【Grant-in-Aid for Scientific Research(S)】
Biological Sciences (Medicine, dentistry, and pharmacy Ⅱ)

Title of Project : The role of glial cells in neuropathic pain

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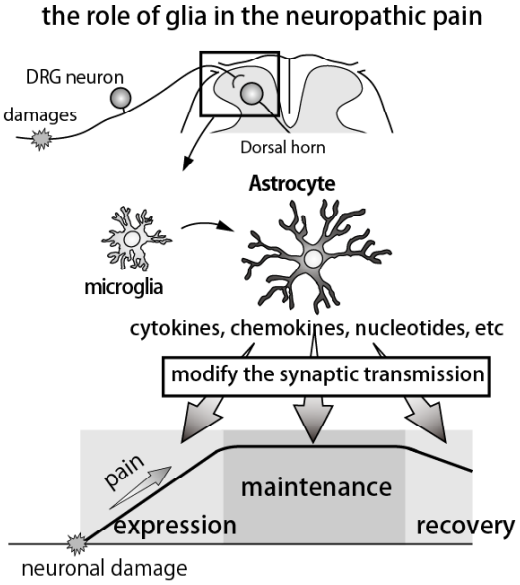
Research Area : Neurochemistry/Neuropahrmacology
Keyword : Neurotransmitter/receptor, Glia, Neuropharmacology, Neuropathic Pain

【Purpose and Background of the Research】

There are over 22 million patients suffering from neuropathic pain without effective medicines in the world. To create new drugs against the pain is now the important issue. For this purpose, we have to clarify the mechanism responsible for the expression of neuropathic pain as soon as possible. We have established the important role of microglia in the mechanism and identified many molecules that drive microglia to initiate the pain (Nature 2003, 2005). However, it is unknown how and when these molecules interact each other and what kind of the relationship between microglia and astrocytes which are also activated after nerve damages. The aim of this project is to clarify the role of glia in neuropathic pain signaling.



【Research Methods】

For the aim, we examine the mechanism of the activation and function of astrocytes after the nerve damages related to the function of microglia as mentioned below.

1. Astrocytic molecules (cytokines, chemokines, receptors and/or transcriptional factors) whose expression are increased in the spinal dorsal horn after nerve damages will be identified by transcription analysis in the long range time-course (development, maintenance and recovery phases of the pain).
2. Among the molecules identified in the experiment 1, the important molecules closely related to the neuropathic pain will be selected and the function of the molecules in the pain will be clarified by behavioral pharmacological methods.
3. The relationship between the important molecules in the pain signaling of astrocytes and spinal microglia activation in the spatial-temporal analysis will be examined.
4. The expression pattern of the vesicular nucleotide transporter (VNUT) in the spinal dorsal horn after nerve damages will be examined in order to know the role of VNUT being important for the release of nucleotides.
5. The effects of the important molecules identified above experiments will be examined by electrophysiological method and two-photon imaging analysis using dorsal horn slices attached dorsal root neurons (in vitro) and the pain animal models of several KO mice .

【Expected Research Achievements and Scientific Significance】

From the findings on the glia-neuron signaling pathway, we are able to understand the mechanism of neuropathic pain. We have a possibility to create new drugs for treating neuropathic pain.

【Publications Relevant to the Project】

1. Tsuda M, Shigemoto-Mogami Y, Koizumi S, Mizokoshi A, Kohsaka S, Salter MW, Inoue K: P2X4 receptors induced in spinal microglia gate tactile allodynia after nerve injury. ***Nature*** 424: 778-783, 2003
2. Koizumi S, Shigemoto-Mogami Y, Nasu-Tada K, Shinozaki Y, Ohsawa K, Tsuda M, Joshi BV, Jacobson KA, Kohsaka S, Inoue K. UDP acting at P2Y6 receptors is a mediator of microglial phagocytosis. ***Nature*** 446, 1091-1095, 2007

【Term of Project】 FY2011-2015

【Budget Allocation】 149,600 Thousand Yen

【Homepage Address and Other Contact Information】

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