

3836179 STNS/M : MAJOR : NEUROSCIENCE ; M.Sc. (NEUROSCIENCE)

KEY WORD : G-PROTEIN / MORPHINE / RAT BRAIN / REVERSE-  
TRANSCRIPTASE POLYMERASE CHAIN REACTION

SUKIT KAEWSUK : THE STUDY OF G-PROTEIN mRNA SUBUNITS  
IN DIFFERENT AREAS OF RAT BRAIN BY RT-PCR AND EFFECTS OF ACUTE  
AND CHRONIC MORPHINE ADMINISTRATION. THESIS ADVISOR :  
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589-330-7

The present work investigated changes in gene expression of specific subtypes of GTP-binding proteins (G-protein) following acute and chronic morphine injection in rats. A reverse-transcriptase polymerase chain reaction (RT-PCR) assays was developed in which two sets of primers were used to amplify multiple subtypes of  $G_{\alpha}$  and  $G_{\beta}$  mRNA. Individual subunits were then identified by the restriction pattern of the RT-PCR products.

First, the distribution of  $G_{\alpha}$  and  $G_{\beta}$  subunits mRNA in four brain regions believed to be associated with drug addiction : prefrontal cortex, striatum, nucleus accumbens (NAc) and locus coeruleus (LC) were determined. It was found that  $G_{\alpha o}$  mRNA levels in NAc and prefrontal cortex are greater than in LC and striatum. The level of  $G_{\alpha i1}$  mRNA in prefrontal cortex , NAc and LC are greater than in the striatum. The amounts of  $G_{\alpha i2}$  mRNA were equal in all areas. The  $G_{\beta 2}$  mRNA was expressed at higher level in NAc as compared to prefrontal cortex and LC.

Second, changes of expression of the  $G_{\alpha}$  subunits ( $G_{\alpha o}$ ,  $G_{\alpha i1}$ ,  $G_{\alpha i2}$  and  $G_{\alpha i3}$ ) and  $G_{\beta}$  subunits ( $G_{\beta 1}$ ,  $G_{\beta 2}$  and  $G_{\beta 3}$ ) following morphine injection were measured. Acute doses (30mg/kg) caused an increase of  $G_{\alpha o}$  and  $G_{\beta 1}$  mRNA in prefrontal cortex and decrease in  $G_{\alpha i1}$  and  $G_{\alpha i2}$  in the same area. There were no changes in other brain regions. Chronic morphine administration, twice a day for 14 days, resulted in an increase of the mRNA level of  $G_{\alpha i1}$ ,  $G_{\alpha i2}$  and  $G_{\beta 1}$  in prefrontal cortex and no change in  $G_{\alpha o}$  and  $G_{\beta 2}$  levels. In striatum, NAc and LC there was no change of  $G_{\alpha i o}$  and  $G_{\beta}$  subunits.

This work has shown that both acute and chronic morphine administration cause specific changes of G protein expression in selected brain areas of rats. The information obtained can be used to further investigate the molecular changes that occur in the mammalian brain following repetitive intake of drugs as in cases of addiction.