CHAPTER VI

CONCLUSION

In the present study, using the immunohistochemical technique, the effect of serotonin depletion on chemically-induced trigeminal nociception, NMDA receptor NR1 subunit phosphorylation and expression was studied. The following are the conclusions of our findings.

1. Activation of trigeminal nociceptive pathway, indicated by Fos expression in dorsal horn neuron in TNC, was demonstrated by topical application of IS on exposed dura for 30 minutes. However, low-pH CSF (pH 4.7) application cannot activate trigeminal nociception.

2. PKC phosphorylation of NR1 subunit of NMDA receptor at serine-896 in superficial dorsal horn of TNC was rapidly induced (30 minutes) following an dural application of IS and that phosphorylation persisted for long period (up to 2h). However, low-pH CSF (pH 4.7) cannot activate NMDA receptor NR1 subunit phosphorylation.

3. No change in the NMDA receptor NR1 subunit expression in dorsal horn of TNC was observed following dural stimulation.

4. There was a relationship between NMDA receptor NR1 subunit phosphorylation and trigeminal nociception. Our data demonstrated a strong positive correlation between the number of pNR1-ir cells and the number of Fos-ir cells (r^2 = 0.957, $P < .001$). The correlation could be presented by the linear regression of y = 0.520x. It is suggested that NR1 receptor phosphorylation may play a major role in trigeminal nociception and can be used as indicator for trigeminal nociception.

5. Trigeminal nociception was potentiated in the serotonin-depleted state. This nociceptive facilitation was more evident in dural inflammation-induced rats. This study further supports the role of serotonin in the control of trigeminal nociception.

6. Neither serotonin depletion alone nor serotonin depletion combined with dural inflammation altered NMDA receptor NR1 subunit expression in TNC.

7. Serotonin depletion enhanced dural inflammation-induced NMDA receptor NR1 subunit phosphorylation in accordance with trigeminal nociception. Thus, we

would like to suggest that the mechanism of nociceptive facilitation in low serotonin condition may involve the increase in NR1 receptor phosphorylation, not the increase in NR1 expression in TNC. However, immunohistochemical technique cannot quantify total NR1 protein. To confirm this, western blot technique should be performed.

8. In low serotonin condition, there also was a strong positive correlation between the number of pNR1-ir cells and the number of Fos-ir cells ($r^2 = 0.941$, $P < .001$). Besides, the correlation could be presented by the linear regression of $y = 0.706x$. It was noted that the slope of the linear regression was higher than the slope of normal rats. This suggests that low serotonin condition increases the sensitivity of central neuron in TNC and reduction in brain synthesis of serotonin may increase susceptibility of migraine attack in migraine sufferers.