptor sensitivity, which increases the chances of accidental overdose if followed by drugs of abuse (Bandelow, et al.). Opioid antagonists also exhibit paradoxical effects, in that they would be expected to induce anhedonia or depression, but have not been shown to do so more often than placebos (Bandelow, et al.). According to Bandelow, et al., there have been no controlled studies of the effects of opioid antagonists on the overall constellation of BPD symptoms.

### **Psychotherapeutic Interventions.**

Several psychotherapeutic interventions are suggested in the literature. Bandelow, et al. (2010) advocates stimulating the EOS by replacing dangerous, impulsive behaviors with more socially acceptable methods, such as moderate exercise, artistic endeavors and forging safe, reliable relationships (which sounds a bit idealistic) . Fonagy, Luyten and Strathearn (2011) recommend therapy that focuses on “mentalization”- the recognition of the mental states of self and others. They posit that by focusing on the patient’s current mental experience while activating the attachment system, he or she can learn to imbue chaotic emotional states with meaning and coherence, thus enhancing self-regulation.

According to Schore (2003b), the primitive emotional states experienced by extremely dysregulated individuals are not cognitive, but rather, “psychobiological”: They are whole-body experiences that are communicated primarily by the right-brain through unconscious mechanisms such as projective identification (p. 59). Schore opines, “In order to receive these transference communications of traumatically dissociated affect, the therapist must shift from a left to right hemispheric dominant state of evenly hovering attention” (2003b, p. 143). During this right-brain to right-brain dialogue, the self-aware, empathic therapist resonates nonverbally with the client, via



facial expression, prosody, and body posture. In this way, the therapist is able to perceive the client's dysregulation and provide gentle interactive regulation. Through long-term treatment in such a growth-promoting environment, neuronal connections truncated by early trauma can develop (2003b, p. 145). As this process unfolds, dysregulated bodily states evolve into subjective experiences that can be verbally articulated (Stolorow & Atwood, 1992, p. 42, as cited in Schore, 2003b, p. 144).

### **Conceptual Alterations as a Result of this Project**

The research on this topic illuminated the following: (1) the tangential nature of the of extant research, (2) the limited benefits of medication for these patients, and (3) the connection of BPD to post-traumatic stress disorder (PTSD). First, the genetic and neurochemical research seems to be predominantly hypothetical (e.g. Holden, Pakula & Mooney, 1997; Bandelow, Schmahl, Falkai, & Wedekind, 2010). These lines of research are clearly in their infancy, and only mildly suggestive of future direction. For instance, the EOS theory is interesting; however, the evidence of dysregulation seems to point in myriad, often inconsistent, directions.

Second, according to the above studies, medication for BPD patients is rather ineffectual. It is possible that the research mistakenly views BPD patients as too homogeneous a group. Lawson (2000) describes four different character profiles of borderline mothers based on dominant states of fear, helplessness, emptiness and anger. Moreover, there are 53 iterations of BPD based on the DSM definition. It seems intuitive that these various distinctions might manifest neurobiologically, which differences do not seem to be reflected in the research.

Third, BPD is closely related to PTSD. Cozolino (2010) suggests that BPD, "may represent one variant of complex PTSD" (p. 281). Both he and Schore (2003a,b) describe the trauma to which PTSD is attributed as a likely secondary stressor to an initial traumatic attachment history.

This paper describes characteristics and symptoms of BPD, as well as some of the genetic, chemical and psychoneurobiological explanations of the condition. Importantly, these perspectives should not be viewed as discrete, but rather as interdependent, in that, as Schore (2003a) explains, the attachment environment during critical periods of brain growth directly impacts gene expression, by stimulating gene-regulating hormones, such as opioids, that alter the micro-architecture of the brain (p. 33). Also mentioned were various interventions, with an emphasis on long-term psychotherapy focusing on reparative right-brain communication (Schore, 2003b).

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