Neural reflex regulation of systemic inflammation: Potential new targets for sepsis therapy

Fernandez R.

Nardocci G.

Navarro C.

Reyes E.P.

Acuña-Castillo C.

Cortes P.P.

Sepsis progresses to multiple organ dysfunction due to the uncontrolled release of inflammatory mediators, and a growing body of evidence shows that neural signals play a significant role in modulating the immune response. Thus, similar toall other physiological systems, the immune system is both connected to and regulated by the central nervous system. The efferent arc consists of the activation of the hypothalamic-pituitary-adrenal axis, sympathetic activation, the cholinergic anti-inflammatory reflex, and the local release of physiological neuromodulators. Immunosensory activity is centered on the production of pro-inflammatory cytokines, signals that are conveyed to the brain through different pathways. The activation of peripheral sensory nerves, i.e., vagal paraganglia by the vagus nerve, and carotid body (CB) chemoreceptors by the carotid/sinus nerve are broadly discussed here. Despite cytokine receptor expression in vagal afferent fibers, pro-inflammatory cytokines have no significant effect on vagus nerve activity. Thus, the CB may be the source of immunosensory inputs and incoming neural signals and, in fact, sense inflammatory mediators, playing a protective role during sepsis. Considering that CB stimulation increases sympathetic activity and adrenal glucocorticoids release, the electrical stimulation of arterial chemoreceptors may be suitable therapeutic approach for regulating systemic inflammation.

Carotid body

Reflex control of inflammation

Sepsis

Systemic inflammation

Vagus nerve

glucocorticoid

hypoxia inducible factor

tumor necrosis factor alpha

adrenergic system

carotid body

carotid sinus

corticosteroid release

cytokine production

human

hypothalamus hypophysis adrenal system

immune response

immune system

immunomodulation

immunoreactivity

immunoregulation

inflammation

nonhuman

paraganglion

protein expression

reflex

regulatory T lymphocyte

Review

sepsis

signal transduction

vagus nerve