

Inflammation and Brain: Regulation of Systemic Inflammation in Sepsis

Yukio Imamura*, Nao Yoshikawa, Yuki Murakami, Satoko Mitani and Akitoshi Seiyama

Human Health Science, Kyoto University Graduate School of Medicine, Japan

Inflammation is a biological response to harmful stimuli with pathogens or chemical irritants, etc. The inflammation serves as a chemical sign of the wound healing. Various biochemical substances enroll the processes. For example, cytokines (e.g. interleukins) secreted from immune cells such as macrophage, T cell or B cell induces an acute inflammation, trigger the proliferation and/or differentiation of other immune cells and regulate the chemo-attractant migration of immune cells. These acute inflammatory responses are usually ceased when the stimulant is removed and the biochemical reactions are useful to maintain the living organisms.

On the other hand, when the pathogens overwhelm the host organism and the inflammatory response is affecting the whole body, the infected organisms are diagnosed as systemic inflammatory response syndromes (SIRS). The SIRS is closely related to sepsis, which is often confronted with patients in the intensive care unit [1].

Sepsis is accompanied by a remarkably altered and imbalanced cytokine response (known as a cytokine storm). Cytokine storms are fatal immune reactions, which lead to be multiple-organ dysfunctions. The processes finally results in septic encephalopathy. In the septic encephalopathy, blood brain barrier (i.e. a guardian for the brain) is impaired and this would cause the brain to be more affected by the inflammatory mediators [2].

Survivors of severe septic conditions show symptoms with brain dysfunctions including coma, delirium and cognitive memory impairment [3]. It is required to develop the therapeutic strategies for the better outcome of septic encephalopathy. To date, it is reported that a lot of inflammatory mediators such as interleukins, tumor necrosis factor- α , high mobility group box-1, chemokines etc., are involved in the pathogenesis of septic encephalopathy. Thereby, preclinical trials targeting anti-inflammatory mediators have been performed using animal models of septic encephalopathy. However, it is not so well accomplish the better outcome of septic encephalopathy, why?.

Brain employs a unique property for the plastic change, 'plasticity'.

For example, neurotransmitter glutamate and its receptor are critical for the induction of the synaptic plasticity (i.e. plastic changes of neuronal network) of neurons [4]. Since the neurotransmission is spatially and temporally regulated, the aberrant distribution and/or expression of neurotransmitter receptor on neurons after encephalopathy abolished the neuronal plasticity. Probably, it might be difficult to totally recover the synaptic functions in septic encephalopathy.

Recently, it was reported that electrical pulse stimulation of vagus nerve regulated the systemic inflammation. In pre-clinical studies using rodent model of sepsis, vagus nerve stimulation improves the mortality rate of sepsis [5]. This electrical pulse stimulation of neurons effectively reduces the cytokine levels and ameliorates the physiological parameters for the lung injury [6]. Hence, the cranial nerve is important for the regulation of inflammation.

In conclusion, the control of inflammatory mediators and neuronal activity will be a better prognosis of the septic encephalopathy.

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*Corresponding author: Yukio Imamura, Unit for liveable cities, Human Health Science, Kyoto University Graduate School of Engineering and Medicine, Japan, Tel: +81-75-751-3970; Fax: +81-75-751-3970; E-mail: yimamura-ns@umin.net

Received July 24, 2012; Accepted July 24, 2012; Published July 28, 2012

Citation: Imamura Y, Yoshikawa N, Murakami Y, Mitani S, Seiyama A (2012) Inflammation and Brain: Regulation of Systemic Inflammation in Sepsis. *Biochem Pharmacol* 1:e127. doi:[10.4172/2167-0501.1000e127](https://doi.org/10.4172/2167-0501.1000e127)

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