Possible interaction of hippocampal nitric oxide and calcium/calmodulin-dependent protein kinase II on reversal of spatial memory impairment induced by morphine

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1. Introduction

Compelling evidence suggests that mu-opioid receptor agonist, morphine, modulates learning and memory in both human and animal subjects (Bodnar and Hadjimarkou, 2003; Canli et al., 1990; Gallagher et al., 1985). This modulation has been indicated in positive and negative effects by different experimental studies and different types of drug administration (Classen and Mondadori, 1984; McNamara and Skelton, 1992). Many reports have pointed that chronic administration of opioids impairs learning and memory processes in various kinds of memory assessment tasks (Sala et al., 1994; Spain and Newsom, 1991). On the other hand, the effect of acute administration of morphine on memory processes is still controversial. Some studies showed that pre-training acute administration of morphine inhibits the acquisition of memory in different paradigms such as y-maze discrimination (Castellano, 1975), active or passive avoidance (Izquierdo, 1979) and operant tasks (Bruins Slot and Colpaert, 1999). On the contrary, Jensen et al. showed an inverted U shaped dose-response curve following acute intra-cerebroventricular (i.c.v) post-training injection of morphine in rats tested in passive avoidance task (Jentsch and Taylor, 1999). Improving effect of acute pre-test administration of morphine has been reported in amnesia induced by pre-training injection of morphine (Zarrindast and Rezayof, 2004). Previous studies have indicated that hippocampal-dependent memory also can be affected by opioids in the Morris water maze task (Li et al., 2001; McNamara and Skelton, 1991). It has been demonstrated that pre-training repeated exposure to morphine impaired acquisition while post-training administration of morphine did not alter consolidation of spatial memory in water maze task (McNamara and Skelton, 1991). Further, it has been reported that i.c.v injections of morphine has no effect on the retrieval of spatial memory in Morris