

An Opioid Deficit in Borderline Personality Disorder: Self-Cutting, Substance Abuse, and Social Dysfunction

Borderline personality disorder is far more common than has been previously recognized, with a prevalence rate as high as 5.9% in the general population (1). The disorder has high morbidity and mortality: these patients have higher rates of suicide and poor functioning and utilize more mental health resources than most patients with axis I diagnoses (2). Psychotherapeutic treatments for borderline personality disorder typically show partial efficacy, and while patients may respond to medications in a circumscribed and often transient manner, there are currently no pharmacologic treatments for borderline personality disorder approved by the Food and Drug Administration. Patients are, therefore, left without the benefit of reliable and effective therapies. Furthermore, pharmacotherapeutic and neurobiological research that might inform treatment in borderline personality disorder has made less progress than one would hope, especially considering the seriousness and pervasiveness of the disorder.

The article in the current issue by Prossin and colleagues (3) holds promise for helping to move the field forward. They present evidence that patients with borderline personality disorder suffer from a definitive abnormality in opioid activity. While there has been a great deal of interest in the opioid system in borderline personality disorder (4), until this study, the role of opioids in borderline personality disorder was largely theoretical with little empirical support. The few pieces of evidence—reviewed by Stanley and Siever (4)—include 1) decreased endogenous opioids, especially beta-endorphins and met-enkephalins, in self-injurers with cluster B personality disorders (predominantly borderline personality disorder) compared to individuals without self-injury (5); and 2) a reported association between a μ -opioid gene polymorphism and borderline personality disorder. Prossin and colleagues, however, are the first to measure μ -opioid receptor binding directly in the brains of living patients with borderline personality disorder.

They used a μ -opioid ligand, [^{11}C]carfentanil, to examine binding in the cerebral cortex of patients with borderline personality disorder during induction of neutral and sad sustained emotional states. The participants were female patients with borderline personality disorder and matched healthy comparison subjects. During the neutral state, the patients showed more μ -opioid binding in regions of the prefrontal cortex, in the reward center (accumbens), and in the amygdala, while the comparison subjects showed more μ -opioid binding in the thalamus. μ -Opioid binding in the prefrontal cortex during the neutral mood correlated negatively with neuroticism in borderline personality disorder. During induced sadness, neurotransmission mediated by μ -opioid receptors was greater in the patients than in the comparison subjects. An important feature of the study is that it experimentally manipulated the subjects' emotional state, since opioid ligand binding is likely to be state dependent. The authors interpreted the greater baseline μ -opioid receptor availability in borderline personality disorder as perhaps reflecting a deficit in endogenous circulating opioids. The results also seem to suggest that enhancement of endogenous opioid availability during sad mood is greater in patients with borderline

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personality disorder than in healthy subjects, which might reflect a compensatory response and is consistent with lower levels of endogenous opioids in self-injurers (5).

Opioid-Deficit Model

How might abnormal opioid activity help to explain the symptoms and etiology of borderline personality disorder? For decades, researchers have theorized that at least one behavior common in borderline personality disorder—self-cutting—relates to abnormalities in opioid activity. It has long been noted that patients with borderline personality disorder report that they engage in self-cutting not as a suicidal act but, rather, as a means to relieve psychic pain. Many patients report that they do not feel physical pain at the moment when they cut themselves; instead, cutting engenders feelings of relief or well-being. One view of cutting in borderline personality disorder is that it represents a method of endogenous opioid generation. In this view, patients learn to cut themselves, thereby releasing opioids, which reward their behavior. This, coupled with evidence that patients with borderline personality disorder who do not cut themselves are less symptomatic than those who do, led to efforts to treat borderline personality disorder with opiate antagonists by eliminating the positive feedback from cutting. While we know of no large-scale randomized, controlled trial, pilot studies on the efficacy of opiate antagonists showed mixed results (reviewed in reference 4) and overall showed that while opiate antagonists may slightly decrease cutting behavior, they do not improve the intrapsychic distress that leads to the cutting (6). This lack of diminished distress is consistent with the model of opioid deficiency.

Thus, a promising way of construing cutting behavior in borderline personality disorder is to consider that these patients may have a preexisting deficit in endogenous opioids. According to this view, patients are self-medicating by cutting themselves, attempting to attenuate severe intrapsychic distress that healthy individuals—without such a deficit—would not be experiencing. This is consistent with the observation that opiate antagonists might decrease cutting behavior by rendering ineffective the patient's attempts to treat his or her pain (thereby decreasing the frequency of cutting) but would not relieve the underlying intrapsychic distress. A deficit in opioids is also consistent with the high rate of opiate abuse in borderline personality disorder, as patients may be compensating for a deficit in endogenous opioids. Not only is there a high rate of opiate abuse in borderline personality disorder, but there is also a high rate of borderline personality disorder among patients seeking substance abuse treatment; for instance, 44.1% of individuals seeking buprenorphine treatment have borderline personality disorder (7). Clinically, it has been noted that individuals with borderline personality disorder who are taking opiates report feeling euthymic rather than euphoric, while withdrawal is associated with sustained dysphoria.

An opioid-deficit theory of borderline personality disorder might explain far more than the self-injurious behavior of these patients. For example, their extraordinary difficulties in social behavior may also be linked to a preexisting deficit in endogenous opioids. The endogenous opioid system not only regulates pain but also has an important role in social behavior. This system, through μ -opioid receptors, has long been implicated in regulation of emotional and stress responses. Reductions in its function have been associated with attachment behavior deficits and anxiety-like responses in animal models. In many species, the soothing and comforting that infants receive from maternal grooming and touching is mediated through the opioid system (8). In human beings, opioids are involved in normal and pathological emotion regulation (9) in addition to their more traditional role in modulating the sensory and affective dimensions of pain (10). In short, there is reason to think that endogenous opioids facilitate normal social function in healthy individuals.

If the proposed model is accurate, then a deficit in endogenous opioids might go some way toward explaining not only cutting behavior and substance abuse in borderline personality disorder but also the almost ubiquitous social dysfunction observed in

this condition. Gunderson has argued for a greater focus on interpersonal dysfunction in understanding borderline personality disorder, stating that the relational style characteristic of the disorder “offers the best discriminators for the diagnosis” of borderline personality disorder (11). Mood shifts and self-destructive behaviors in borderline personality disorder seem to arise specifically in response to interpersonal triggers (12). Furthermore, the domains of intrapsychic pain and interpersonal dysfunction in borderline personality disorder are closely linked.

Clinical Implications

The findings of Prossin and colleagues have both broad and specific clinical implications. Broadly, they lend support to a model of an opioid deficit in borderline personality disorder that may be “hard wired” (consistent with the high heritability of borderline personality disorder). This view could provide a heuristic model to help patients and clinicians understand the social disruption in borderline personality disorder. The satisfaction that normally accompanies closeness to other people both in early attachment and throughout life may elude patients with borderline personality disorder. If these individuals do not have sufficient endogenous opioids, then the continual craving for relationships and heightened reaction to their loss is understandable. Such a model could provide a better understanding and improve management of disappointment in relationships for patients. It might also destigmatize the disorder; the difficulty in forming a therapeutic alliance, for example, could be reconstrued as the result of an opioid deficit. Furthermore, it provides support for targeting the μ -opioid receptor as a novel molecular target for pharmacotherapy in borderline personality disorder.

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