



Biomedical and Obesity Research Core

Nebraska Center for the Prevention of Obesity Diseases through Dietary Molecules

Workshop Training Series

Obesity, Cognitive and Motor Functions -Animal behavior services at BORC

June 20, 2019

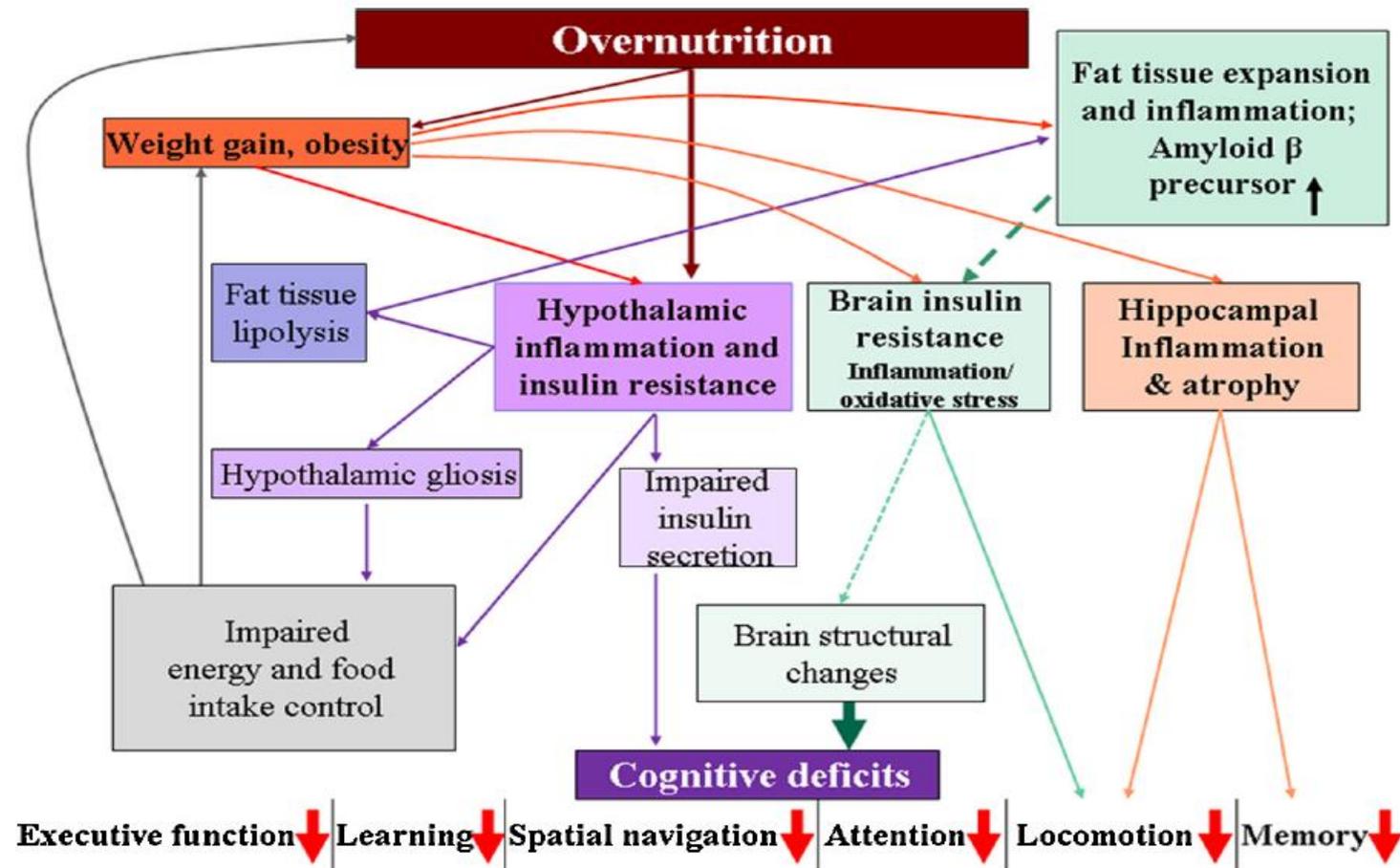
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Dietary Molecules

Obesity is associated with cognitive and motor function impairment

- Healthy obese subjects have some deficits in learning, memory, and executive function relative to non-obese individuals.
- Cognitive performance declines with decreased physical activity and aerobic fitness, which often accompany, if not simply underlie or contribute to, increased fatness and high energy consumption.
- Anxiety and stress-related mental disorders are strongly associated with obesity
- Weight loss improves cognitive function affecting some of the very same cognitive parameters impaired in the obese state.
- Obesity affects motor control capabilities, degrading daily functions and health.

Effects of obesity on the brain and cognitive function



Animal Behavior Research Equipment

[Grip Strength System](#)

[ROTOR-ROD™ System](#)

[SR-LAB™ Startle Response System](#)

[Place Conditioning Preference](#)

[Barnes Maze](#)

[Morris Water Maze](#)

[The Radial Arm Maze](#)

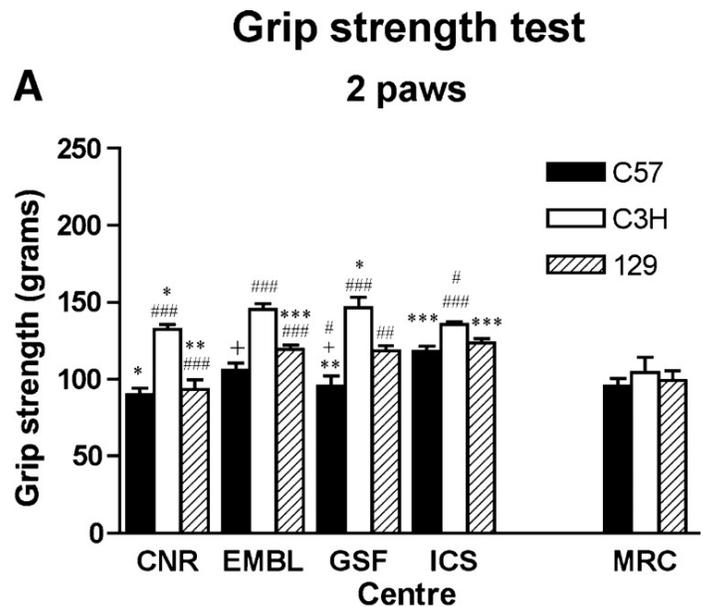
Animal Grip Strength System

The Grip Strength test is used to evaluate motor function and deficit in rodent models



- Animal Grip Strength System measures hind limb and fore limb grip strength.
- Gauge mountings are horizontally and vertically adjustable to accommodate both rats and mice.
- Peak force values (tension and compression) are automatically captured.
- Able to connect to desktop or laptop for quick data recording.

Grip Strength Test



A cross-laboratory study of grip strength test.
Physiological Genomics Published Vol. 34 no. 3, 243-255

- Forelimb (2 paws) grip force measurements of 3 mouse strains in 5 Eumorphia centers (CNR, EMBL, GSF, ICS, and MRC).
- Bars represent the means (\pm SE) of grip strength measurement (in grams of force) averaged across 3 trials.
- The ANOVA revealed a statistically significant effect of strain, center and a statistically significant strain center interaction

Treadmill

The treadmill is an apparatus used to evaluate the effects of exercise and different intensity training on physical health, cognitive and mental health. Scientists usually use it to phenotype different genetic of disease model, assess the recovery of motor and locomotion function from injuries, investigate the drug effects on motor function.



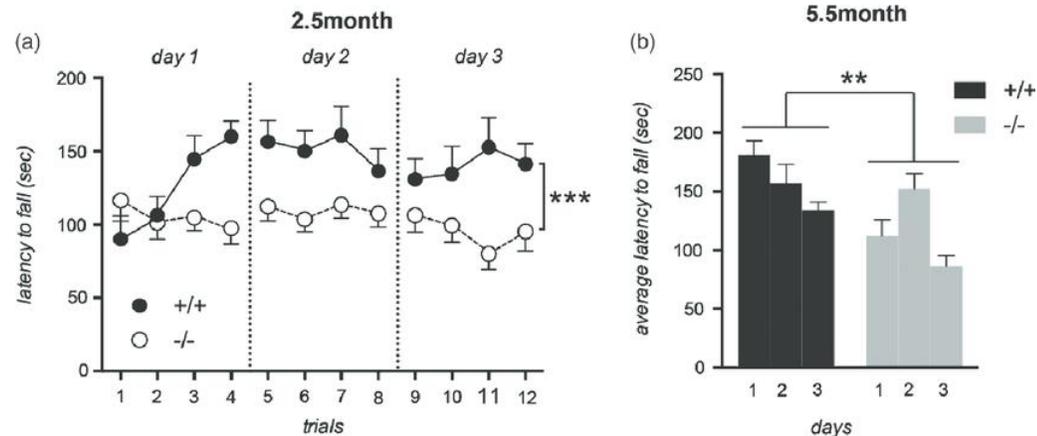
ROTOR-ROD™ System



- Utilize the 'fear of falling' instinct as a natural motivator.
- Measures motor function, motor learning, coordination, and equilibrium in both rats and mice.
- The speed control ramp is constructed of segments that are accelerating, constant or decelerating in any mix.
- Record RPM, fall latencies and distances traveled automatically.

<https://www.youtube.com/watch?v=v56MtrmWAs0>

Motor Function Test



CDKL5 mutated animals fell down earlier compared with the respective WT
Genes Brain and Behavior 15(5) · March 2016

The motor performance was evaluated in 2.5-month-old animal and re-tested in the same animal when 5.5 months old.

(a) Each point represents the latency to fall down during the three consecutive days of the test.

(b) shows performance of the same animal at 5.5 months of age, analysed by pooling the trials of each day to limit motivation and motor learning bias.

The overall evaluation of performance (from trial 1 to 12) indicates that CDKL5 mutated animals fell down earlier compared with the respective WT

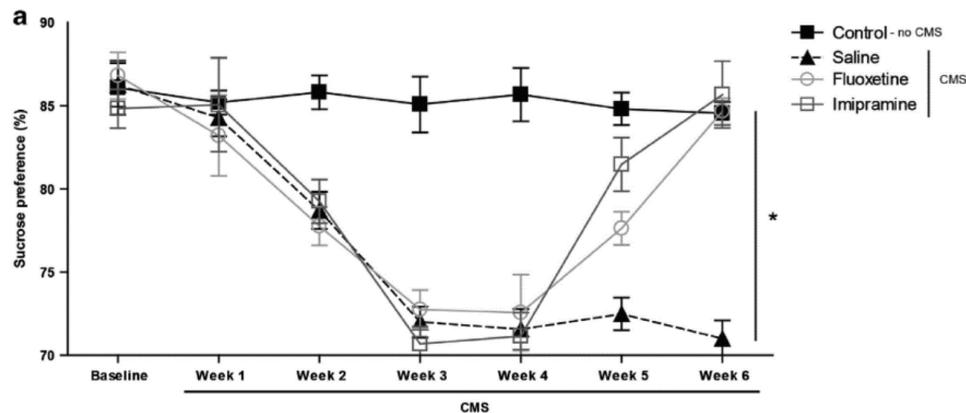
Place Preference Enclosure Equipment



1. Place preference is a form of Pavlovian conditioning in which a distinctive environmental cue (the positive conditioned stimulus or CS+) becomes associated with a motivationally significant event (the unconditioned stimulus or US).
2. Place conditioning is most often used with rodents (rats, mice) to study the positive (rewarding) or negative (aversive) motivational effects of objects (e.g., food pellets, novel toys) or experiences (e.g., brain stimulation, drug intoxication, drug withdrawal, illness, wheel running and copulation).

https://www.youtube.com/watch?time_continue=82&v=RKTa6EuTsnQ

Place Preference Test



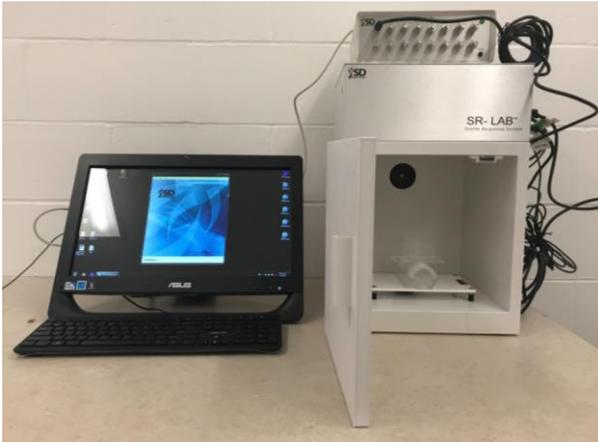
- **Animals exposed to chronic mild stress (CMS) revealed a significant decrease in sucrose preference when compared with control animals.**
- **The administration of antidepressants in the last 2 weeks of the CMS protocol significantly reversed this behavioral phenotype**

Animals exposed to chronic mild stress revealed a significant decrease in sucrose preference.

Transl Psychiatry (2013) 3, e266

The SR-LAB Startle Response System

The SR-LAB™ Startle Response System is the world's most widely used system for startle reflex measurement and by far the most successful for fear potentiated startle and pre-pulse inhibition testing.



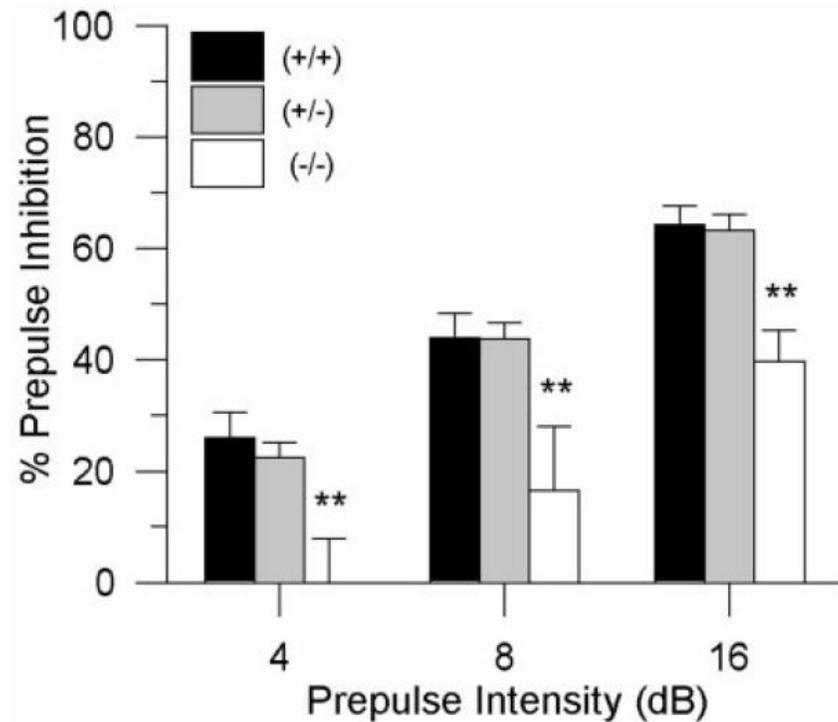
Experimental paradigm

- Acoustic startle reflex
- Fear-potentiated startle
- Pre-pulse inhibition
- Delay and trace conditioning

Application

- drug toxicity,
- auditory system physiology,
- neurodevelopment
- behavioral genetics.

Pre-pulse Inhibition Test



PPI was significantly disrupted in the DAT (dopamine transporter) knock-out mice at each pre-pulse intensity, compared with both DAT wild type and DAT heterozygous mice

Equipment For Spatial Learning And Memory -Barnes Maze

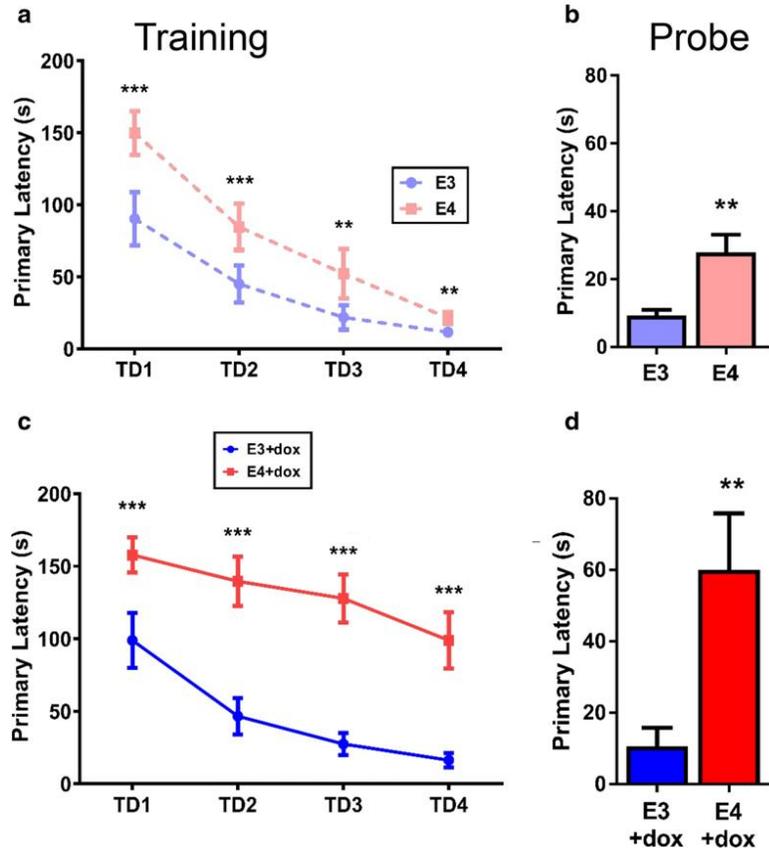
The Barnes maze is a spatial memory task that requires subjects to learn the position of a hole that can be used to escape the brightly lit, open surface of the maze.



- The task relies on the innate preference of rodents for dark, enclosed spaces over open areas.
- The Barnes maze consists of a flat, circular disk with a number of holes around its perimeter that permit the subject to exit the maze into an escape box.
- Subjects are presumed to learn the location of an escape hole using spatial reference points that are either fixed outside the maze (extra-maze cues) or on the maze in relation to the escape hole (proximal cues).
- **Errors** (indicated by the animal placing its nose or forepaws at the edge of a hole that did not lead to the escape chamber), **latency** (which is the time it takes to find the platform), and **the distance and time** traveled to get to the escape hole **are measured**.

<https://www.youtube.com/watch?v=MBwoYJ7MdI8>

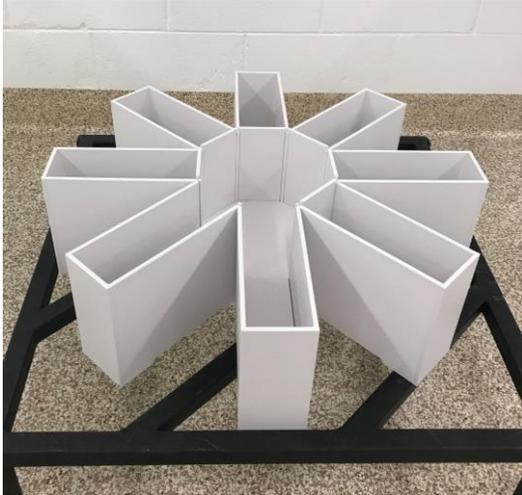
Spatial Learning And Memory Test



- Barnes maze spatial learning and memory in untreated and doxorubicin-exposed human APOE3 and APOE4 knockin mice.
- Reduction in latency to the target hole is recorded as a measure of training in this spatial learning task.
- Compared to APOE4 mice, APOE3 mice showed significantly shorter latencies during all four training days and during individual trials on training day 1, in both untreated (a) and treated (c) cohorts.
- A 72-h probe trial for untreated animals (panel b) and doxorubicin-exposed animals (panel d) showed lower latency for APOE3 mice compared to APOE4 mice, irrespective of treatment.

Equipment for spatial learning and memory

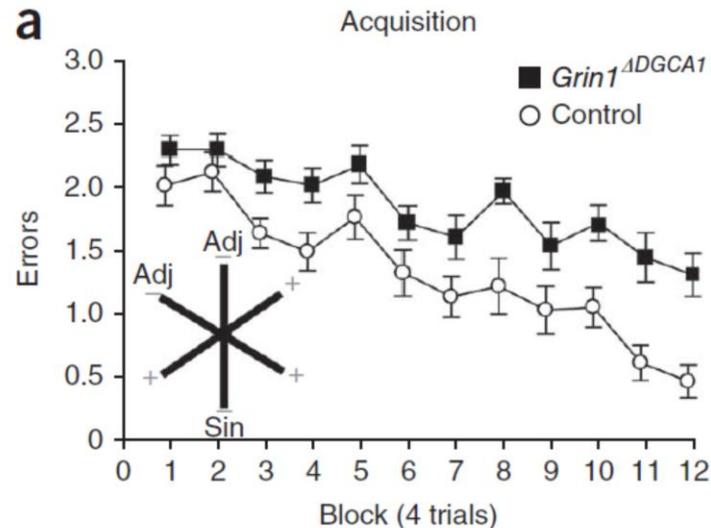
-Radial Arm Maze



- There are multiple version of experimental design for radial arm maze.
- Investigators measure the amount of time it takes for animals to find the arm leading to food, as well as the number of times it traverses an arm it has previously visited (error).
- **Reference memory** is assessed when the animals only visit the arms of the maze which contains the reward. The failure to do so will result in reference memory error.
- **Working memory** is assessed when the animals enter each arm a single time. Re-entry into the arms would result in a working memory error.

<https://www.youtube.com/watch?v=8LAvXj65JNl>

Long-term Spatial Reference Memory Test



- ***Grin1*^{ΔDGCA1}: NMDARs (neurotransmitters) are lacking in dorsal and ventral hippocampal CA1 pyramidal cells, specifically in adulthood**
- ***Grin1*^{ΔDGCA1} mice made significantly more spatial reference memory errors.**

***Grin1*^{ΔDGCA1} mice were impaired in learning a radial maze task**
Nature Neuroscien volume 15, number 8

Equipment for spatial learning and memory

-Morris Water Maze

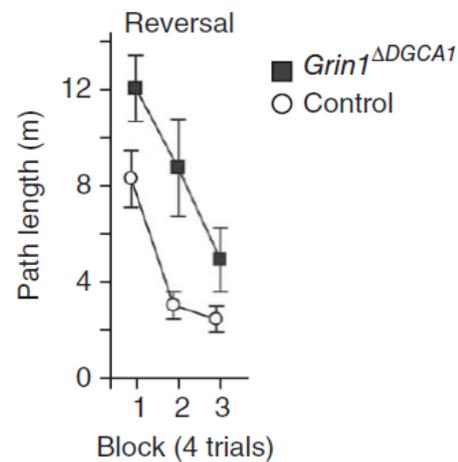
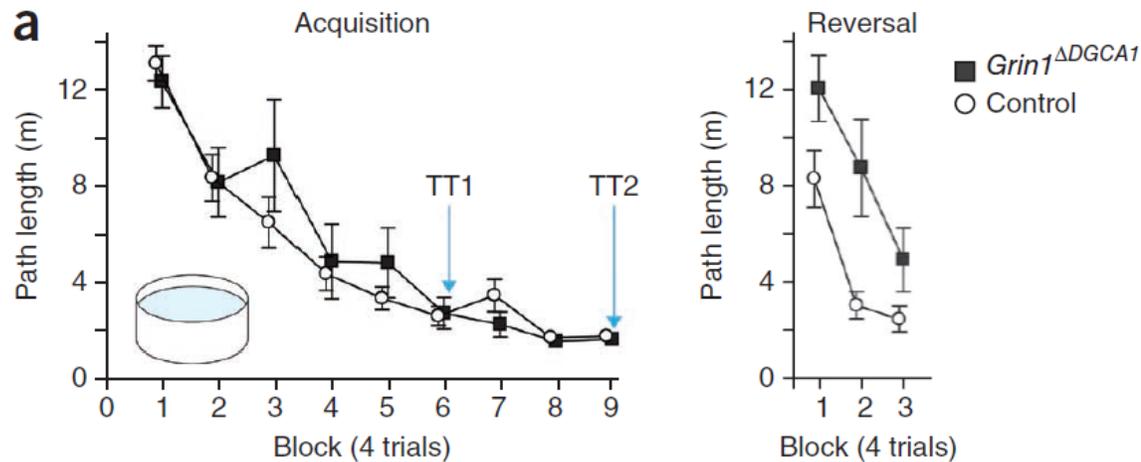


The Morris water maze (MWM) is a test of spatial learning and reference memory for rodents that relies on distal cues to navigate from start locations around the perimeter of an open swimming arena to locate a submerged escape platform.

- MWM learning impairments are independent of locomotor effects
- **Spatial learning** is assessed by length of path traveled by animals to locate the escape platform.
- **Reference memory** is determined by preference for the platform area when the platform is absent.
- Reversal and shift trials enhance the detection of spatial impairments.

<https://www.youtube.com/watch?v=leHLL4vcbCc>

Spatial Reference Memory Test



- Controls and *Grin1*^{ΔDGCA1} mice demonstrated similar path lengths during acquisition of memory in the fixed-location, hidden-escape-platform water maze task.
- Reversal trials (platform was moved to the opposite quadrant of the pool) showed that the path lengths of *Grin1*^{ΔDGCA1} mice were significantly longer than those of controls

The path lengths of *Grin1*^{ΔDGCA1} mice were significantly longer than those of controls
Nature Neurosciences volume 15, number 8

Thank you