Abstract:

Due to the persisting lack of reliable animal models of cognitive impairment with good translational validity, researches strive to discover new ways and tools to replicate symptoms of human neurodegenerative diseases in rodents. Recently, biperiden, an M1-selective muscarinic antagonist, has been proposed as a potential tool for generating fast screening models of mnemonic deficits such as seen in patients with Alzheimer's disease. Being highly selective for the M1 receptor, a predominant type of muscarinic acetylcholine receptors in the brain involved in cognitive processes, it has been speculated to possibly only influence cognition without causing sensorimotor side effects. Studies assessing the usability of this drug reported conflicting results. We have decided to expand the experimental data and evaluate biperiden's validity in several variants of the Morris water maze.

The results of this study showed no significant effect of biperiden on cognitive flexibility, tested by reversal learning. In delayed-matching-to-position paradigm, which tests assesses working memory, we found a difference in performance between the two experimental groups; however, it cannot be unequivocally attributed to a memory impairment. No effects were observed in visible platform task, confirming a lack of sensorimotor side effects. We found an increase in escape latencies in the counter-balanced acquisition paradigm, pointing to a disruptive influence on memory acquisition. In probe trials, a significant decrease of time spent in the target quadrant was observed, suggesting a memory retention impairment. In conclusion, taking into account the conflicting results from other studies, biperiden does not seem reliable enough to serve as a tool for generating models of cognitive impairment, and as such we would not recommend its use in this field.