State-dependency is a phenomenon concerning interoceptive stimuli and their subsequent impact on the ability of an organism to successfully retrieve a memory. The current study utilized a Pavlovian avoidance conditioning procedure to train, reactivate, and test avoidance memory expression in rats following treatment with the NMDA receptor antagonist, MK-801. Previous studies have demonstrated that MK-801 impairs memory, therefore we sought to establish MK-801-induced deficits for reconsolidation in adult rats in our laboratory, and hypothesized that MK-801 would block the reconsolidation of avoidance memory to ensure efficacy of the drug in our hands. Given that MK-801 has been shown to be state-dependent in other studies using peripheral injections, we hypothesized that we would find state-dependent reconsolidation deficits when infusing directly into the central nervous system and, in particular, the hippocampus. Experiment 1 demonstrated significant deficits in a reconsolidated memory for Pavlovian fear conditioning following MK-801 injection immediately after reactivation, but no effect when the memory was not reactivated, confirming that MK-801 worked to impair reconsolidation in a reactivation-dependent manner. Experiment 2 confirmed and extended prior findings that peripheral injection of MK-801 impaired avoidance memory for reconsolidation in a state-dependent manner, and that the window of susceptibility to impairment by MK-801 is less than 6 hours. Experiment 3 showed that intracerebroventricular (icv) infusions of MK-801
produced similar memory impairment as in Experiment 1, but that this finding was state-dependent as in Experiment 2. Experiment 4 showed that bilateral hippocampal infusion of MK-801 produced reconsolidation impairments similar to Experiments 1, 2, & 3; however, we failed to find a state-dependent effect of MK-801 in the hippocampus. The findings discussed here highlight that the issue of state-dependent memory may be more important than previously thought. Our data demonstrate that although a memory may appear to be blocked when tested in the absence of an amnestic treatment, re-administration of the treatment may serve to allow retrieval. This finding is crucial because many of the studies that lead to our current understanding of memory do not use a state-dependent design to assess the possibility of the results being due to a state-dependent effect, rather than actual blockade of memory formation.