Key Function of Complement System in Interactions between Pain and Nociceptors, $C_5a$, and $C_3a$

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Abstract
A part of the immune system that improves (complements) the ability of antibodies and phagocytic cells to clear microorganisms and injured cells from an organism, attacks the pathogen’s cell membrane, and encourages inflammation called complement system. It is main part of immune system. Over thirty proteins and protein pieces compose the complement system, including cell membrane receptors, and serum proteins. The complement system activates by 3 biochemical pathways: the alternative complement pathway, the classical complement pathway, and the lectin pathway. The complement system is a main portion of the innate protection. Effectors of the complement cascade attack microorganisms, activate basophils and mast cells, and promote chemotaxis of white blood cells (WBC). The complement system also has a function in inflammatory hyperalgesia and neuropathic pain. $C_5a$, an anaphylatoxin, is a main effector of the complement cataract and upon banding to $C_5aR1$ receptors on neutrophils it develops a potent neutrophil absorbent. Complement segments also have a direct effect on nociceptors. Injection of $C_3a$ and $C_5a$ into the hind-paw of mice or rats influences behavioral hyperalgesia. Using of $C_3a$ or $C_5a$ to peripheral nerves ex vivo sensitizes C fiber nociceptors. This effect might be mediated by a direct effect of banding $C_5a$ receptors. $C_5a$ activates spinal microglia in neuropathic pain and $C_5a$ block of the complement cascade in the spinal cord reverses neuropathic pain behavior and is also participated in neuropathic pain.

Keywords: Complement System, Pain, Nociceptors, $C_5a$, $C_3a$

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