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2. **Title**

   Effects of the Aversive Stimulus on the Rewarding Effects of a Substance of Abuse and the Development of Substance Dependence

3. **Period**

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4. **Summary**

   [Background] The purpose of the present study is to investigate the involvement of aversion in manifestation and tolerance of the rewarding effects of a substance of abuse and to clarify the mechanism of reward in the development of addiction.

   [Methods] NaCl (salt), quinine, and foot shock were used as aversion, and saccharin and EtOH were used as reward. The influence of aversion on the reward-intake behavior was investigated, and the effects of aversion on the brain reward system was measured by the intracranial self-stimulation (ICSS) experiment using the male Wister rat.

   [Results] NaCl and foot shock increased the total consumption of saccharin and EtOH and decreased the ICSS reward thresholds produced by saccharin and EtOH, respectively. On the other hand, foot shock prevented a decrement of the total consumption of EtOH, and increased the ICSS reward thresholds produced by EtOH.

   [Conclusions] The present study suggested that aversion (NaCl and foot shock) increased the reward value of saccharin and EtOH, respectively, whereas foot shock prevented the development of tolerance of the rewarding effects of EtOH. These effects of aversion (NaCl and foot shock) on the rewarding effects of saccharin and EtOH were demonstrated to be mediated through the brain reward system.