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Correspondence

Is the OLETF Rat a Good Model of Central Sensitization?

Kyoko Miyasaka[1,*] and Akihiro Funakoshi[2]

[1]*Department of Clinical Physiology, Tokyo Metropolitan Institute of Gerontology, 35-2 Sakaecho, Itabashiku, Tokyo l73-0015, Japan*
[2]*Department of Gastroenterology, Kyushu Cancer Center, Fukuoka 811-1395, Japan*

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Otsuka Long-Evans Tokushima Fatty (OLETF) rats, developed as a model of non-insulin-dependent diabetes mellitus, are naturally occurring cholecystokinin-A receptor (CCK-AR) gene knockout rats (1). Although the possibility that the OLETF rats possess other gene abnormalities is not excluded, none of these abnormalities besides the CCK-AR gene has been cloned. OLETF rats have revealed several abnormal functions including a decrease in exploratory behavior, increase in anxiety, impaired learning, disturbance of regulation of body temperature, and so on (2). We recently reported (3) that OLETF rats showed hyperalgesia in response to acute thermal pain as well as disturbed responses to thermal pain. Based upon this recent report (3), Félix et al. proposed (correspondence) that OLETF rats might be useful as a model of central sensitization – a possible relevance to fibromyalgia.

Fibromyalgia has been a poorly understood syndrome characterized by diffuse chronic pain with other somatic symptoms and suggested to be a syndrome of dysfunctional central pain processing (4). Psychogenic factors may be involved in the pain of fibromyalgia syndrome. It has been known that anxiety, depression, or somatizing personality traits may predispose some patients with fibromyalgia to the development or maintenance of the syndrome and that physical or psychological trauma or certain viruses may be partly responsible for initiating the events that lead to fibromyalgia (4). As OLETF rats show anxiogenic behavior, some common feature of mood disturbance between OLETF rats and fibrmyalgia patients might exist.

However, the most common symptoms accompanying fibromyalgia are poor-quality sleep, morning stiffness, and fatigue (4). These symptoms could not be evaluated appropriately in the animal study. At least, OLETF rats did not seem to have poor sleep. In addition, our observation that OLETF rats showed thermal hyperalgesia and disturbed responses to thermal pain represented a dysfunction of central pain processing. However, the major complaint of patients with fibromyalgia syndrome is chronic sustained pain. We could not examine whether OLETF rats feel chronic pain. 5-Hydroxytryptamine (5-HT) and 5-hydroxyindole acetic acid (5-HIAA) contents were increased in some parts of the brain of OLETF rats. Unfortunately, we did not examine the effect of 5-HT inhibitors or agonists on pain sensation, so that we could only suggest the involvement of 5-HT function in the disturbance of pain processing. Whether 5-HT function is altered in patients with fibromyalgia has been inconclusive (4).

Taken together, we wonder whether the OLETF rat would be a model of fibromyalgia syndrome, although this animal could be useful to examine the molecular mechanism of pain processing in the central nervous system.

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*Corresponding author. miyasaka@tmig.or.jp
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