Interactive effects of a protein kinase AII inhibitor and testosterone on spatial learning in the Morris water maze.


Source
Department of Pharmacology and Toxicology, Pharmaceutical Sciences Research Center, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran.

Abstract
Neurohormones such as testosterone (TE) are important in modulation of learning and memory. In the present study, we investigated the interactive effects of pre-training bilateral intra-hippocampal infusions of testosterone and H-A^8, a selective PKAII inhibitor, on spatial acquisition in the Morris water maze (MWM). Different doses of TE (\(1 \times 10^{-4}, 1 \times 10^{-3}, \text{and } 1 \times 10^{-2} \mu g/\text{side}\)) and H-A^8 (\(5 \times 10^{-5}, 1 \times 10^{-4} \mu M/\text{side}\)) were administered 3 min before start of the training each day. Control animals received bilateral intra-hippocampal infusions of DMSO as vehicle for TE and H-A^8. Animals were trained for 4 days and each day included one block of four trials. The results of this study showed that bilateral infusion of TE (\(1 \times 10^{-4} \mu g/\text{side}\)) or H-A^8 (\(1 \times 10^{-4} \mu M/\text{side}\)) impaired spatial learning as indicated by significant increases in escape latency and traveled distance compared to the control group. Although pre-training bilateral infusions of a low concentration of either TE (\(1 \times 10^{-4} \mu g/\text{side}\)) or H-A^8 (\(1 \times 10^{-4} \mu M/\text{side}\)) into the CA1 region of the hippocampus did not affect learning capabilities, but the combination of the low doses of the drugs led to significant deficits in spatial acquisition. Overall, our data suggest that spatial acquisition was affected by PKAII inhibition or TE administration. Moreover, when co-administered, these drugs had a negative synergistic impact on acquisition.