Alzheimer's disease (AD), a progressive neurodegenerative disorder, is the most common form of dementia in humans and is clinically characterized by cognitive decline. The exact cause of AD remains elusive but the sporadic type is mainly related to aging and other risk factors such as diabetes and metabolic disturbances. The aim of the present study was to investigate the central effects of increasing doses of ICV streptozotocin (STZ), a diabetogenic drug, on cognitive performance in the rat. Cognitive functions were evaluated in the Morris Water Maze, Delayed Alternation and Passive Avoidance Tests.

**METHODS**

- Surgery: Male Wistar rats received a single infusion of 5 µL of STZ (1.5, 3 and 4.5 mg/kg) or vehicle (citrate buffer) over 2.5 minutes administered bilaterally into the lateral ventricles.
- Morris Water Maze (MWM): Rats placed into a circular tank containing water; learn to find a fixed and invisible escape platform positioned beneath the surface of the water using extra-maze visual cues. The animals were given 4 training sessions over 4 consecutive days (Day 1 to Day 4). Each training session consisted of 4 consecutive trials, each separated by 60 seconds. For each trial, the animal was placed in the maze at one of two starting points equidistant from the escape platform. The animal was left on the escape platform for 60 seconds before starting a new trial. 24 hours after the end of the acquisition (Day 5), rats were submitted to a 60-sec probe trial where the platform was removed. The behavior of animals was analyzed using a video-tracking system.
- Delayed Alternation (DA): Rats were placed in a Skinner box fitted with a house light, two retractable levers located on either side of the food receptacle and a food pellet dispenser. After having learnt the lever press, rats were then submitted to 15 delayed alternation sessions (S1 to S15). Each session consisted of 36 successive trials separated by 10 seconds. Each trial consisted of presenting the animal first with one lever (left or right). A lever-press resulted in the delivery of a food pellet, the retraction of the lever and 2.5 seconds later, both levers were presented. The animal had to learn to press on the lever opposite to that previously presented to gain a food reward (non-matching to sample). Incorrect responses (presses on the same lever) were not reinforced.
- Passive Avoidance (PA): Rats placed individually into the light compartment of a two-compartment box, received a 0.8 mA foot-shock when they entered the dark compartment. 48 hours later the rat was placed again in the light compartment and the rat's latency to cross to the dark compartment was recorded (cut-off time = 180 seconds).

**RESULTS**

**CONCLUSION**

These results suggest that ICV injection of STZ induces learning and memory deficits in the MWM in the rat. A modest learning, working memory and attention impairment was also observed during the acquisition of a Delayed Alternation task. Similar results were observed at 1.5 and 2.25 mg/kg in a second study, confirming the presence of cognitive impairment using the Morris Water Maze and the Delayed Alternation Tests. In conclusion, ICV injection of STZ induces cognitive alternations reminiscent of deficits observed in AD and serves as a relevant alternative model for testing novel therapeutic approaches targeted for AD treatment.