Involvement of the dorsal hippocampal GABA-A receptors in histamine-induced facilitation of memory in the Morris water maze

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Several types of learning and memory processes are regulated by the hippocampus which is an important subcortical structure in the mammalians’ brain. Previous investigations have shown that different receptor systems in the CA1 region of hippocampus are involved in learning and memory functions. Investigating the possible influence of dorsal hippocampal GABA-A receptors on histamine-induced spatial facilitation in adult male Wistar rats was the focus of the current study. Rats were bilaterally implanted with dorsal hippocampal (CA1) cannulae, recovered from surgery and then trained in Morris water maze (MWM) for 4 consecutive days. A block of four trials was given each day. All drugs were injected into CA1 regions, 5 min before training. Pre-training intra-CA1 microinjection of muscimol, a GABA-A receptor agonist, at the dose of 0.01 or 0.02 μg/rat, increased the traveled distance or the escape latency and traveled distance to the hidden platform, respectively, indicating a water maze spatial acquisition impairment. Intra-CA1 administration of bicuculline, a GABA-A receptor antagonist however, significantly decreased the escape latency and traveled distance to the hidden platform, suggesting a spatial learning facilitation. On the other hand, pre-training intra-CA1 microinjection of the subthreshold dose of muscimol plus different doses of histamine (0.025, 0.05 and 0.1 μg/rat) did not alter the histamine response. Meanwhile, the co-administration of the ineffective dose of bicuculline together with histamine potentiated the spatial learning. Moreover, bilateral infusion of histamine (0.025, 0.05 and 0.1 μg/rat) by itself, facilitated the spatial learning. Notably, the drug injections had no effect on swimming speed during the MWM training sessions. Our results suggest that the dorsal hippocampal (CA1) GABA-A mechanism(s) may influence the histamine-induced facilitation of spatial acquisition.

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1. Introduction

The spatial memory refers to the ability of the animal to locate a particular place using spatial cues. Activation of the cAMP-dependent protein kinase A (cAMP response element-binding protein (PKA/CREB) signaling pathway in dorsal hippocampus (the CA1 region) may play a distinctive role in spatial memory acquisition (Mizuno et al., 2002; Naghdil et al., 2005). Furthermore, investigations have indicated that hippocampal lesions lead to impaired performance in different tasks depending on what spatial information are used (Silvers et al., 2003).

In addition, gamma-aminobutyric acid (GABA) which is the major inhibitory neurotransmitter in the brain, is known to affect learning and memory processes (Castellano et al., 1996; Nakagawa et al., 1999). Several investigations have indicated that GABAergic receptor agonists and antagonists impair and facilitate memory retrieval, respectively (Castellano and McGaugh, 1990; Nakagawa and Iwasaki, 1995; Nazari-Serenjeh et al., 2011). GABA induces its effects via three subtypes (α1–6, β1–4, γ1–3, δ, ε, θ and π) (Zheng et al., 2009). Hippocampal pyramidal cells tend to express different GABA-A subunits (α1–6) (Fritschy and Brunig, 2003). Among the several GABA-A subunits, α1 subunit is found to abundantly express through most of the adult brain regions (McKernan et al., 1991). Hence, competent brain performance in both spatial and non-spatial tasks might depend on the

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