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Trauma: The Mind/Body Connection

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My favorite introduction to this topic is a cartoon – it's the one of the zebra saying "I'm stressed," whose stripes are unwinding on the ground. We all know from both intuition and experience that there is an obvious mind/body connection in traumatic stress. Who has not felt the adrenaline rush with pounding heart and shaking hands from a near-miss in the car? The response happens within seconds and lasts for minutes. The physiological "fight or flight" reaction to stress is hard-wired in us. It is a protective reaction to danger that helps us cope with a saber-toothed tiger or a potential mugger.

Can we extrapolate from this acute reaction to the negative long-term consequences of chronic stress and posttraumatic stress disorder (PTSD)? Recent research points to biological differences among acute stress reaction, chronic stress, and posttraumatic stress disorder. Delineating these differences and the implications for treatment of these stress states is the current struggle. We are growing in our understanding of the biological impact of trauma on symptomatology, memory, and vulnerability. There is probably no better example in mental health of the "whole person" biopsychosocial model than PTSD. This article highlights some of the more salient psychobiological changes in persons diagnosed with PTSD. First, however, I would like to say a few words about the overall physiology of the human mind/body.

Human Physiology

The body is an exquisitely complex system of pathways with many cellular interactions and activating/feedback loops. For example, there are 100 billion

nerve cells, each having 200,000 synapses. There are now over 100 identified neurotransmitters. The brain interacts with the endocrine glands (e.g. pituitary, thyroid, adrenal), activating them to secrete hormones which are carried by the blood stream throughout the body to take part in intracellular metabolism. Each cell in the body has 100,000 genes. We now know that gene expression turns on and off in response to internal signaling substances. When hormones reach a high enough level, they turn off the activating brain cells (a negative feedback loop). This glimpse of the body's metabolism (even if you do not have a medical background) is important in understanding the psychobiology of PTSD.

Psychobiology is the study of molecular/structural changes in the brain that relate to psychiatric syndromes. These changes create a cascade of complex actions within the brain and throughout the entire body. Against the backdrop of human physiology, it is not surprising that the psychobiology of PTSD is complex and involves many systems. Further, when early childhood abuse and neglect are contributing factors, there is the added element of the developing brain's response to abnormal attachments to caretakers and the shaping of faulty circuitry and emotional dysregulation. (A recent study of adolescents with a history of physical/sexual abuse showed abnormal electroencephalogram readings in 54% as compared with 27% of controls with no abuse.) There is now an early literature on the "psychobiology of attachment."

Bessel van der Kolk, a leading theorist, researcher, and clinician in the field of traumatology, cleverly captures the impact of trauma on the mind/body with the phrase "the body keeps the score"

(1996). A number of psychobiological abnormalities in PTSD are currently being explored. There is not yet a cohesive picture (that may take another decade of research), but there are some important findings with which clinicians should be familiar. I will begin by describing the major neurohormonal imbalances linked to traumatic experience and will then move into some of the physiological manifestations of PTSD. Finally, I will conclude with general treatment implications for working with this population.

Neurohormonal Dysregulation - The HPA Axis

The **hypothalamic-pituitary-adrenal (HPA)** axis plays a major role in the stress reaction. The hypothalamus (a structure in the middle part of the brain) releases corticotropin-releasing factor (CRF), which stimulates the release of adrenocorticotrophic hormone (ACTH) from the pituitary. The pituitary, a small gland at the base of the brain, is the "master endocrine gland"; it has feedback loops with endocrine glands throughout the body. The hormone ACTH, in turn, stimulates the release of cortisol from the adrenal cortex (the outer layer of the adrenal gland). Cortisol is a steroid hormone which affects all cells and maintains physiologic integrity within the body. As cortisol levels increase, the release of CRF by the hypothalamus is, in turn, suppressed, as are the corresponding production of ACTH by the pituitary gland and cortisol by the adrenal cortex. Thus, the negative feedback of the HPA loop (see diagram) regulates the level of cortisol in the bloodstream.

Studies over decades have consistently shown a positive correlation between the severity of a stressor and the level of cortisol in the bloodstream. A severe

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stressor increases cortisol levels. In PTSD, however, recent studies have shown unexpectedly low cortisol levels (although there may be cortisol surges at times) and a greater number of cellular cortisol receptors. Because the blood cortisol level is low, the normal negative feedback of the HPA loop is not activated; the hypothalamus continues to secrete CRF. The corresponding pituitary response, however, is blunted (by a mechanism that is unclear) and the levels of ACTH in the bloodstream are lower than would be expected. Elevated CRF is a significant finding in PTSD, since CRF affects not only the pituitary but also other brain structures (such as the amygdala, which is intricately involved in threat perceptions).

The dexamethasone (an oral form of an adrenal steroid) suppression test in PTSD yields unusual results. In normal subjects, dexamethasone will suppress the adrenal release of cortisol. The brain reacts to a high adrenal steroid level (from a pill) and turns off the hypothalamic-pituitary stimulation of the adrenal cortex. This test has been used in the study of depression, in which there is a subtype of nonsuppression. In PTSD, there is supersuppression of cortisol release in victims of child abuse, combat veterans, and earthquake survivors. A dose of dexamethasone smaller than that used in the standard depression test suppresses cortisol levels in these cases.

There is significant dysregulation of the HPA axis in PTSD. We do not yet know all the implications, but what is clear is that a major mind/body pathway for reaction to stress has gone awry. PTSD patients have a low tolerance to stress. The increased CRF level may be related to anxiety and the re-experiencing of traumatic events. We are beginning to postulate the relationship between specific psychobiological abnormalities and possible clinical manifestations.

Other Influences

Adrenergic (related to adrenaline or norepinephrine) **hyper-reactivity** is a well established abnormality in PTSD. Norepinephrine is secreted by the adrenal medulla (the central part of the adrenal gland, which is located just above the kidney) and in the brain. Norepinephrine is the major neurotransmitter for the sympathetic nervous system. The sympathetic nervous system is mobilized in the fight-or-flight

response, causing increased blood flow to the major muscles (including the heart) and induction of a hyperalert state of readiness. In PTSD, adrenergic hyper-reactivity appears to be associated with hyperarousal, hypervigilance, anxiety/panic and irritability/rage. Adrenergic activity in the brain may also be related to flashbacks and spontaneous abreactions, the re-experiencing of the traumatic material. A number of studies have shown increased levels of 24-hour urine epinephrine and norepinephrine excretion in combat veterans compared with patients with other psychiatric diagnoses. Elevated levels of these hormones in the bloodstream may be experienced by the post-trauma patient as anxiety, panic, and agitation.

Serotonergic dysfunction is probable in persons diagnosed with PTSD, as evidenced primarily by drug studies. Serotonin, a major neurotransmitter in the brain, appears to mediate a number of core symptoms of PTSD. The selective serotonin reuptake inhibitors (SSRI's) increase serotonin levels and appear to be first-line medications for the treatment of PTSD.

Opioid dysregulation is another interesting feature of PTSD. There is an increased release of endorphins, in response to stimuli reminiscent of the trauma, that results in stress-induced analgesia (numbness, lack of pain). This endogenous opioid secretion is probably related to the "addiction to trauma" syndrome, both the re-enactment and self-mutilation. Patients often report a "high" after cutting or burning themselves. It has also been postulated that opioid dysregulation is connected to the high rate of chemical dependency in the survivor population.

Recent studies have focused on the hypothalamic-pituitary-thyroid axis. In PTSD, there is increased thyroid activity, with T3 elevation (T4, the hormone secreted by the thyroid gland, is converted to T3 by cells throughout the body). As early as 1927, there was report of a clear history of traumatic stress in 85% of more than 3000 cases of hyperthyroidism. Many of the agitation symptoms of hyperthyroidism are similar to the hyperarousal symptoms in PTSD.

Physiological Manifestations
Sensitization and kindling phenomena have been proposed as a model for PTSD. This model implies that sensitization of areas of the brain by traumatic stress can

eventually lead to kindling, or autonomous electrical activity in these areas. Kindling is thought to be a mechanism involved in seizure activity. By analogy, it may be that kindling plays a part in the intrusive symptomatology in PTSD. The anticonvulsants serve as both antikingling and mood-stabilizing agents and are often useful in the treatment of PTSD.

Neuroimaging studies have revealed some interesting findings. Magnetic resonance imaging (MRI) brain studies indicate significantly smaller **hippocampal volumes** (indicative of permanent structural change) in both combat veterans and child abuse victims with PTSD. The hippocampus is located within the medial temporal lobe, just posterior to the amygdala. The MRI data collected so far suggest that the severity of traumatic exposure, the severity of PTSD symptoms, and the severity of cognitive deficits are all related to hippocampal volume.

Magnetic resonance spectroscopy (MRS) shows that there is actual alteration of the **hippocampal neurons**. The hippocampus is implicated in learning and memory, particularly explicit memory for events. There are neurological case reports in the literature of patients with hippocampal damage who develop amnesia for explicit cognitive information, but can still learn implicitly. The hippocampus can be conceptualized as the cognitive map for the amygdala, which assigns emotional significance to sensory input. It is not yet known whether the hippocampal damage predisposes one to the development of PTSD or is a direct effect of the psychobiology of the disorder. However, difficulties in learning and memory (e.g., traumatic amnesia) are prominent clinical findings in PTSD and are often treatment challenges.

Functional neuroimaging techniques, such as positron emission tomography (PET), create maps of cerebral blood flow/brain activity. Preliminary studies suggest that provocation of symptoms of PTSD (e.g., by telling the story) results in increased activity within paralimbic structures, as well as perhaps the amygdala and visual cortex. Broca's area, which is involved in speech, is deactivated. This may explain the difficulty trauma survivors have in verbal expression of the trauma, in addition to fragmentation of memory. Traumatic memory may be primarily emotional;

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indeed, the popular literature is now referring to "emotional memory". This functional neuro imaging research is limited by the small number of subjects studied, yet the findings in five studies are convergent and open the door to future models.

Finally, I would like to call attention to the **medical concerns** of patients with PTSD. In our clinical experience at The Center, more than 60% of our patients have significant medical illnesses. Common problems include migraine headaches, irritable bowel syndrome, chronic pelvic pain, adult-onset diabetes, and fibromyalgia. Clearly, there is an impact of chronic stress on multiple systems. A number of immune disorders (e.g., rheumatoid arthritis and mixed collagen vascular disorder) are evident in PTSD patients as well. It is not surprising that severe trauma may have an impact on the body's immune system. Medical illness is often compounded by the trauma survivor's difficulty with trusting caregivers (who may or may not be educated and sensitive to trauma

issues), tolerating invasive procedures, and feeling deserving of self-care. These clinical observations of medical comorbidity point the way to future research.

Treatment Implications

As knowledge of the psychobiology of PTSD grows, so do relevant treatment implications, particularly with regard to medication management. The treatment of PTSD should be integrative and stage-oriented. Wise psychopharmacologic choices should be based on a comprehensive understanding of the patient; consideration must be given to movement in psychotherapy, significant psychosocial stressors (particularly revictimization), as well as any comorbid medical conditions. PTSD is a complex human response to overwhelming trauma that involves long-term symptoms and maladaptive patterns. The survivor's life experience is an interplay of biological, psychological, and social aspects; effective treatment must address the whole experience. This has been a survey of the current thinking and research in the

psychobiology of trauma. We are on the edge of discovery; the next decade should be exciting!

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