

# **Increased locomotor response to amphetamine induced by the repeated administration of the selective kappa-opioid receptor agonist U-69593**

José Antonio Fuentealba, Katia Gysling, María Estela Andrés

## **Abstract**

Acute administration of kappa opioid receptor (KOR) agonists decreases both dopamine (DA) extracellular levels in the nucleus accumbens (NAc) and locomotor activity. Opposing to its acute effects, recent studies show that chronic administration of KOR agonists potentiates both stimulated DA release and induced locomotor activity. Since KOR agonists have been considered as potential treatment for stimulant dependence, the effects of their repeated administration on psychostimulant actions are of major concern. The present study was undertaken to investigate the in vivo effect of repeated administration of the KOR agonist U-69593 on DA extracellular levels in the NAc and on the locomotor activity challenged with amphetamine. Rats were injected once daily with the selective KOR agonist U-69593 or vehicle for four consecutive days. One-day after the last U-69593 injection, microdialysis studies assessing extracellular DA levels in the NAc and locomotor activity challenged with amphetamine were conducted. Microdialysis studies revealed that preexposure to U-69593 had no effect on basal DA levels but significantly augmented amphetamine-induced DA extracellular levels. Accordingly, amphetamine-induced locomotor activity was also significantly potentiated in U-69593 preexposed rats. These results suggest that long-term effect of KOR activation results in facilitation of amphetamine-induced DA extracellular levels in the NAc accompanied by sensitization of amphetamine-induced increase in locomotor activity.