

PHOSPHODIESTERASE INHIBITION BY SILDENAFIL CITRATE ENHANCES RETENTION OF MAZE LEARNING IN AGED RATS

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Studies evaluating the potential cognitive enhancing effects of sildenafil, a phosphodiesterase type 5 inhibitor (PDE5), have generally utilized young animals. Because the development of compounds to enhance cognition are generally targeted at aging populations, it is important to examine the effect of PDE5 inhibition in aging models. We assessed whether treatment with sildenafil citrate (the active compound of Viagra), a cyclic nucleotide PDE5 inhibitor, would attenuate an age-associated learning and memory impairment in rats tested on a 14-unit T-maze task. Rats were pre-trained in one-way active avoidance of foot shock in a straight runway and the next day received 15 acquisition trials in a foot shock motivated 14-unit T-maze. Performance in this maze paradigm requires accurate responding to avoid mild foot shock and has been shown to be sensitive to age-related changes in central cholinergic and glutamatergic systems. Intraperitoneal (i.p.) injections of sildenafil or vehicle were given 15 minutes before training. The treatment conditions were as follows: vehicle (CN) and sildenafil (V1.5, V3.0, V4.5, or V10.0 mg/kg). One week following acquisition training, all rats received 5 additional trials to assess retention under drug free conditions. Behavioral measures of performance included deviations from the correct pathway (errors), run time from start to goal, shock frequency, and duration. Statistical analysis revealed a significant aged-related increase in errors committed during acquisition and retention. Treatment with sildenafil did not improve acquisition in any age group, but did significantly enhance retention of maze learning (3 mg/kg) in aged animals. These results suggest that sildenafil may prove useful in improving memory consolidation mechanisms that become less efficient in normal aging and impaired in dementia.