Borderline personality disorder is a heritable brain disease

The prevailing view among many psychiatrists and mental health professionals is that borderline personality disorder (BPD) is a "psychological" condition. BPD often is conceptualized as a behavioral consequence of childhood trauma; treatment approaches have emphasized intensive psychotherapeutic modalities, less so biologic interventions. You might not be aware that a large body of research over the past decade provides strong evidence that BPD is a neurobiological illness—a finding that would drastically alter how the disorder should be conceptualized and managed.

Neuropathology underpins the personality disorder

Foremost, BPD must be regarded as a serious, disabling brain disorder, not simply an aberration of personality. In DSM-5, symptoms of BPD are listed as: feelings of abandonment; unstable and intense interpersonal relationships; unstable sense of self; impulsivity; suicidal or self-mutilating behavior; affective instability (dysphoria, irritability, anxiety); chronic feelings of emptiness; intense anger episodes; and transient paranoid or dissociative symptoms. Clearly, these clusters of psychopathological and behavioral symptoms reflect a pervasive brain disorder associated with abnormal neurobiology and neural circuitry that might, at times, stubbornly defy therapeutic intervention.

No wonder that 42 published studies report that, compared with healthy controls, people who have BPD display extensive cortical and subcortical abnormalities in brain *structure* and *function*.[1] These anomalous patterns have been detected across all 4 available neuroimaging techniques.

Magnetic resonance imaging. MRI studies have revealed the following abnormalities in BPD:

- hypoplasia of the hippocampus, caudate, and dorsolateral prefrontal cortex
- variations in the CA1 region of the hippocampus and subiculum
- smaller-than-normal orbitofrontal cortex (by 24%, compared with healthy controls) and the mid-temporal and left cingulate gyrii (by 26%)
- larger-than-normal volume of the right inferior parietal cortex and the right parahippocampal gyrus
- loss of gray matter in the frontal, temporal, and parietal cortices
- an enlarged third cerebral ventricle
- in women, reduced size of the medial temporal lobe and amygdala
- in men, a decreased concentration of gray matter in the anterior cingulate
- reversal of normal right-greater-than-left asymmetry of the orbitofrontal cortex gray matter, reflecting loss of gray matter on the right side
- a lower concentration of gray matter in the rostral/subgenual anterior cingulate cortex
- a smaller frontal lobe.

continued

Henry A. Nasrallah, MD
Editor-in-Chief

BPD must be regarded as a serious, disabling brain disorder, not simply an aberration of personality and behavior

To comment on this editorial or other topics of interest, visit www.facebook.com/CurrentPsychiatry, or go to CurrentPsychiatry.com and click on the "Contact Us" link.

Current PSYCHIATRY

Editorial Staff
EDITOR John Baranowski
MANAGING EDITOR Erica Vonderheid
ASSOCIATE EDITOR Patrice Kubik

Art & Production Staff
CREATIVE DIRECTOR Mary Ellen Niatas
ART DIRECTOR Pat Fopma
DIRECTOR, JOURNAL MANUFACTURING Michael Wendt
PRODUCTION MANAGER Donna Pituras

Publishing Staff
PUBLISHER Sharon J. Spector
MARKETPLACE ACCOUNT MANAGER Linda Wilson
DIRECTOR OF NEW MEDIA Amy Park
CONFERENCE MARKETING MANAGER Kathy Wenzler
Subscription Services: (800) 480-4851

Editor-in-Chief Emeritus
James Randolph Hillard, MD

Frontline Medical Communications
CHAIRMAN Stephen Stoneburn
EVP DIGITAL BUSINESS DEVELOPMENT/CFO Douglas E. Grose
PRESIDENT/CEO, CLINICAL CONTENT DIVISION Marcy Holeton
PRESIDENT/CEO, MEDICAL NEWS DIVISION Alan J. Imhoff
PRESIDENT, CUSTOM SOLUTIONS JoAnn Wahl
EXECUTIVE DIRECTOR, OPERATIONS Jim Chicca
VP, MARKETING & CUSTOMER ADVOCACY Jim McDonough
VICE PRESIDENT, CUSTOM PROGRAMS Carol J. Nathan
VICE PRESIDENT, MULTICHANNEL CUSTOM SOLUTIONS Margo Ullmann
CORPORATE DIRECTOR, RESEARCH & COMMUNICATIONS Lori Raskin
CORPORATE CIRCULATION DIRECTOR Donna Sickles

In affiliation with Global Academy for Medical Education, LLC.
VICE PRESIDENT, MEDICAL EDUCATION & CONFERENCES Sylvia H. Reitman, MBA
VICE PRESIDENT, EVENTS David J. Small, MBA

FRONTLINE MEDICAL COMMUNICATIONS
7 Century Drive, Suite 302
Parsippany, NJ 07054
Tel: (973) 206-3434
Fax: (973) 206-9378
www.qhc.com

Published through an educational partnership with Saint Louis University
SAINT LOUIS UNIVERSITY

In an analysis of MRI studies,[2] correlation was found between structural brain abnormalities and specific symptoms of BPD, such as impulsivity, suicidality, and aggression. These findings might someday guide personalized interventions—for example, using neurostimulation techniques such as repetitive transcranial magnetic stimulation and deep brain stimulation—to modulate the activity of a given region of the brain (depending on which symptom is most prominent or disabling).

Magnetic resonance spectroscopy. In BPD, MRS studies reveal:

- compared with controls, a higher glutamate level in the anterior cingulate cortex
- reduced levels of N-acetyl aspartate (NAA; found in neurons) and creatinine in the left amygdala
- a reduction (on average, 19%) in the NAA concentration in the dorsolateral prefrontal cortex.

Functional magnetic resonance imaging. From fMRI studies, there is evidence in BPD of:

- greater activation of the amygdala and prolonged return to baseline
- increased functional connectivity in the left frontopolar cortex and left insula
- decreased connectivity in the left cuneus and left inferior parietal and the right middle temporal lobes
- marked frontal hypometabolism
- hypermetabolism in the motor cortex, medial and anterior cingulate, and occipital and temporal poles
- lower connectivity between the amygdala during a neutral stimulus
- higher connectivity between the amygdala during fear stimulus
- deactivation of the opioid system in the left nucleus accumbens, hypothalamus, and hippocampus
- hyperactivation of the left medial prefrontal cortex during social exclusion
- more mistakes made in differentiating an emotional and a neutral facial expression.

Diffusion tensor imaging. DTI white-matter integrity studies of BPD show:

- a bilateral decrease in fractional anisotropy (FA) in frontal, uncinated, and occipitofrontal fasciculi
- a decrease in FA in the genu and rostrum of the corpus callosum
- a decrease in inter-hemispheric connectivity between right and left anterior cingulate cortices.

Genetic studies

There is substantial scientific evidence that BPD is highly heritable—a finding that suggests that brain abnormalities of this disorder are a consequence of genes involved in brain development (similar to what is known about schizophrenia, bipolar disorder, and autism).

A systematic review of the heritability of BPD examined 59 published studies that were categorized into 12 family studies, 18 twin studies, 24 association studies, and 5 gene-environment interaction studies.[3] The authors concluded that BPD has a strong genetic component, although there also is evidence of gene-environment (G×E) interactions (ie, how nature and nurture influence each other).

The G×E interaction model appears to be consistent with the theory that expression of plasticity genes is modified by childhood experiences and environment, such as physical or sexual abuse. Some studies have found evidence of hypermethylation in BPD, which can exert epigenetic effects. Childhood abuse might, therefore, disrupt certain neuroplasticity genes, culminating in morphological, neurochemical, metabolic, and white-matter aberrations—leading to pathological behavioral patterns identified as BPD.

continued on page 32

continued from page 20

The neuropsychiatric basis of BPD must guide treatment

There is no such thing as a purely psychological disorder: Invariably, it is an abnormality of brain circuits that disrupts normal development of emotions, thought, behavior, and social cognition. BPD is an exemplar of such neuropsychiatric illness, and treatment should support psychotherapeutic approaches to mend the mind at the same time it moves aggressively to repair the brain.

Henry A. Nasrallah, MD
Editor-in-Chief

References

1. McKenzie CE, Nasrallah HA. Neuroimaging abnormalities in borderline personality disorder: MRI, MRS, fMRI and DTI findings. Poster presented at: 52nd Annual Meeting of the American College of Neuropsychopharmacology; December 8-12, 2013; Hollywood, FL.
2. McKenzie CE, Nasrallah HA. Clinical symptoms of borderline personality disorder are associated with cortical and subcortical abnormalities on brain magnetic resonance imaging (MRI). Poster presented at: 26th Annual Meeting of the U.S. Psychiatric and Mental Health Congress; September 31-October 3, 2013; Las Vegas, NV.
3. Amad A, Ramoz N, Thomas P, et al. Genetics of borderline personality disorder: systematic review and proposal of an integrative model. Neurosci Biobehav Rev. 2014;40C:6-19.