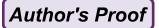
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Freud's prediction that one day neurobiology would be systematically considered as part of psychoanalytic practice is now beginning to come to fruition. We have preliminary data on the neurobiological aspects of borderline personality disorder (BPD) such that it is actually possible to begin to build bridges between psychotherapeutic technique and what we know about brain functioning in this particular disorder [1, 2]. In this chapter, I will point out what I believe are linkages between the therapeutic action of psychotherapy and our knowledge from research on BPD that it is neurobiologically based. In this integrative effort, I will explore both the possible ways in which psychotherapy changes the brain and how we might shape psychotherapeutic efforts with patients who have BPD to incorporate our knowledge of neurobiology.

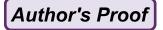
How Psychotherapy Changes the Brain

In our efforts to examine the way that psychotherapy changes the brain, we must navigate the choppy waters of biological reductionism. Mind is the activity of the brain [3], but all aspects of experience cannot be reduced to the causal consequences of brain mechanisms alone. Schwartz et al. [4] clarified that contemporary physics departs from classical physics by supporting the notion that intrinsic mental contents – feeling, knowing, and effort – are primary causal factors. They note that the conscious act of willfully altering the mode by which experience is processed can change the cerebral mechanisms used. Hence, psychological treatment of disorders that have a substantial neurobiological component in their etiology can be a realistic and reasonable goal.

This approach to bridging neurobiology and psychotherapy is best viewed as an example of what Kendler [5] has called explanatory dualism. Psychology and biology represent two useful explanations of similar phenomena but each uses different language to describe those phenomena.

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Kandel [6, 7] was a pioneer in the efforts to identify underlying mechanisms in how psychotherapy might change the brain. Using the marine snail Aplysia, he noted that when learning takes place in this organism, the number of synapses doubled and tripled as a result of the learning. He stressed that psychotherapy is a form of learning about one's self that probably results in similar changes at the synaptic level. Subsequent to Kandel's efforts, functional neuroimaging became sufficiently advanced to begin to differentiate how medication and psychotherapy may influence anatomically different brain areas, at least in some preliminary work by Goldapple et al. [8]. In a comparison of patients who received cognitive-behavioral and SSRIs for depression, psychotherapy appeared to work from the "top down" while medication worked from "the bottom up."

Another study of depressed patients [9] raises intriguing possibilities about the impact of the therapy on the brain. These investigators randomly assigned 23 patients with major depression to either short-term dynamic psychotherapy or to fluoxetine treatment. Both groups received 16 weeks of treatment. 5-HT_{1A} receptor density was estimated both before and after treatment using photoemission tomography (PET). When they examined their results, they noticed that psychotherapy increased the binding to 5-HT_{1A} receptors, but antidepressant medication did not alter the 5-HT_{1A} receptor density in these patients. They concluded that psychotherapy leads to changes in the molecular structure of the synapse in patients with major depression. While this mechanism cannot necessarily be translated directly to BPD, it is nevertheless true that serotonergic problems have been identified as fundamental to the neurobiology of BPD [10].

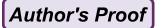
Much literature is devoted to the notion that emotional dysregulation is the fundamental problem in BPD [11]. Hence, there is considerable interest in how one can self-direct the regulation of emotional response. Preliminary work suggests that the prefrontal cortex may be one brain area that is critically important in this attempt to regulate one's emotions [4]. Tourette syndrome is an interesting model to study this phenomenon, since it is predominantly a disorder of self-regulation. It involves chronic motor and facial tics. Most patients with this disorder have premonitory urges, which indicate to the patients when the tics might be coming. These sensory motor impulses are suppressible, although not indefinitely. Peterson et al. [12] studied this phenomenon of tic suppression in children using neuroimaging techniques. They found that some children with Tourette syndrome were better than others at using conscious effort to suppress the tics. Those who were particularly good at it activated the frontal cortex during the effort to suppress the tics and ultimately had larger volumes of the frontal cortex and fewer symptoms. Those who were less adept at suppressing tics did not have the same plastic response. They had smaller volumes of the frontal cortex and more symptoms of the disorder. This elegant study demonstrates that brain volume actually increases in the frontal area as a result of psychological effort to regulate one's impulses.

This introduction to some of the thinking about how psychotherapy changes the brain has primarily been focused on diagnostic entities other than BPD. As we enter a more specific consideration of BPD, it will be useful to first discuss what is known about the neurobiology of BPD.

The Neurobiology of Borderline Personality Disorder

BPD has a multifactorial etiology [13]. Many have experiences of early abuse and neglect. Prospective research [14] has clearly linked borderline symptoms in adults to childhood sexual abuse and neglect. However, significant numbers of borderline patients do not have such histories in the many retrospective studies that have been conducted.

From a neurobiological perspective, transference involves the representation of others distributed in a network of neural units whose simultaneous activation constitutes the representation [15]. However, with BPD, there are other phenomena that are highly relevant in understanding the clinical



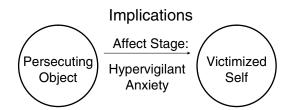


Fig. 13.1 The affect state of anxiety and hypervigilance associated with HPA hyperreactivity is linked to a specific internal object relationship involving a persecuting object and a victimized self

challenges presented by these patients. The BPD patient's hypervigilance may be linked to the heightened arousal of the hypothalamic-pituitary-adrenal axis. Borderline patients also show greater left amygdalar reactivity to standard pictures of faces with various emotional expressions. Using morphing technique with photographs of emotional faces, researchers have found that patients with BPD identify emotional states in others more rapidly than controls. Problems linked to the anterior insula may make it more difficult for patients to maintain a cooperative relationship with others. All these phenomena converge to delineate unique transference problems in the treatment of BPD patients. Each contributing factor will be elaborated in this chapter.

Hyperreactivity of the HPA Axis

One consequence of early interpersonal trauma with parents or caregivers is that borderline patients may have a persistent hypervigilance because they need to scan the environment for the possibility of others who may have malevolent intentions toward them. Neurobiological findings are confirming these sequelae of developmental trauma. Rinne et al. [16] studied 39 female BPD patients who were given combined dexamethasone/corticotropin releasing hormone (CRH) tests using 11 healthy subjects as controls. Twenty-four of these women had histories of sustained childhood abuse. Fifteen of them had no histories of sustained childhood abuse. When they examined the results, the chronically abused BPD patients had significantly enhanced adrenocorticotrophic hormone (ACTH) and cortisol responses to the dexamethasone/CRH challenge compared with non-abused subjects. In addition, there were no significant differences between non-abused BPD subjects and normal controls. They concluded that a history of sustained childhood abuse is associated with hyperresponsiveness of ACTH release. Their findings suggest that this hyperreactive physiological state is relevant to this subgroup of borderline patients but not necessarily to those who lack such histories. Sustained childhood abuse appears to increase the CRH receptors' sensitivity.

Knowledge of the hyperresponsiveness of the HPA axis fits well with our understanding of the pattern of internal object relationships in BPD. Because we understand that internal object relationships are created through building blocks of self-representations, object representations, and affects linking the two, we can infer that an anxious and hypervigilant affect state would be linked to a perception of others as persecuting and the self as victimized [2] (Fig. 13.1).

Hence, there is an expectation of malevolence in the environment, and the borderline patient may misread the intentions of others as persecuting in a way that creates repetitive conflict with others. States of arousal undermine the capacity to accurately mentalize the internal states of others. Hypervigilant misperceptions appear to be related to amygdalar hyperactivity, and a review of recent research in that area is illuminating.



The Role of the Amygdala

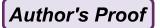
One function of the amygdala is to increase vigilance and to facilitate an individual's evaluation of the potential for novel or ambiguous situations [17]. A functional MRI study [18] comparing six female BPD patients with six female control subjects found that the amygdala on both sides of the borderline patients' brains showed enhanced activation compared to the control group. The investigators concluded that the perceptual cortex in a borderline patient may be modulated through the amygdala in such a way that attention to emotionally relevant environmental stimuli is increased.

Two different studies [11, 17] examined how borderline patients react to standard presentations of faces compared to control subjects. In one study [18], borderline patients showed significantly greater left amygdalar activation to facial expressions of emotion compared with normal control subjects. Of even greater importance, though, was the tendency for borderline subjects, in contrast to controls, to attribute negative attributes to neutral faces. Faces that were without expression were regarded as threatening, untrustworthy, and possibly plotting to do something nefarious. A hyperactive amygdala may be involved in the predisposition to be hypervigilant and overreactive to relatively benign emotional expressions. This misreading of neutral facial expressions is clearly related to the transference misreadings that occur in psychotherapy of borderline patients and in the recreation of "bad object" experiences in the lives of borderline patients. It is also connected to the common observation of therapists that the usual professional boundaries and therapeutic neutrality are experienced by BPD patients as cruel and withholding [19].

Implications for Psychotherapy

These findings have a number of implications for psychotherapists treating someone with BPD. First of all, in keeping with the literature on self-regulation of emotional response, one must recognize that therapeutic change takes effort. Now, this axiom may seem obvious, but in my experience as a consultant and supervisor, many therapists do not sufficiently engage in such conscious efforts. For example, some patients use the entire therapy hour to ventilate about what happened to them since the last session without taking time to think and reflect about the significance of the events they are describing – e.g., the factors that triggered the emotional response and the consequences in terms of interpersonal relationships. The psychotherapist needs to be forthright in interrupting the patient at times and insisting that the patient reflect about the significance of what is being described. In this way, a therapeutic alliance is formed in which the therapist and patient collaborate in pursuit of the commonly held goal of understanding experience and moderating the emotional response. From the standpoint of neurobiology, the therapist is directing mental resources away from lower-level limbic responses and toward higher-level prefrontal functions. The empirically supported psychotherapies for BPD, such as dialectical behavior therapy (DBT), mentalization-based therapy (MBT), and transference-focused psychotherapy (TFP), all feature self-reflective, mindfulness-promoting techniques. Neuroimaging studies support this approach to moderating the hyperreactive amygdalar response. Ochsner et al. [20] have shown that actively rethinking or reappraising feelings causes prefrontal activation that modulates limbic-based negative feelings such as fear. One can readily see a convergence of cognitive therapy and dynamic therapy here as both emphasize working with the patient's cognitions in these situations of strong affect.

A very preliminary pilot study of dynamic psychotherapy shows that frontal activation may be crucial to the effect of MBT [21]. In this pilot study, five patients with BPD and five controls were given brain perfusion single-photon emission tomography (SPET) pre-treatment and post-treatment. All five of the BPD patients showed a lower level of activation in the frontal areas prior to treatment compared to the control group. Each patient then received 16 months of drug-free



mentalization-based psychotherapy following Fonagy and Bateman. Only two of the five BPD patients who completed the treatment underwent the post-treatment repeat SPET.

When the results were examined, the two patients who performed post-treatment SPET showed improvement observable by decreases in impulsivity, self-destructive acts, and unstable affectivity. The post-treatment neural pattern suggested a strong frontal activation in these two subjects, absent in pre-treatment, suggesting more effective cortical modulation of subcortical areas.

Heightened Emotional Sensitivity

The misreading of neutral facial expressions by patients with BPD is only part of the total picture of how these patients read emotional faces. Wagner and Linehan [11] noted in their research that women who were diagnosed as BPD actually were more accurate in the labeling of fearful facial expressions than their non-BPD control subjects. Further research suggests that the situation is more complex.

Blair et al. [22] and Lynch et al. [23] point out that to assess the capacity of BPD patients to respond accurately to emotional expressions, one needs to design a study in which morphing facial expressions shown at varying degrees of intensity are used. They use technology such that faces change gradually and monotonically from neutral expressions to prototypic emotional expressions of maximum intensity. This technology allowed them to evaluate more than accuracy – it can also assess how intense a facial expression had to be before accurate recognition occurs.

Lynch et al. [23] studied 20 individuals with BPD and 20 normal controls using this method. As the facial expressions morphed from neutral to maximum intensity, participants with BPD correctly identified facial affect at an earlier stage than did healthy controls. Participants with BPD were more sensitive than healthy controls in identifying the emotional expressions in general, regardless of their valence. They noted that their results support the contention that heightened emotional sensitivity may be a core feature of BPD. It is possible that the heightened emotional sensitivity is related to the hyperreactive HPA axis and the hyperreactive amygdalar response associated with trauma. However, the results were not stratified in terms of the extent of childhood abuse so such conclusions cannot be drawn clearly. The authors note that their findings are consistent with the notion that emotional dysregulation is central to BPD, and that these individuals overreact to relatively minor emotional expressions and interpersonal cues. Moreover, for those patients who experience early childhood trauma, this hypervigilance to emotional states in others may be adaptive and protective.

Recognizing facial emotions has also been studied by Baron-Cohen et al. [24] through the use of the *Reading the Mind in the Eyes Test* (RMET). This test shows a photograph of a set of eyes and offers four choices that would describe the facial emotional expression reflected by those eyes. Because of the frequent observation that people with BPD distort what they see in others' faces, there has been some inference that BPD patients will not be able to mentalize well when they see these eyes and misunderstand what they reflect. Mentalizing, defined as an imaginative mental activity involved in perceiving and interpreting human behavior in terms of intentional mental states [25], is variable in patients with BPD. It resides on a continuum from being accurate at some moments and wildly inaccurate at others. Bateman and Fonagy [25] stressed that mentalization is intimately linked to the sense of being understood by an attachment figure, and patients with BPD have trouble maintaining mentalization in the context of an intense attachment relationship. The capacity to read faces and link the facial expression to the internal experience of someone is related to both the intensity of the attachment relationship and the presence or absence of strong emotions connected with that person.

Fertuck et al. [26] compared 30 patients with BPD to 25 healthy controls using the test designed for reading eyes. They found that the BPD group performed significantly better than the healthy controls on this test. This enhanced performance is probably related to the greater threat potential



perceived in facial stimuli and the hypervigilance discussed previously. Neutral faces may represent the most ambiguous threat, so there is particular vigilance paid to neutral facial expressions. Indeed, the BPD group did particularly well compared with the controls on faces with neutral emotional valence. This group of investigators stresses that the actual perception of facial expressions is fairly accurate in patients with BPD because of their need to assess moment-to-moment shifts in the emotional states of others for survival purposes. However, the problem area for BPD lies not in the perception of emotional expressions, but in the *interpretation* of emotional expressions. This problem with interpretation is most striking in the neutral faces where there is ambiguity. The difficulty appears to be in assessing whether someone is trustworthy or not. BPD patients appear to have a good deal of difficulty in linking trustworthiness with facial expression and may overreact to minor signs of malevolence.

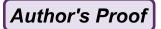
This research helps address a longstanding controversy in the field of BPD: namely, do patients with BPD distort in their perceptions of their therapist? Some clinicians have long noted that these patients seem to have a highly developed sensitivity, sometimes referred to as "radar" for the therapist's countertransference. Other clinicians have noted that distortions of the therapist's intent may border on being delusional. Hence, in light of these research findings on the heightened emotional sensitivity, one could say that both attributes of the BPD patient are accurate. They do have an uncanny way of reading faces, but they may or may not be accurately interpreting what goes on inside the therapist. The accuracy probably varies depending on the state of the attachment relationship, the presence of powerful feelings, and the degree of ambiguity of the facial expression.

Implications for Psychotherapy

Therapists treating patients with BPD need to recognize that mentalizing resides on a continuum from being accurate at some moments to absent at others, based on the affective state of the patient and the intensity of the attachment to the therapist. One of the clinical implications is that therapists must be aware that the patient may be accurately tuning in to a not-yet conscious feeling state in the therapist. This implication is consonant with the time-honored cautionary note that Searles [27] and others have noted that whenever a patient has an apparently paranoid perception of the therapist, a good starting point is for the therapist to assume that there may be a kernel of truth in the perception. Clinicians should also remember that neutral faces represent the most ambiguous threat. Hence, therapists need to be aware of nonverbal communications that they are sending out to patients. The proverbial "blank screen" face is not appropriate for the treatment of BPD, and therapists will do much better to engage in a warm and spontaneous dialog with the patient while respecting the fact that the patient may be somewhat suspicious of their motives.

Therapists can also help the patient with BPD by helping them to elaborate on their perceptions and the interpretations of those perceptions. Therapists may usefully ask what it was in their facial expression or in their manner that made the patient assume malevolence when the therapist intended none. One can also actively elicit alternative perspectives from the patient, a cornerstone of MBT, to help the patient begin to explore in more detail the subjectivity of others. The therapist must also keep in mind that the patient may be misinterpreting and overreacting to small changes in facial expression that really are ambiguous from the patient's perspective.

Research repeatedly demonstrates that patients with BPD have a bias toward the perception of anger, rejection, or social threat [28]. The functional imaging studies have found abnormalities of the prefrontal-amygdalar neurocircuitry aiding affect regulation in BPD subjects, as noted previously. Hence, clinicians must be aware that the capacity for rational thinking is often interfered with because of strong emotion. Some of the emotional arousal seen in borderline patients contributes to the alterations of facial emotion recognition and interpretation of those faces. One implication of this phenomenon is that it may be useful to postpone any exploratory or interpretative work until the intense emotional state of the BPD patient has settled down. Pine [29] has coined the phrase "strike"



while the iron is cold" (p. 153) to indicate this need to allow for the passage for the time before attempting to engage the patient in a useful exploration of his or her perceptions.

Mirror Neurons and Mentalization

Current evidence supports the notion that mentalization relies, in part, upon internal simulations of the perceived emotions and mental states of others [30–33]. This hypothesis is strengthened by studies which demonstrate that imitating facial expressions of others induces the emotional content of those expressions in the imitator [34].

Mirror neurons in the premotor cortex appear to automatically trigger unconscious internal simulations of the observed behaviors of others so that the observer may reconstruct their mental states and emotions [30, 32, 35]. Mirror neurons are activated by *either* performance of goal-directed behaviors, like grasping or frowning, or observation of them in others [32, 35–39]. Gallese [37] hypothesizes that there is a broad array of "mirror matching mechanisms" present in the human brain that enable intersubjective communication and attribution of intentionality.

For example, representations of the frowning facial expression of another person may register in the superior temporal sulcus and fusiform gyrus of the observer [30, 31]. Nonconscious, temporoparietal representations of the frowning facial expression may activate mirror neurons in the premotor cortex [30, 31], which appear to automatically trigger unconscious simulations of frowning in the observer [32, 33, 39]. Simulations of frowning are believed to trigger the associated feeling and mental states (e.g., anger) [30].

Research suggests that conscious discernment of feeling states of self and others relies on the encoding of such *feeling state representations* in two areas of the right somatosensory cortex known as the insula and SSII [35, 40–43]. The SSII and insular regions appear to be important in generating nonconscious neural representations of feeling states associated with different emotions [34, 41]. Investigators propose that the medial prefrontal cortex reads the neural representations of self and other feeling states conveyed by SSII and insular regions [43]. This observation is relevant to the role of the medial prefrontal cortex (e.g., anterior cingulate cortex and paracingulate gyrus) in conscious attention to emotional states of the self and others [44, 45].

The anterior insula may be of particular significance since it mediates communication between the limbic system and mirror neurons, i.e., it helps replay observed actions and determines the emotional reactions to them. While the anterior insula traditionally is associated with sensing physiological states in the body, it strongly reacts to adverse or uncomfortable occurrences and social interactions, such as unfairness, risky choices, or impending loss of social status. The anterior insula also responds to the intentions and emotional states of others and imbues them with feelings. The anterior insula plays a key role in research involving trust in patients with BPD.

Neuroimaging and Trust in BPD

Using neuroimaging techniques involving two simultaneous functional MRIs, King-Casas et al. [46] utilized a trust game to study the differences between patients with BPD and normal controls. In brief, two players are involved in an economic trust scheme. One is designated as the Investor and invests money, while the other is designated as the Trustee and pays money. Brain activity is measured in the anterior insula of the Trustee during the game.

Fifty-five subjects with BPD were recruited for this ten-round, economic exchange game with healthy partners. In essence, the task studied the capacity to maintain cooperation and repair broken cooperation. BPD patients played the Trustee role against a healthy Investor. These dyads were compared to other teams in which the Trustee was a healthy control. In the game, the Investor invests



money, while the Trustee repays money. If both cooperate, both benefit from the exchange, much more so than if the Investor keeps most of the money. This task requires trust between the players, which builds up through repeated fair offers.

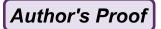
The Investor has \$20 and can choose to give any amount to the Trustee. The amount chosen is automatically multiplied by 3. The Trustee can then give back any amount that he or she chooses, knowing that it is a ten-round game. The healthy controls tend to return about 33% of what they receive from the Investor. The patients with BPD started out the same way, but after round 4, they started giving less. The Investors reacted by investing less. The healthy Trustees reacted strongly to small investments by the Investor. They had large activations in the anterior insula, which suggested that they recognized that they were not being treated fairly. By contrast, the Trustees who had BPD showed no relationship between what was given them and activations in the anterior insula. The researchers inferred that patients with BPD assume that no one is trustworthy, and therefore they expect everyone to be unfair. In essence, the BPD subjects lacked the "gut feeling" that the relationship was in jeopardy – i.e., they failed to mentalize the other player's motivation and intent. It is important to note that the face of the other player was not visible to them, so that they were simply relying on their general assumptions regarding the trustworthiness of others.

The researchers concluded that BPD patients are impaired in their anterior insular activation – i.e., they do not accurately and usefully evaluate a planned action by another person with negative consequences. Hence, they have major problems in their capacities to cooperate in a task. The better outcomes were accomplished through a coaxing strategy, in which wary Investors who transferred small amounts of money are encouraged by generous returns, which signals trustworthiness. However, the healthy players used this strategy twice as often as BPD subjects. A separate study, using a similar game, from a different center [47] also found that BPD patients show less trust during interpersonal interactions.

Implications for Psychotherapy

The problems involving cooperation reflected in this study have significant implications for the notion of the therapeutic alliance in psychotherapy, which research has consistently shown to be a critical ingredient in the outcome of psychotherapy [48]. It is well known that one cannot assume a therapeutic alliance when treating a patient with BPD in the same way one can with patients who are organized at a higher psychological level [49]. The problem, of course, is that the patient cannot assume that the therapist is trustworthy, so it makes it difficult for a borderline patient to cooperate in the formation of a therapeutic alliance involving a collaborative pursuit of common goals. The therapeutic alliance with BPD patients must be regarded as an achievement of the therapy, not an automatic phenomenon. Hence, it is useful as a therapist to validate the patient's difficulty in trusting the therapist with comments such as, "I understand why it would be difficult for you to trust my good intentions in therapy, given what you've experienced with authority figures in the past." One may also say, "I recognize that I will need to earn your trust over time, and I'm prepared to attempt to do that."

The difficulties in trust also have implications for the use of transference interpretation. We know that TFP is one of the empirically validated treatments for BPD and can be highly effective [50]. When the patient is in a position of not trusting the therapist, he or she may experience a transference interpretation in a persecutory manner, a misunderstanding of what is going on inside the patient that reflects the untrustworthiness and malevolence of the therapist. Transference interpretation has to be preceded with a series of interventions of a more supportive nature, including empathic validation, supportive strategies, and efforts to encourage the patient to elaborate on his or her feelings. Transference interpretations tend to be much more effective when attention to building a therapeutic alliance precedes them.



Clinicians must remember that, particularly in those borderline patients who experience significant childhood trauma, there is a prominent object relations paradigm present as depicted in Fig. 13.1 of this chapter. In other words, the paradigm of persecuting object and a victimized self is likely to be either on the surface or just below the surface much of the time. Although idealization may also be present in the transference to the therapist, one must keep in mind the fragile and tenuous state of such idealizations. Split off from the more negative paradigms of persecuting object and victimized self, the idealized units may rapidly disappear if the therapist makes even a small empathic error from the standpoint of the patient.

Timetables for Change and the Neurobiology of Learning

Clinicians have long noted that patients with BPD who have experienced early childhood trauma often are slow to change. Past neuronal associations developed through intense, repeated experiences early in life are likely to remain strong, even when the therapist is providing insight through interpretation. Psychotherapists need to be aware that nonhippocampal learning that is implicit and procedural in nature may be particularly refractory to interpretive strategies. Early trauma may be encoded without going through the declarative hippocampal system.

Insight may be quite useful when hippocampal learning is involved because quick, new ways of looking at new information and adapting to new situations may be possible when the information is stored in a declarative hippocampal mode [51]. However, insight has separate and different effects than repeated experience has on changing what has been learned in the past. Another aspect of understanding therapeutic change in the psychotherapy of patients with BPD is that implicit memories will require multiple exposures over an extended period of time for change to be achieved. In other words, there is a good deal of new experience provided in the therapist–patient relationship, and it will take a good deal of time to gradually modify the neural networks involving self and other that have been ingrained early in childhood [52].

Implications for Psychotherapy

Early trauma is common in BPD patients. In many cases the internal object relationships associated with those childhood experiences of abuse or neglect are encoded in implicit procedural memories. Although the psychotherapist may observe the derivatives of those early experiences in the patient's mode of relatedness, one must have modest expectations for the impact of insight provided through interpretation on these patterns. It may be useful to explain to patients that the timetable for therapeutic change is different for different kinds of problems. Patients may find it helpful if they are told that research suggests that a period of at least 12 months is needed before substantial changes are noted.

Conclusions 366

Neurobiological research on BPD has now advanced to the point where bridges between psychotherapy and brain changes are possible. Indeed, many of the fundamental psychodynamic ideas about BPD are bolstered by the findings of neurobiological research. We are gaining greater insights into how psychotherapy changes the brain. We are also able to capitalize on our knowledge of neurobiology to inform particular psychotherapeutic strategies.



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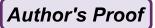
We know that early childhood trauma leaves its mark in a hyperreactive HPA axis and a hyporeactive amygdala that can be linked to a particular pattern of internal object relations involving a persecuting object, a victimized self, and an affective state of hypervigilant anxiety. These brain changes in part contribute to the heightened emotional sensitivity of patients with BPD. We know that their capacity to read faces may be impressively accurate but also subject to misinterpretations of intent in others, particularly under powerful affect states or intense attachment relationships. Transference phenomena involving difficulties in perceiving others as trustworthy can also be connected to faulty activation in the anterior insula. Regulation of the amygdala and other subcortical structures by the frontal cortex is another area of impairment in BPD, and preliminary data suggest that psychotherapy may actually increase frontal activation as a brain correlate of increased reflectiveness. Finally, the impact of interventions must be geared to the type of memory involved. Hippocampal and nonhippocampal memories respond differentially to insight and repeated experience. Over time, a new neural network of self and other is formed that supercedes the old neural network, but the old neural network never disappears entirely. Hence, all the empirically validated therapies for BPD are long term in nature, requiring at least 12 months if not more to make substantial change.

There are many implications for the psychotherapist that can be drawn from these findings. Therapeutic change takes effort. The dynamic therapist must be directive at times to encourage the patient to reflect on affect states rather than simply using the therapy to ventilate. Therapists must also be willing to entertain the possibility that the patient is picking up on early nonverbal signs of the therapist's affect state that are outside of the therapist's awareness. Indeed, therapists must be conscious of what nonverbal signals they are giving out as they listen to the patient. In that regard, and classical "blank screen" visage is contraindicated when treating patients with BPD. Therapists [AU1] who respond naturally and spontaneously to the patient may facilitate the formation of a therapeutic alliance with the patient, which is a therapeutic achievement, rather than a "given," with BPD patients. Transference interpretation must be carefully timed such that it is postponed until the way is paved with empathically validating comments.

Since change in psychotherapy requires this concurrent presence of old maladaptive neural networks and new adaptive networks, it may be useful to help patients understand that many of the features of the disorder will take a good deal of time to change. In educating the patient about these differences, one also helps the patient maintain hope over the course of an extended therapy.

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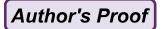
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Author Queries

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Queries	Details Required	Author's Response
AU1	Please check the sentence starting with "In that regard" for completeness.	
AU2	Please update Ref. [9].	

