CHAPTER I

INTRODUCTION

Nowadays, stress is a serious problem in modern society because it causes many disorders such as depression, anxiety and metabolic disease (Pacak and Palkovits, 2001). To cope with stress and maintain the homeostasis, the living organism will be adapted during the long-term stress via the output of stress system which is hypothalamic pituitary adrenal gland (HPA) and locus ceruleus/norepinephrine (LC/NE) system. Unfortunately, this adaptation may cause many physiological and psychological disorders especially heart disease, metabolic disease and mental illness (Tsigos and Chrousos, 2002). In addition, previous studies have shown that chronic stress involves in drug abuse and preference behavior such as place preference or sweet food preference (Dess et al., 1988; Wongwitdecha and Marsden, 1996). Ely and co-workers (1997) further revealed that acute stress did not affect sweet food ingestion but chronic stress increased ingestion of sweet food independent of hunger. Various hormones and neurotransmitters such as corticosteroid and β-endorphin have been suggested to play a role in this process. The functions of these hormones are terminating the stress response by acting at the central stress system within the brain including brain related to sweet food intake (Herman et al., 1996; Sawchenko et al., 1996).

Mesocorticolimbic dopaminergic system is predominantly involved in stress response and behavioral change, the alteration of this system has been suggested to regulate the preference behavior (Nestler et al., 2001). Previous studies reported that increased dopamine (DA) level in nucleus accumbens (NAc) led to an increase in sweet food intake (Phillips et al., 1993). Moreover, local infusions of DA receptor antagonist into the NAc inhibited DA release and decreased sweet food intake (Hajnal and Norgren, 2001). There are some suggestions that chronic stress increased DA level at the NAc and related to sweet food intake. Therefore, chronic stress can modulate the sweet food intake behavior by affecting dopamine level at the NAc.

However, there is a little known information about the mechanism underlying the changes of DA in response to chronic stress.

Opioids receptors are widely distributed in the central nervous system especially in the neurons of reward system and play roles in modulation of their functions (Blackburn et al., 1988; Mansour et al., 1987). In addition, more evidence suggested that opioid receptor was subjected to change during stress (Drolet et at., 2001; Dumont et al., 2000). For example, rats exposure to acute stress produced immediate analgesia in several pain tests (Mogil et al., 1996; Vacarino and Kastin, 2001), whereas chronic-stress rats exhibited hyperalgesia (Gamaro et al., 1998). The decreases of pain thresholds have been suggested to alter response of endogenous opioid system. There is much evidence shown that opioid ligands modulated the mesocorticolimbic system by altering dopaminergic neuron activity (Shippenberg and Bals-Kubik, 1995; Spanagel et al., 1992). For an example, intravenous injection of morphine increased dopamine level in terminal region of mesocorticolimbic dopaminergic system (Gysling and Wang, 1983). Relating to the change of food preference behavior by opioid-induced dopaminergic activity, MacDonald and co-workers (2004) found that infusion of DAMGO ([$_D$-Ala^2, *N*-Me-Phe^4,Gly^3-ol] Enkephalin), μ-opioid agonist, at the ventral tegmental area (VTA) or nucleus accumbens (NAc) increased dopamine level in NAc accompanied with sweet food intake. On the other hand, naloxone, a non-selective opioid antagonist, decreased DAMGO-induced sweet food intake (Clifford et al., 2002). Taken together, chronic restraint stress may possibly cause the alteration of opioid activity in mesocorticolimbic dopaminergic system, leading to the change in dopamine level and induction of sweet food intake behavior.

Therefore, the objectives of this study were, as follows:

1) To examine the effect of chronic restraint stress on sweet food intake

2) To determine whether opioid receptor and what type of opioid receptor mediates chronic stress-induced sweet food intake.

3) To examine effect of chronic restraint stress on changes of the neurotransmission which is dopaminergic neurotransmission involves in sweet food intake.

We hypothesized that chronic restraint stress can increase sweet food intake. Opioid receptor antagonist can reverse sweet food intake in rats exposure to chronic restraint stress.