Opioid Modulation of Working Memory: Intraseptal, but Not Intraamygdaloid, Infusions of β-Endorphin Impair Performance in Spatial Alternation

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The effect of β-endorphin on spatial working memory was examined following microinfusions of β-endorphin into the medial septal area and central amygdaloid nucleus in Long–Evans male rats. Working memory was assessed by spatial alternation in a T-maze. β-Endorphin, 250 and 1000 ng/site, respectively, and muscimol, 20 ng/site, were infused into the medial septal area or central amygdaloid nucleus prior to behavioral testing. The hippocampal theta rhythm was examined following intraseptal infusions of β-endorphin and muscimol. In the medial septal area, β-endorphin and muscimol impaired choice accuracy and reduced the power of hippocampal theta rhythm. The degree of reduction in the power of hippocampal theta rhythm was correlated with the magnitude of behavioral impairment of choice accuracy in spatial alternation. In the central amygdaloid nucleus, β-endorphin (1000 ng) and muscimol (20 ng) did not affect choice accuracy. The results suggest that septal, but not amygdaloid, opioid, and GABAergic activity modulate spatial working memory and hippocampal physiology.


The central opioid system has an important influence on memory. Opioid agents that are administered intracranially or systemically alter performance in a variety of behavioral tasks. Generally, opioid agonists impair, whereas antagonists improve, mnemonic functions (for reviews see Gallagher, Fanell, & Bostock, 1985; Gold, 1992; Izquierdo & Netto, 1985; McGaugh, 1989).

A role of the central opioid system in memory storage is suggested by studies using avoidance tasks that indicate a change in retention following systemic opioid manipulations (Flood, Cherkin, & Morley, 1987; Introvini-Collison, McGaugh, & Baratti, 1985; Izquierdo, 1980; Martinez et al., 1981; McGaugh, Introvini-Collison, & Nagahara, 1988; for reviews see McGaugh, 1989, 1992). However, systemic opioid manipulations also influence performance in behavioral tasks that require working memory (Canli, Cook, & Miczek, 1990; Gallagher, King, & Young, 1983; Gallagher, Bostock, & King, 1985; Spain & Newman, 1991). Working memory is a short-term memory that stores information for a single trial of an experiment, but not for subsequent trials, which is different from reference memory that stores general information for an entire experiment (Olton, Becker, & Handelmann, 1979). The results from studies examining the effects of opioid agents on a variety of behaviors suggest that the central opioid system can modulate different kinds of memory and mnemonic processes.

Opioid receptors and opioid-sensitive neurons that are located in specific areas of the brain may be the targets affected by opioid manipulations in the modulation of memory (Bostock, Gallagher, & King, 1988; Gold, 1992; McGaugh, Introvini-Collison, Cahill, Kim, & Liang, 1992). The medial septal area (MSA, the medial septal nucleus and the vertical limb of the diagonal band) and the amygdala (AMG) are most likely to have an important role in opioid-mediated memory because these areas have been shown to influence a variety of mnemonic functions.

Opioid manipulations in the MSA influenced performance in different behavioral tasks (Bostock, Gallagher, & King, 1988; Ragazzino, Parker, & Gold, 1992). The neural mechanisms underlying opioid-mediated memory remain unclear. The MSA regulates hippocampal physiology (Bland, 1986). GABAergic manipulations in the MSA impaired working memory that was associated with an impairment of hippocampal physiology (Givens & Ol-