LENTIVIRUS OVEREXPRESSION OF CREB IN THE DORSOLATERAL STRIATUM IMPAIRS LONG-TERM MEMORY FOR PLACE LEARNING: EVIDENCE FOR A COMPETITIVE INTERACTION BETWEEN THE STRIATUM AND THE HIPPOCAMPUS


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Extensive research has shown that the hippocampus and the dorsolateral striatum are necessary for place and response learning, respectively. We reported that learning-induced phosphorylation of the transcription factor CREB is sustained in the hippocampus and the dorsolateral striatum of rats that use place and response strategies, respectively (Colombo et al., 2003). In addition, we reported that overexpression of CREB in the dorsal hippocampus facilitates long-term memory (LTM) for place learning (Brightwell et al., 2007) and overexpression of mutant CREB in the striatum impairs LTM for response learning (Brightwell et al., 2008). In the present study, we overexpressed CREB chronically using a Lentivirus vector in the dorsolateral striatum to test the hypotheses that increasing CREB levels in the dorsolateral striatum facilitates LTM for response learning and alters hippocampus-dependent place learning. Two weeks following intra-striatal infusion, experimental (CREB) and control (LacZ and saline) rats were trained on a response task in a water plus-maze. All rats were given a 4-trial memory retention test at 1, 2, 3, 4 and 6 weeks. After completion of response testing, all rats were trained on a place task and tested for place memory after 6 days. Western blotting confirmed a significant increase in the levels of total CREB in the CREB-treated rats in comparisons with controls. For response learning, there were no differences among treatment groups in escape latency or trials to criterion (9/10 correct choices). LacZ- and saline-treated rats were pooled for subsequent analyses. There were no differences between CREB-treated and control rats in memory for response training at any of the time points tested and both groups performed near ceiling thus we were unable to test the facilitatory effect of CREB overexpression in the striatum on LTM for response memory. There was no difference between controls and CREB-treated rats during acquisition of the place task. At test, however, controls showed a significant decrease in the numbers of trials to reach criterion in comparison to training whereas CREB-treated rats did not. The impairment in place memory exhibited by CREB-treated rats is consistent with a competitive interaction of the striatum on the hippocampus. Taken together, the present results suggest that the strong memory trace formed in the dorsolateral striatum during response training competes with the hippocampus either during place-learning or during recall and control of behavioral output.

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