

Robinson's *Gilead*, Khaled Hosseini's *The Kite Runner* and *A Thousand Splendid Sons*, Cormac McCarthy's *All the Pretty Horses* and *The Road*, Richard Powers's *The Echo Maker*, Kate Grenville's *The Secret River*, and Azar Nafisi's *Reading Lolita in Tehran*.

Extensive commentaries and new writings on topics related to psychological trauma are available contemporaneously in texts such as Tal (1995), the Air Force Academy's literary journal *War, Literature, and Art*, and periodic special articles and issues of journals in the traumatic stress field such as the *Journal of Trauma and Dissociation* (e.g., Gold, 2004; Goldsmith & Satterlee, 2004), *Journal of Psychological Trauma, Trauma, Violence and Abuse*, and *Journal of Aggression, Maltreatment, and Trauma*.

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See also: Movie Depictions of Psychological Trauma

LOCUS CERULEUS

The locus ceruleus (LC) is a small (needle-sized) bluish nucleus of 25,000 neurons on each side of the dorsorostral pons, an area within the brainstem. These 50,000 neurons

are highly elaborated (“arborized”) and provide 70% to 90% of the nervous system’s norepinephrine (NE). The LC is the noradrenergic component of the fear-response circuitry, and plays a central role, especially in acute and posttraumatic stress. Psychotropic medications that are specifically useful for the treatment and secondary prevention of acute PTSD symptoms, act by blocking activation of neurons in the LC postsynaptically. For example, propranolol, a postsynaptic NE beta receptor antagonist (Beta blocker), administered in the immediate aftermath of motor vehicle accidents has been found to be efficacious for the secondary prevention of PTSD (Pitman et al., 2002; Vaiva et al., 2003).

The LC is the primary location of the neurotransmitter norepinephrine in the brain. The LC transmits neural signals throughout the brain: “this small nucleus innervates a greater variety of brain areas than does any other single nucleus yet described” (Aston-Jones, Valentino, Van Bockstaele, & Meyerson, 1994). The neural pathways from the LC to other brain areas (*Ascending efferents*) can be conceptualized as the main ‘alarm siren’ of the brain. The most extreme activation of LC efferents occurs during (and in the immediate aftermath of) acute traumatic events in which there is an actual threat to personal survival or to physical integrity. In military veterans with PTSD, LC activity also abruptly increases during the startle response (such as in response to sudden noise and abrupt awakening). Sudden decrease in LC activity has been implicated in the pathophysiology of psychogenic fainting and in a range of other conversion and dissociative symptoms including *La Belle Indifference*. However, LC plays only a minimal role in mood disorders and is unaffected in psychotic disorders.

The LC also is linked to the rest of the body via “*descending efferents*,” which activate the sympathetic arm of the autonomic nervous system (ANS) via projections to preganglionic sympathetic neurons in the spinal cord. Furthermore, the LC simultaneously inhibits the parasympathetic arm of the ANS via projections to the vagus nerve (via the nucleus ambiguus). The resulting abrupt change in

sympatho-vagal ratio results in physical symptoms of fear: palpitations, sweaty palms, cold sweat, hyperventilation, dilated pupils, upper abdominal discomfort (gastric vasoconstriction), dry mouth, jaw clenching, decreased vocalization, muscle tensing, tonic immobility, and increased pain threshold.

Neural projections into the LC (*afferents*) emanate primarily from other parts of the brain's fear circuits, and provide highly processed information concerning external survival-relevant stimuli. *Inhibitory afferents* from the anterior cingulate cortex and GABA-ergic afferents from the rostral medulla inhibit LC activity. The LC receives extensive serotonergic projections from the Raphe nuclei. The therapeutic effects of the antidepressant selective serotonin reuptake inhibitors (SSRIs) in PTSD are due partly to this serotonergic pathway.

Excitatory afferents into the LC originate in the amygdala and a midbrain area involved in pain and defensive behaviors (the periaqueductal gray). Excitatory (and possibly excitotoxic—causing damage to brain cells) non-NMDA glutamatergic activation of the LC (originating in the ventrolateral-rostral medulla) occurs during extreme stress (Aston-Jones et al., 1994). During more chronic stress, NE synthesis in the LC is increased by corticotropin releasing hormone (CRH).

The LC is the only brain nucleus in which neuron loss has been observed in PTSD. In a postmortem study of the right hemisphere's LC, three WWII veterans with war-related PTSD were found to have about 30% fewer neurons in comparison to four healthy veterans (Bracha, Garcia-Rill, Mrak, & Skinner, 2005). Most of the psychophysiological research in PTSD is consistent with a hyperresponsiveness of the LC target neurons to NE, possibly a compensatory upregulation of LC postsynaptic receptors after trauma-induced loss of LC neurons. This pathophysiological mechanism may be clinically conceptualized as “burning out” or “overuse injury” to the LC in PTSD—similar to the nonpsychiatric example of cartilage loss in the knees of aging professional athletes. Acute and/or subacute tachycardia in an otherwise healthy young individual is a useful clinical marker of LC overactivity. Drugs of abuse that

increase the activity (firing) of the LC neurons (e.g., Yohimbe and Cocaine) aggravate PTSD symptoms.

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See also: *Biology, Brain Structure, and Function, Adult; Biology, Brain Structure, and Function, Child; Biology, Neurochemistry; Conditioned Fear*

LONGITUDINAL STUDIES

See: *Research Methodology*