

Lab. 5



To demonstrate amnesic effect of drug in rat using Morris water maze apparatus

Presented by:

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Experimental models for AD

1. Spontaneous models:

- Aged animals can serve as natural models of memory deficits and dementia.
- Dogs have been pointed out as suitable animal models for AD as they have an identical A β sequence to humans .
- Other species, including cats, goats, sheep, and monkeys spontaneously show plaque pathology and some species even exhibit taupathies
- The use of these models for experimental research is considerably limited by availability, economical (based on long lifespan) and ethical reasons.

2. Transgenic models:

- The discovery of AD--associated genes has generated a number of transgenic animal models through introducing mutant genes into the existing genetic makeup or modifying genes of interest using gene targeting technology in an attempt to model some features of human AD
- Numerous transgenic models have been created in rats and mice.
- Because of their larger size, rats are more liable than mice to studies involving complex techniques. Also, more background behavioral data exist for the rat than for the mouse, and rats have long been the preferred small animal species for behavioral characterization

3. Interventional models:

a. Chemically--induced interventional models:

- Scopolamine--induced memory deficits
- Intracerebroventricular (ICV) streptozotocin--induced memory deficits
- Heavy metal--induced memory deficits
- Colchicine--induced memory deficits
- Okadaic acid--induced memory deficits
- Ethanol--induced memory deficits
- Sodium azide--induced memory deficits

b. Lesion--induced interventional models:

- Lesioning can be achieved by surgical (i.e. cerebral--ischemia) or electrolytic procedures (i.e. chronic exposure to electroconvulsive shock), and intraparenchymal or intracerebroventricular microinjections of neurotoxic substances.
- The resultant brain lesions cannot be precisely described since lesion characteristics depend on the type of agent employed and its ability to cause selective harm to different subtypes of neurons, nerve fibers passing through the affected area, glial cells and blood vessels.

Morris water maze

- The Morris water maze is widely used to study memory and learning.
- Animals are placed in a pool of water that is colored opaque with powdered non-fat milk or non-toxic paint, where they must swim to a hidden escape platform

Procedure

- The main component of the water maze set up should be a round pool, about **6 feet in diameter** and about **3 feet deep**. If you are recording the task with a video camera, make sure all sides of the maze are within the camera's field of view.
- Fill up the water maze with tap water, which should be close to 26°C.
- Periodically check the water temperature so that it is within one degree of 26°C.

- Place the escape platform in the center of the pool. During training, it must be exposed, **one inch** above the water.
- This teaches the rat that there is a platform, and that it is the way to get out of the water.
- Later, after the animal is trained and ready for testing, the escape platform will be just below the surface of the water, and will not be visible because the water will be made opaque with milk or non-toxic paint.
- Now, the water maze is ready for training the animals.

Pre-training for the water maze

- For the water maze training, the platform should be in the center of the pool and exposed one inch above the surface, so the animal knows that it's there. The water should be within one degree of 26°C.
- Each animal will undergo three consecutive trials. First, place the animal on the platform for twenty seconds.

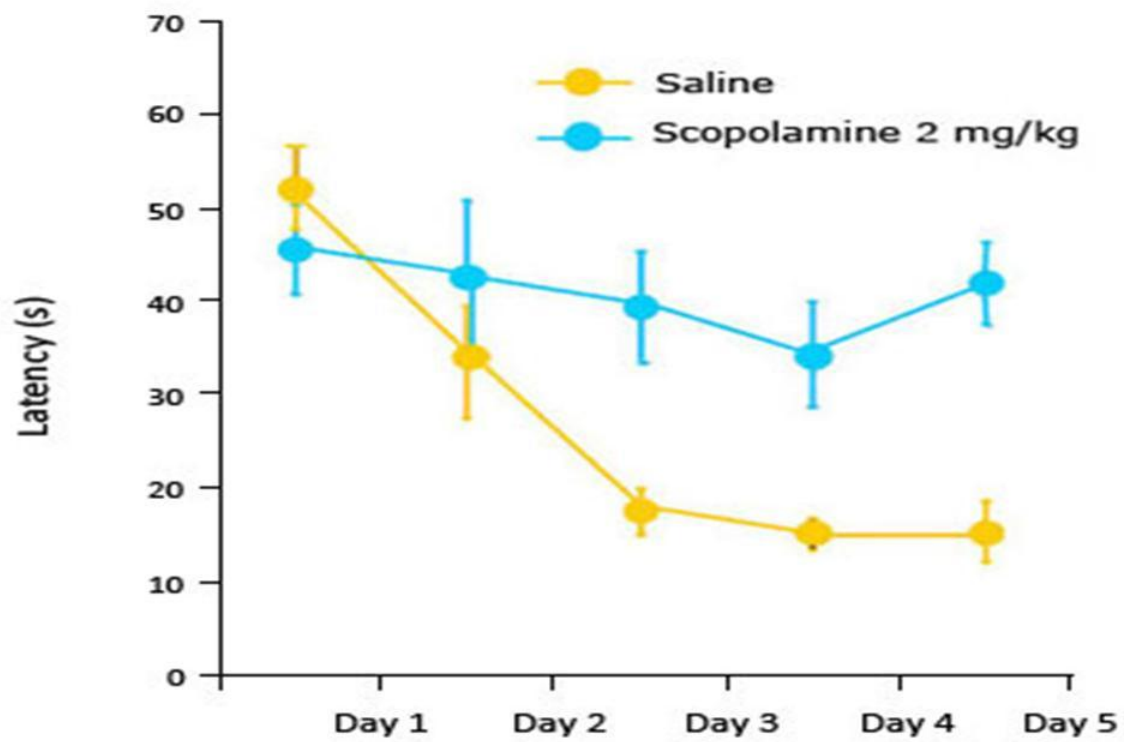
The water maze has 4 starting positions: north, south, east, or west. Take the animal to one of these positions. Lower the animal into the water by supporting it with your hand and bringing it down gently into the water tail-end first. Let the animal swim/search for the platform for a maximum of 60 seconds. At first, the animal may swim around the edge of the pool looking for a way out. Eventually, the animal will learn to search for the platform and climb up.

- Once the rodent reaches the platform, stop the timer, and record the time. If it doesn't find the platform in 60 seconds, then record the time for this trial as one minute.
- Do not pick up the animal if it fails to reach the platform.

Teach the animal that it must swim to the platform.

Therefore, gently guide the animal to the platform with your hand. Let the animal sit on the platform for 15 seconds. If it falls or jumps off, gently guide it back. This will train the animal that it must stay on the platform to be rescued from the pool.

- Repeat the same procedure for two more trials, starting at a different direction for each trial.
- Once the animal has completed all three trials, dry it off with a towel. Repeat the three-trial training process for all the animals consecutively. Keep the directions the same for all of them, and record their times.
- Now that the animals are trained, they are ready to perform the water maze test.



Repeated treatment with the amnesic scopolamine during training impairs acquisition memory for the platform location. Normal acquisition is observed in the vehicle-treated rats as a decrease in latency to find the platform over 5 days of training.