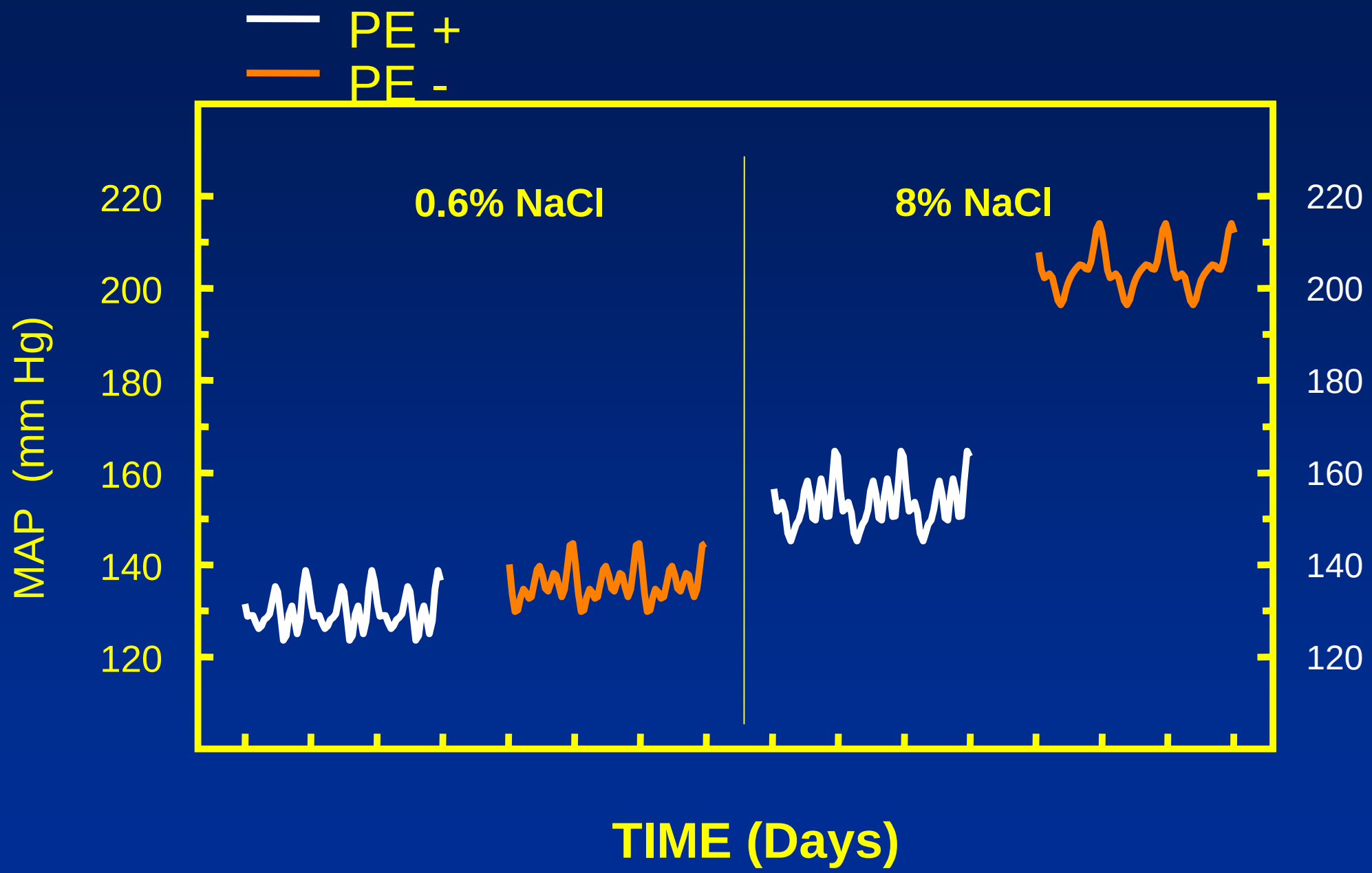
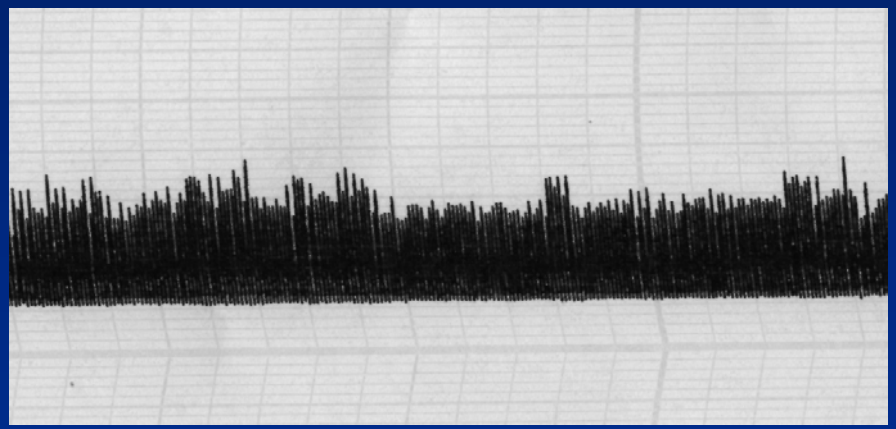
Circadian rhythm of blood pressure and plasma sodium

Mean Arterial Pressure (mm Hg)
160
140
120
100
80
60
40
24
12
24
12
24
12
24
12
24
Clock Hour

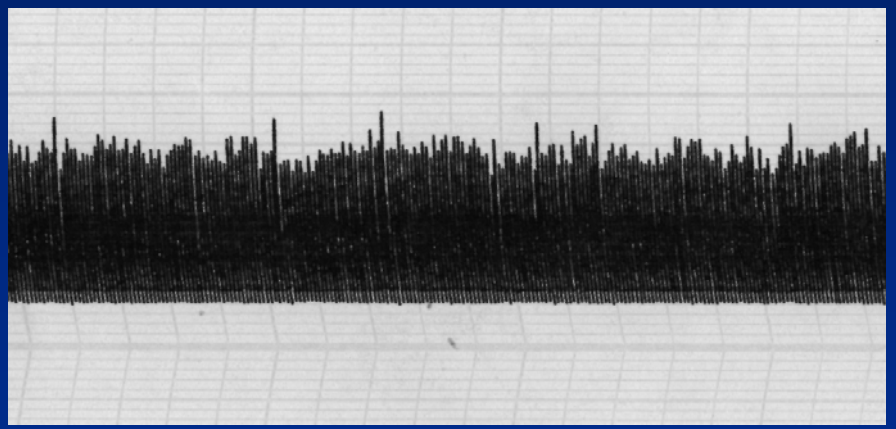


Fang, et al., AJP 281:R1934 2001

Circadian rhythm of sympathetic nervous system activity

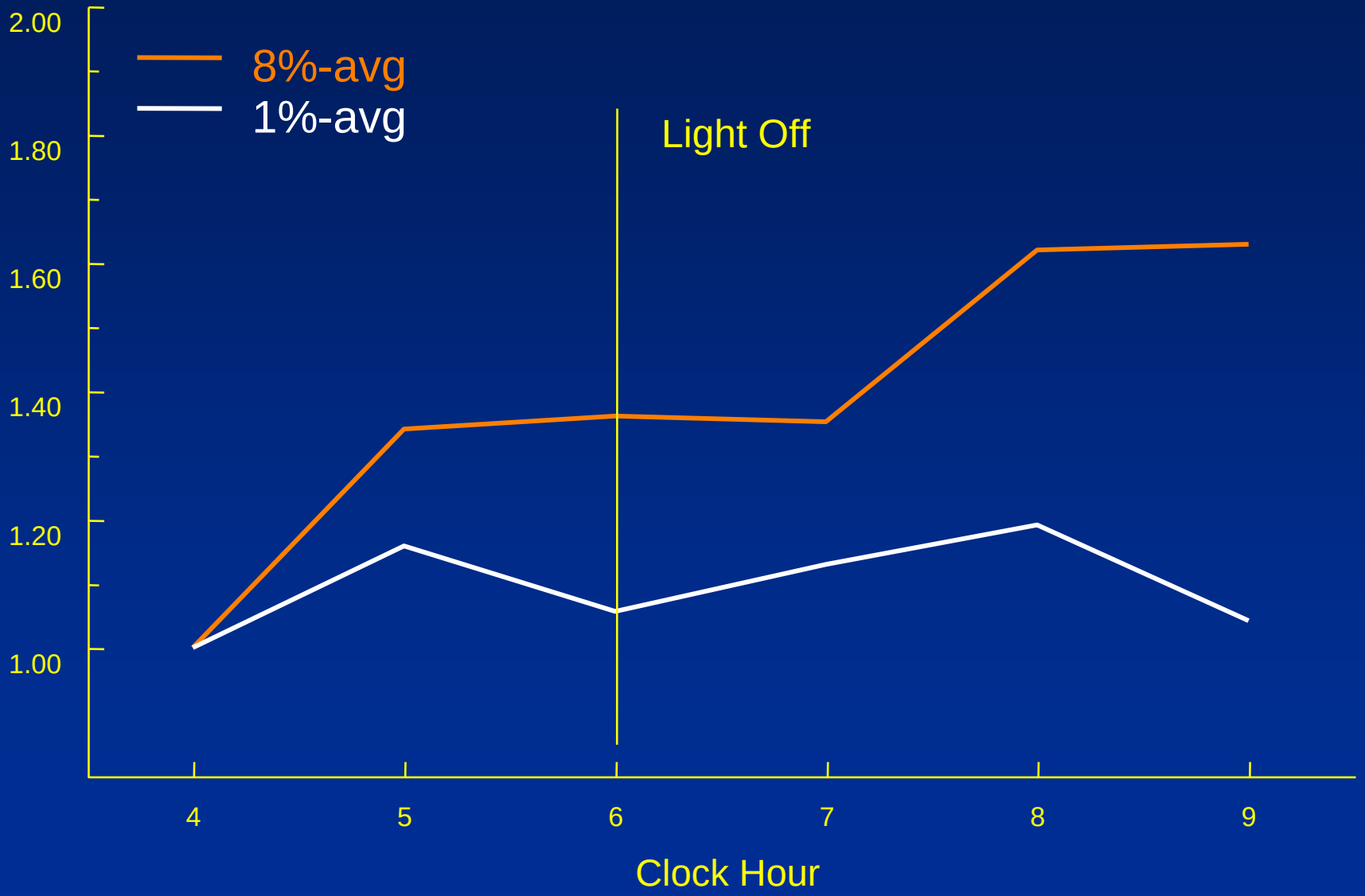


16:00 h

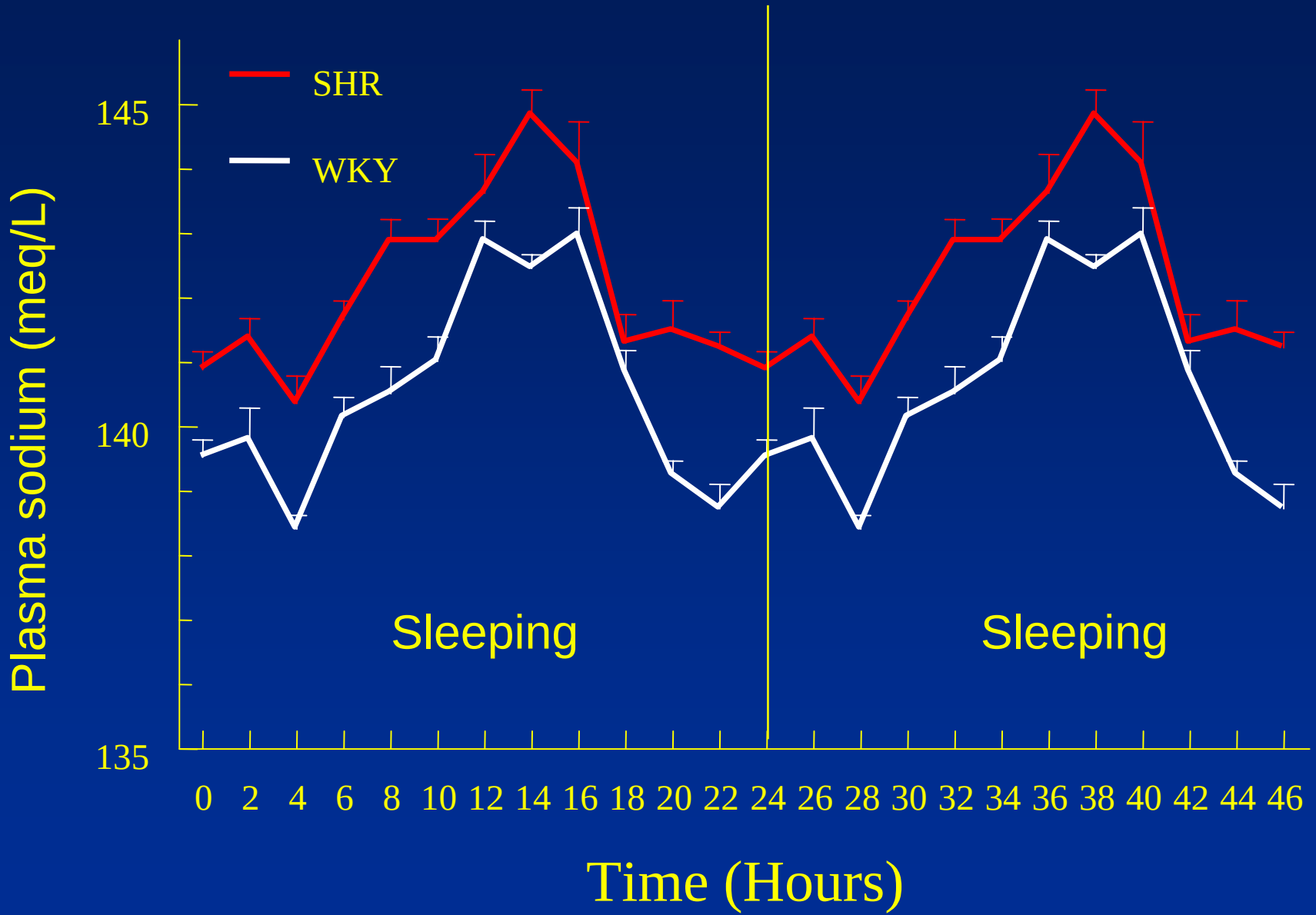


19:00 h

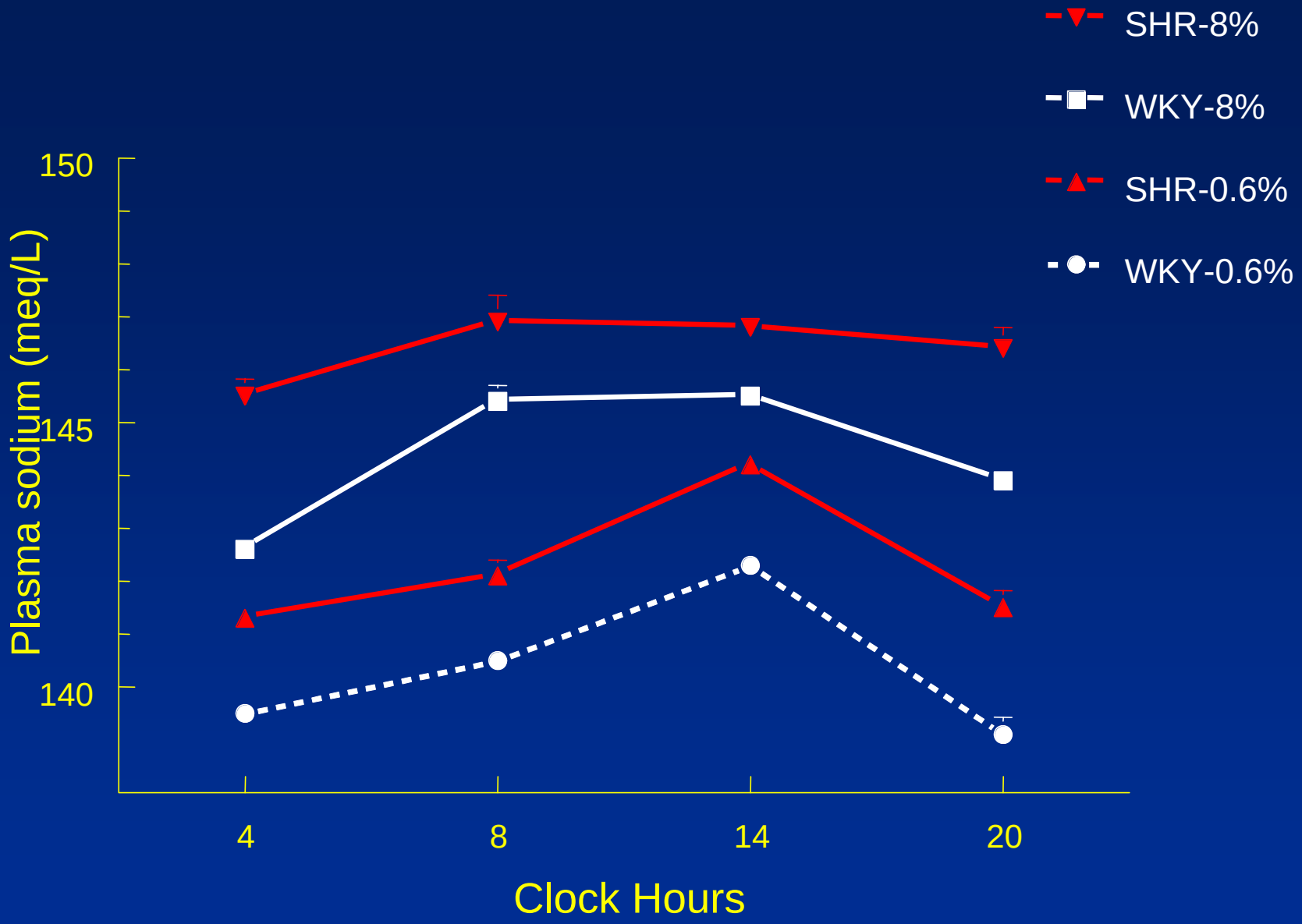
Circadian rhythm of sympathetic nervous system activity at time of awakening



Plasma Sodium Rhythm in WKY vs. SHR



Fang, et al., AJP 278:R1490-R1507, 2000



Fang, et al., AJP 278:R1490-R1507, 2000

Methods to measure blood pressure and heart rate

- Tail cuff
- Tethered catheter
- Telemetry: gold standards

Methods to measure blood pressure and heart rate

- Tail cuff
  - Easy to do
  - Inexpensive
  - Good for longitudinal studies

  - But
  - About 20 mm detection limit
  - Relative worse in mice
  - Greatly effected by stress

Methods to measure blood pressure and heart rate

- Tail cuff
- Tethered catheter
  - Very good for acute studies
  - Inexpensive but labor (surgery) intensive
  - Much more accurate than TC

  - But
  - Prone to stress from tethering
  - Can lose patency
  - Use heparin to maintain patency

Methods to measure blood pressure and heart rate

- Tail cuff
- Tethered catheter
- Telemetry: gold standards
  - Very accurate
  - Circadian cycle monitored easily (set it and forget it)
  - But large transmitter for small animals
  - Battery life relatively poor
  - Very expensive (up to $500/mouse)

Methods for MAP Measurement in Mice

- Tail Cuff (Kroger et al.)
- Acute Catheterization (Tian et al.)
- Chronic Catheterization
- Telemetry

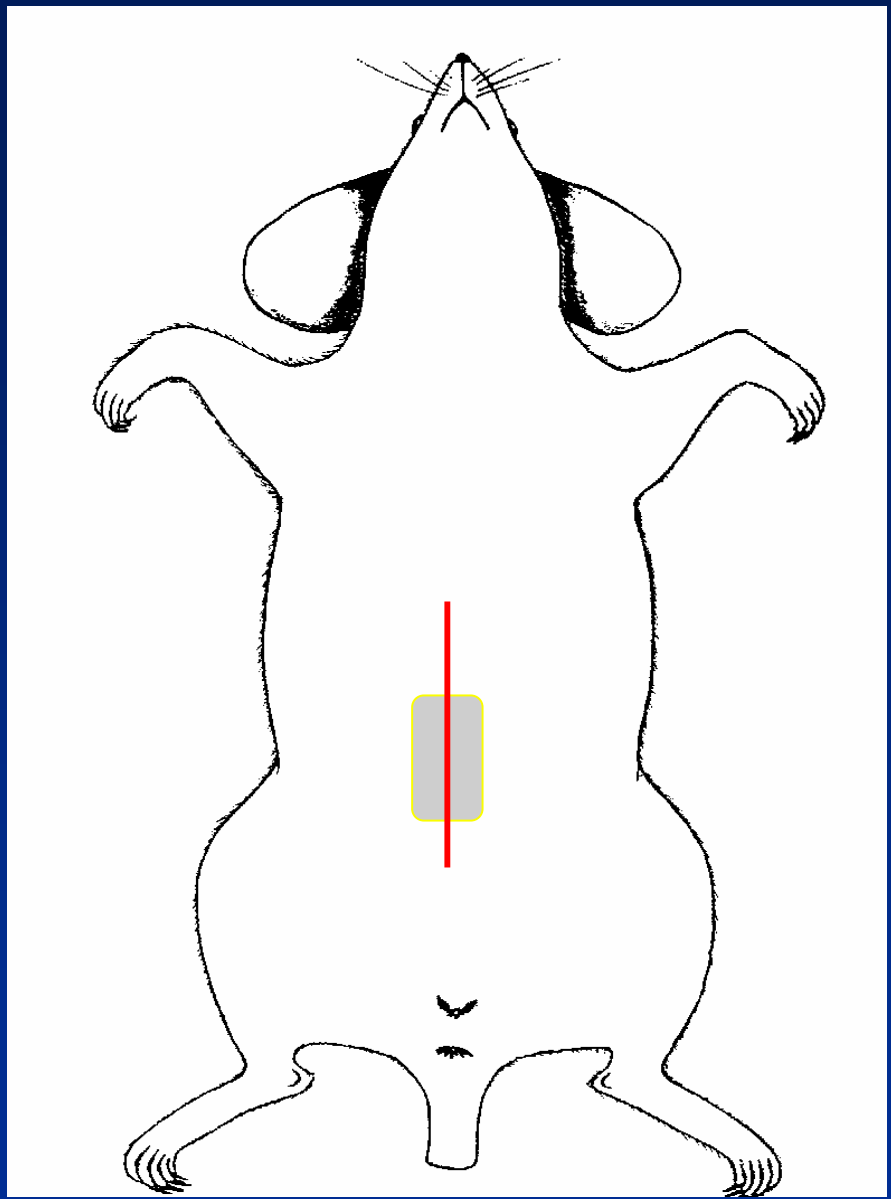
Telemetric Recording in Mice: A Comparison of Carotid and Abdominal Aorta Implantation

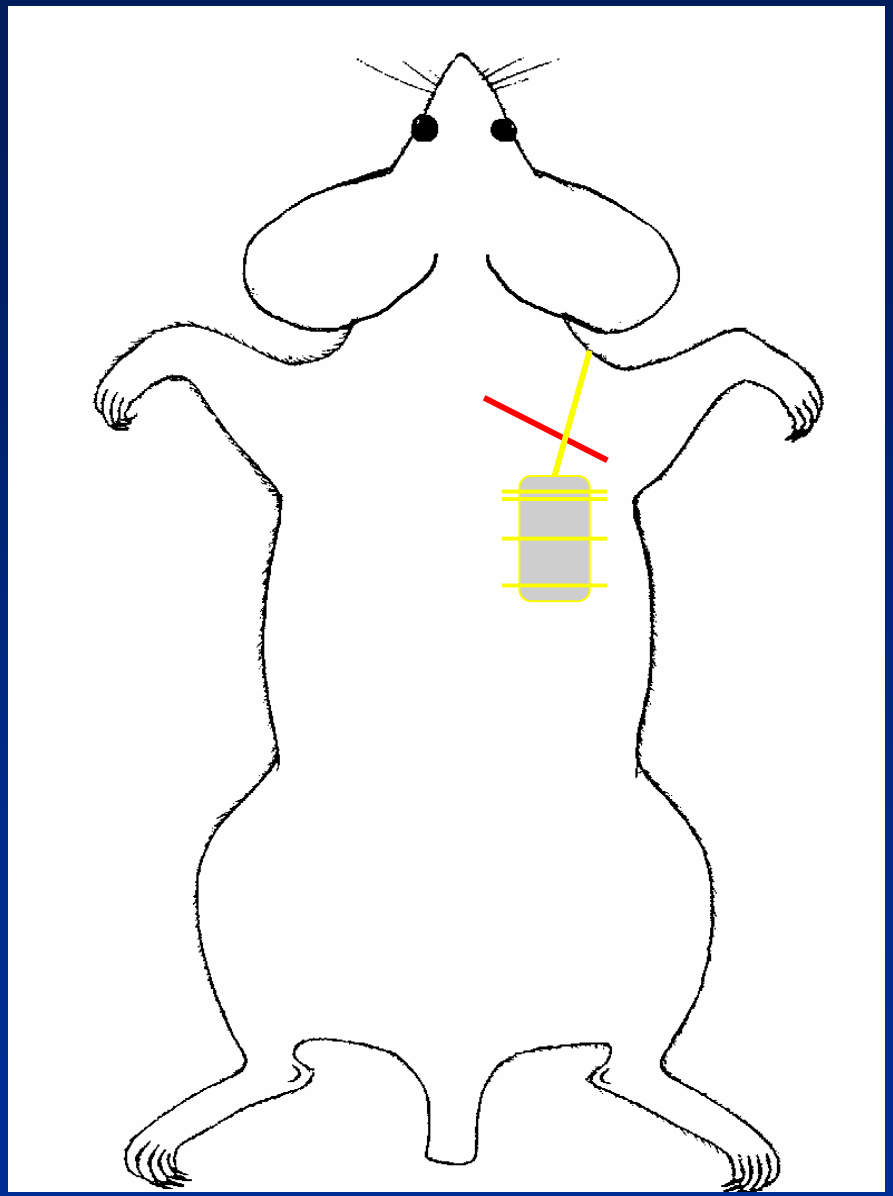
The effect of a high NaCl diet on MAP and HR in mice

Carlson and Wyss. *Hypertension*, 35: e1-e5, 2000

Abdominal Aorta Implantation

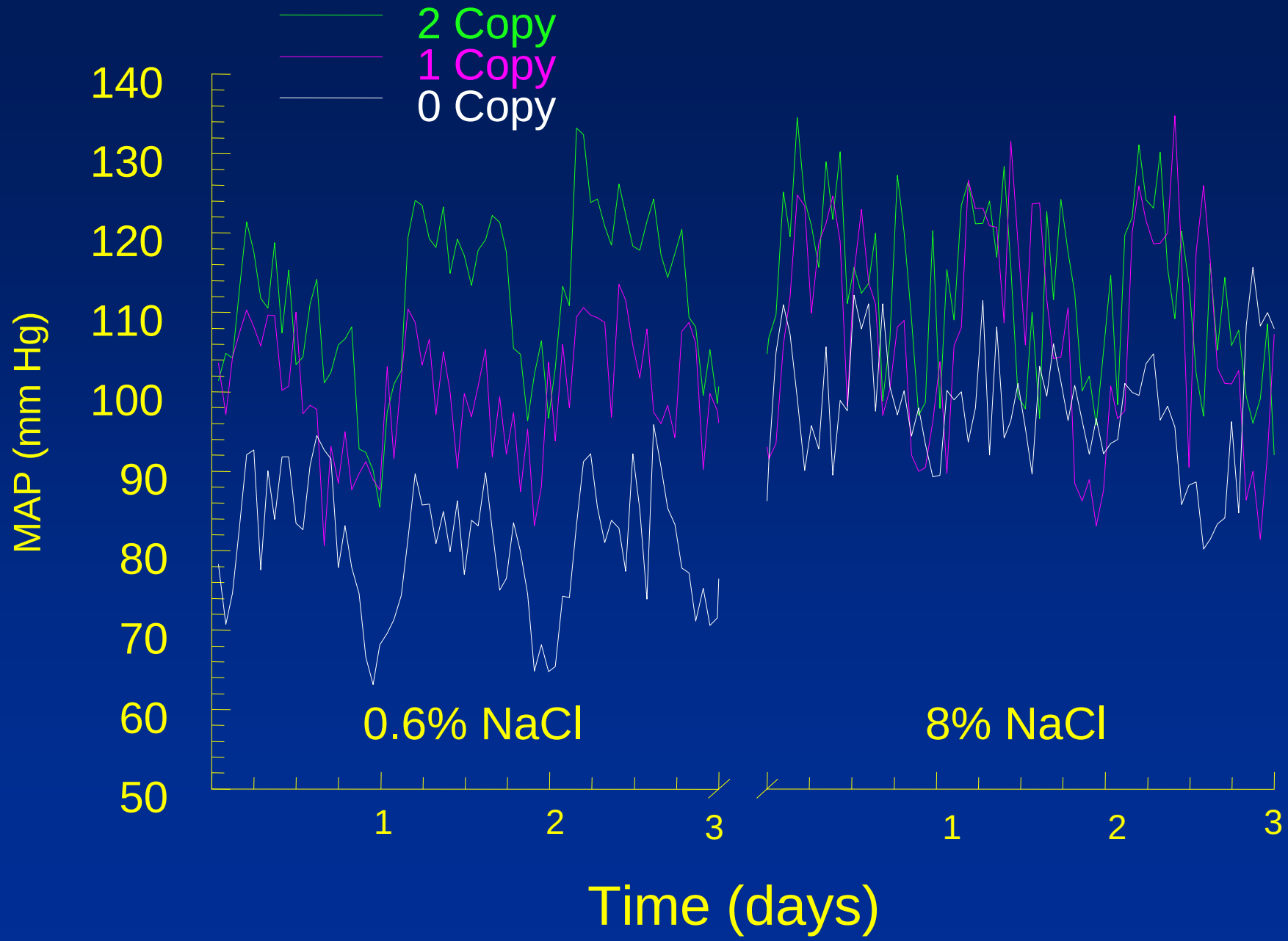
- Sterile conditions
  - Hair removed
  - Disinfection
- Isoflurane anesth.
- Minimal disturbance of aorta
- Minimal occlusion time
- Catheter smoothness
- Probes warmed
- Minimal Vet-bond
- Post-op heating





Carotid Artery Implantation

- Isoflurane or injectable anesthesia
- Aseptic conditions
- Incision from right shoulder to mid-scapular region
- Slide probe under skin
- Suture through muscle around probe
- Sutured to skin


2 Copy
1 Copy
0 Copy
140
130
120
110
100
90
80
70
60
50
MAP (mm Hg)
0.6% NaCl
8% NaCl
1
2
3
1
2
3
Time (days)

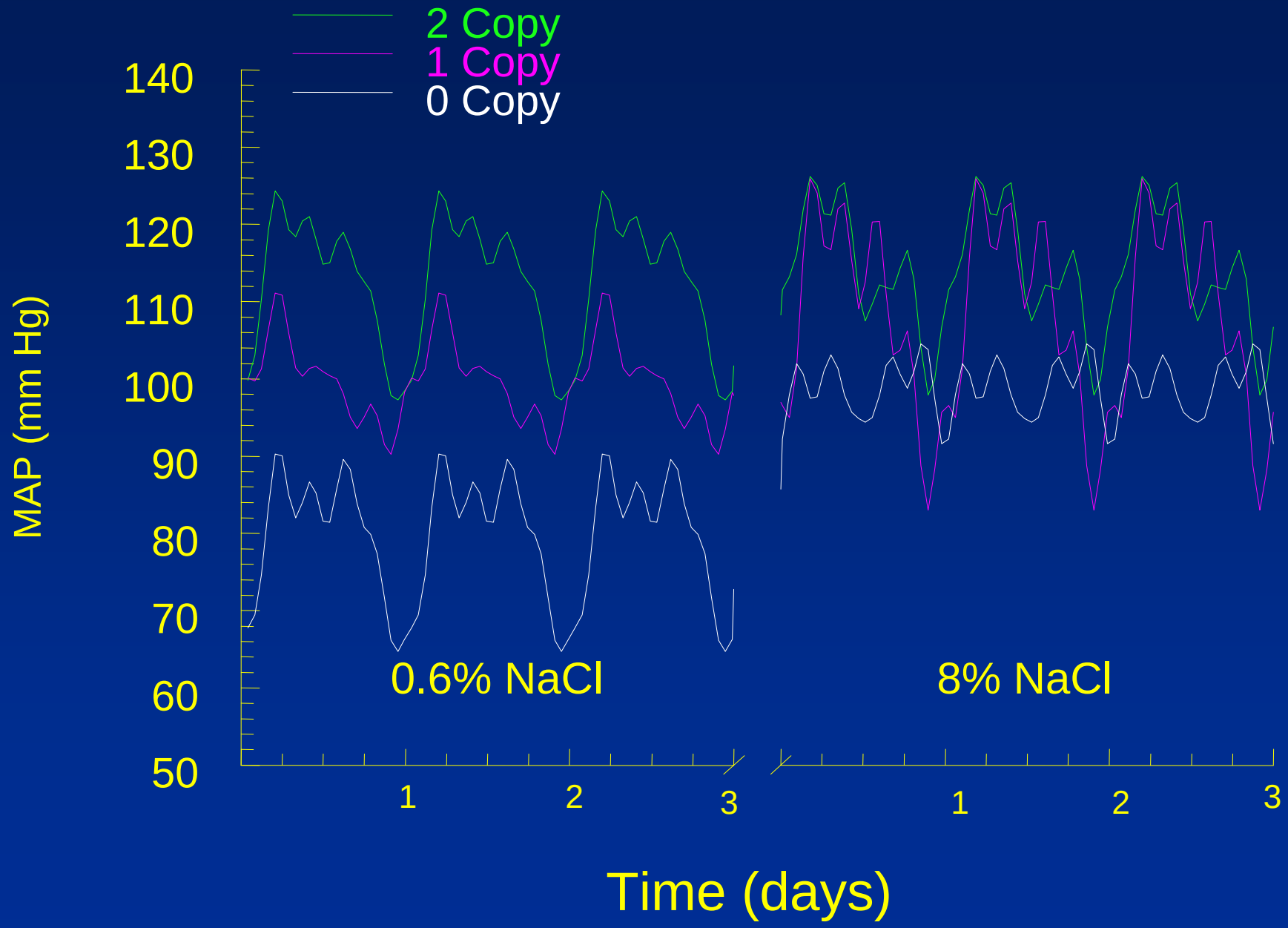

2 Copy
1 Copy
0 Copy
140
130
120
110
100
90
80
70
60
50
MAP (mm Hg)
0.6% NaCl
8% NaCl
1
2
3
1
2
3
Time (days)

Table 1. Mean Arterial Pressure (MAP) and Heart Rate in 2 Copy (+/+; n=7), 1 Copy (+/-; n=7) and 0 Copy (-/-; n=6) ACE Knockout Mice Maintained on a Basal (0.6%) NaCl Diet

	+/+	+/-	-/-
24-Hour MAP Rhythm (3-day averages):			
MESOR (mm Hg)	111.8 ± 4.2	100.0 ± 3.5*	80.7 ± 3.7*#
Amplitude (mm Hg)	19.8 ± 0.6	12.6 ± 0.5*	17.7 ± 0.7
Acrophase (Hour)	01:16 ± 1.0	10:01 ± 0.7#	02:11 ± 0.7
Peak (mm Hg)	126.2 ± 3.6	111.4 ± 1.0*	93.4 ± 1.8*#
Nadir (mm Hg)	93.5 ± 4.1	84.7 ± 2.9	64.4 ± 0.7*#
24-Hour MAP Rhythm (3-day averages):			
Heart Rate (bpm)	551.7 ± 14.1	555.1 ± 12.0	457.9 ± 9.8*#

* $p < 0.05$ versus the +/+ group; # $p < 0.05$ versus all other groups

Surgical Protocol

- Anesthesia
  - Ketamine (100 mg/kg) - Xylazine (15 mg/kg) diluted in 0.9% NaCl
  - Isoflurane (inhalant)
- 7-Day Recovery Period

Do a cost benefit assessment before you dive in.

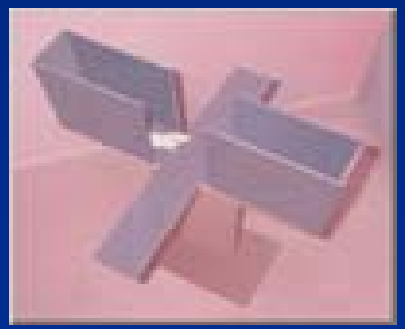
Other hormones

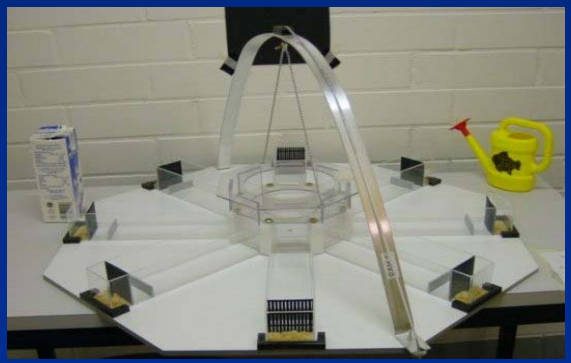
Behavior

- Cognition

  Learning and memory
- Motor function
- Sensory function
- Motivation

Behavioural tasks



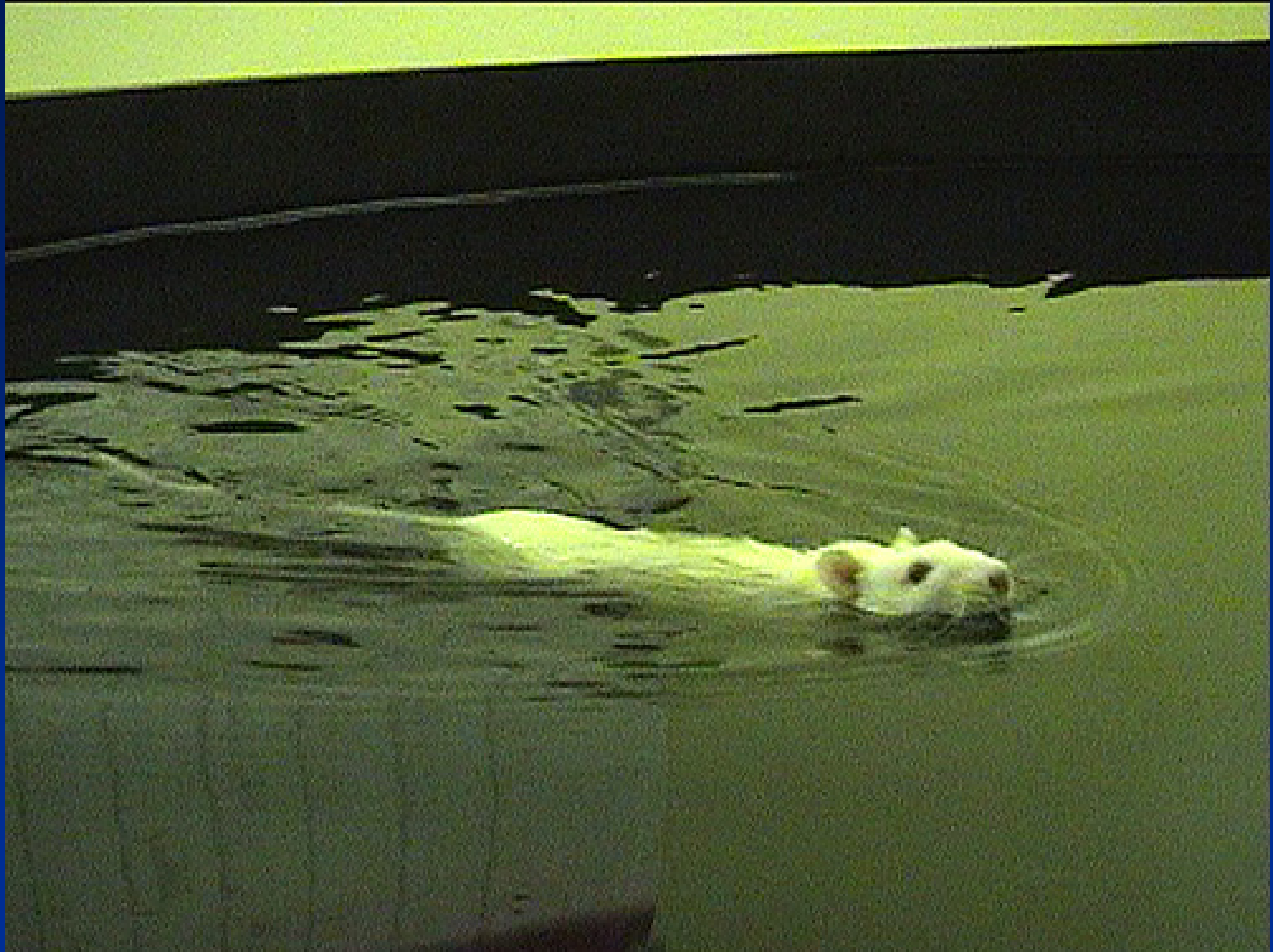


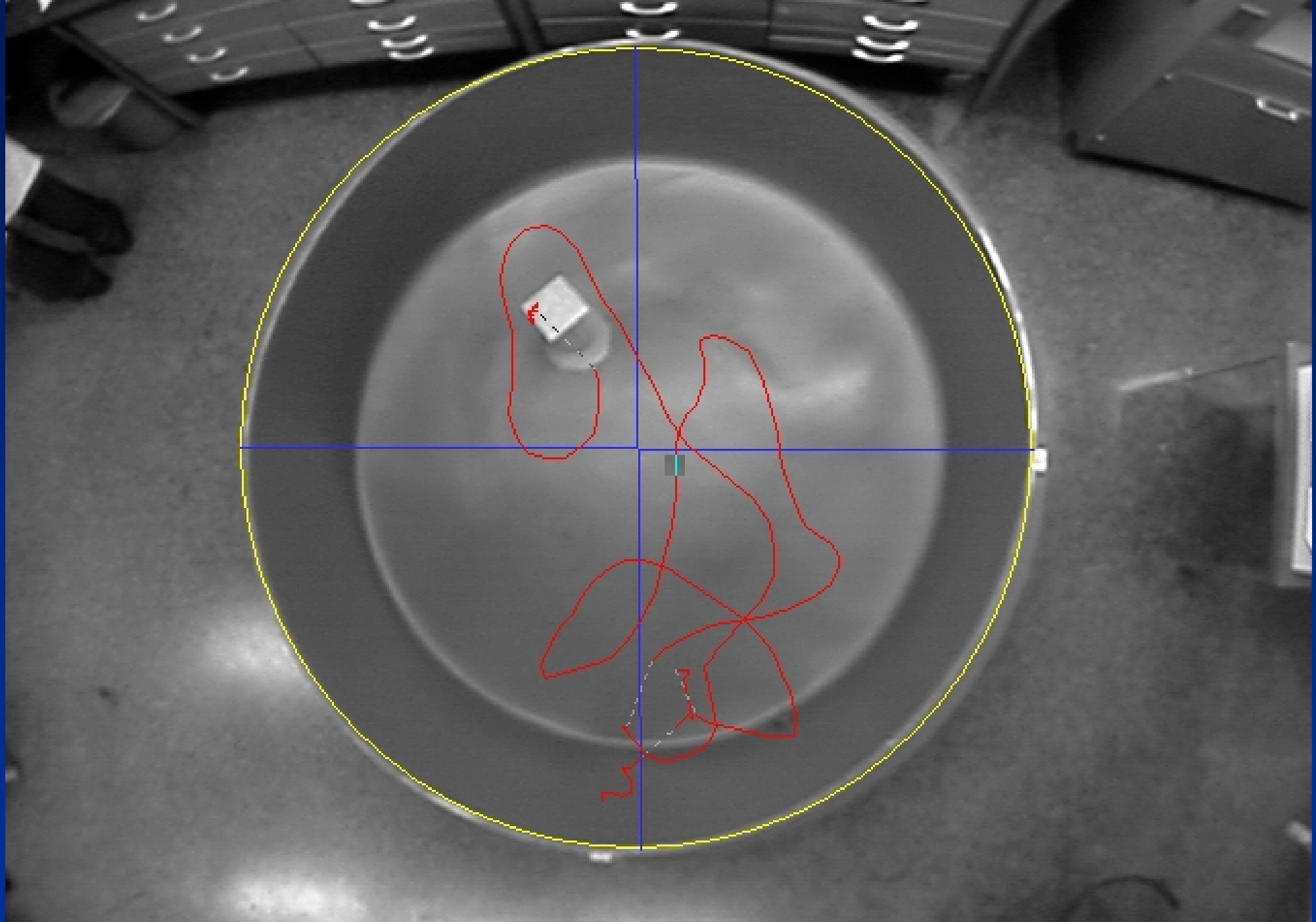
Behavior

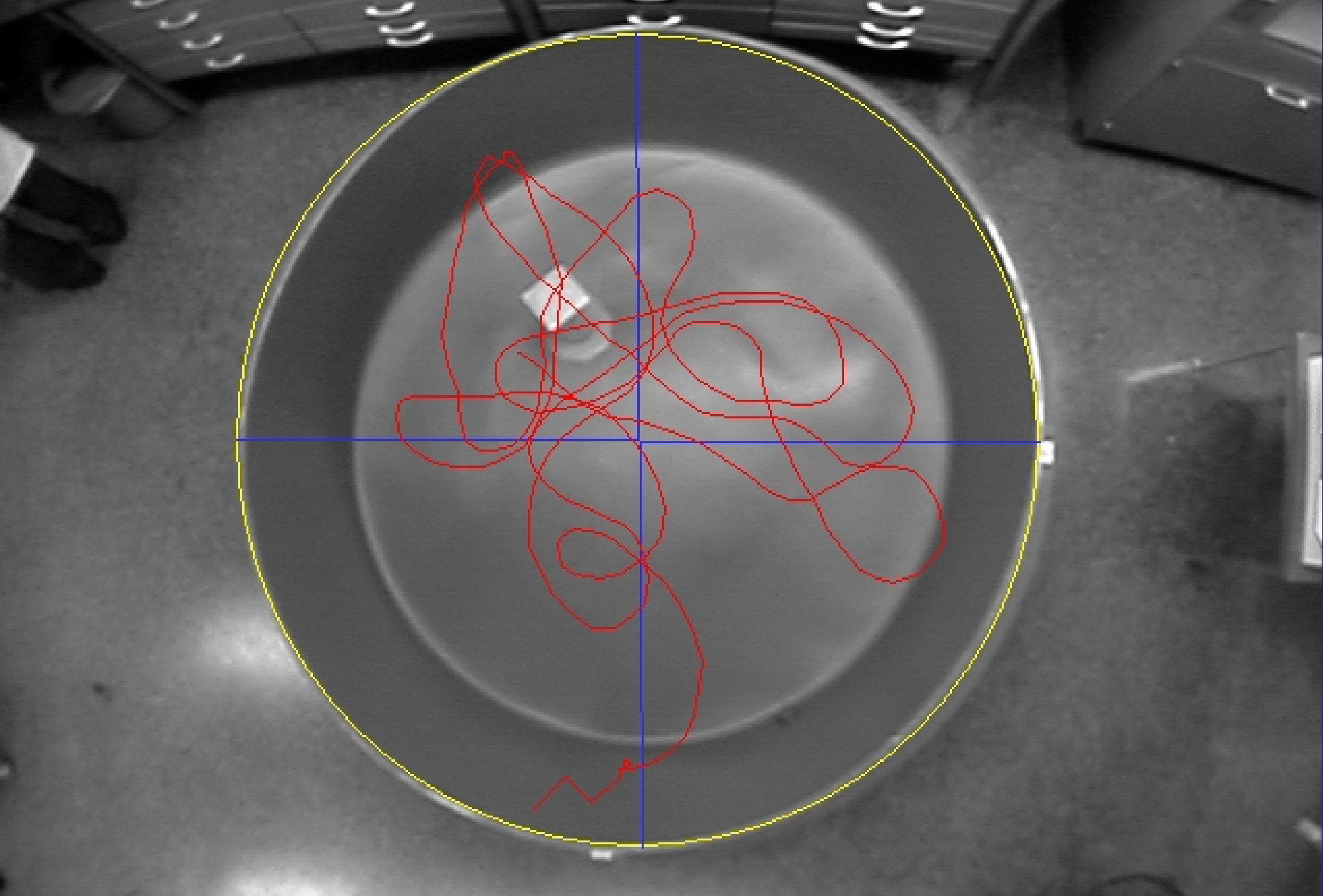
- Cognition

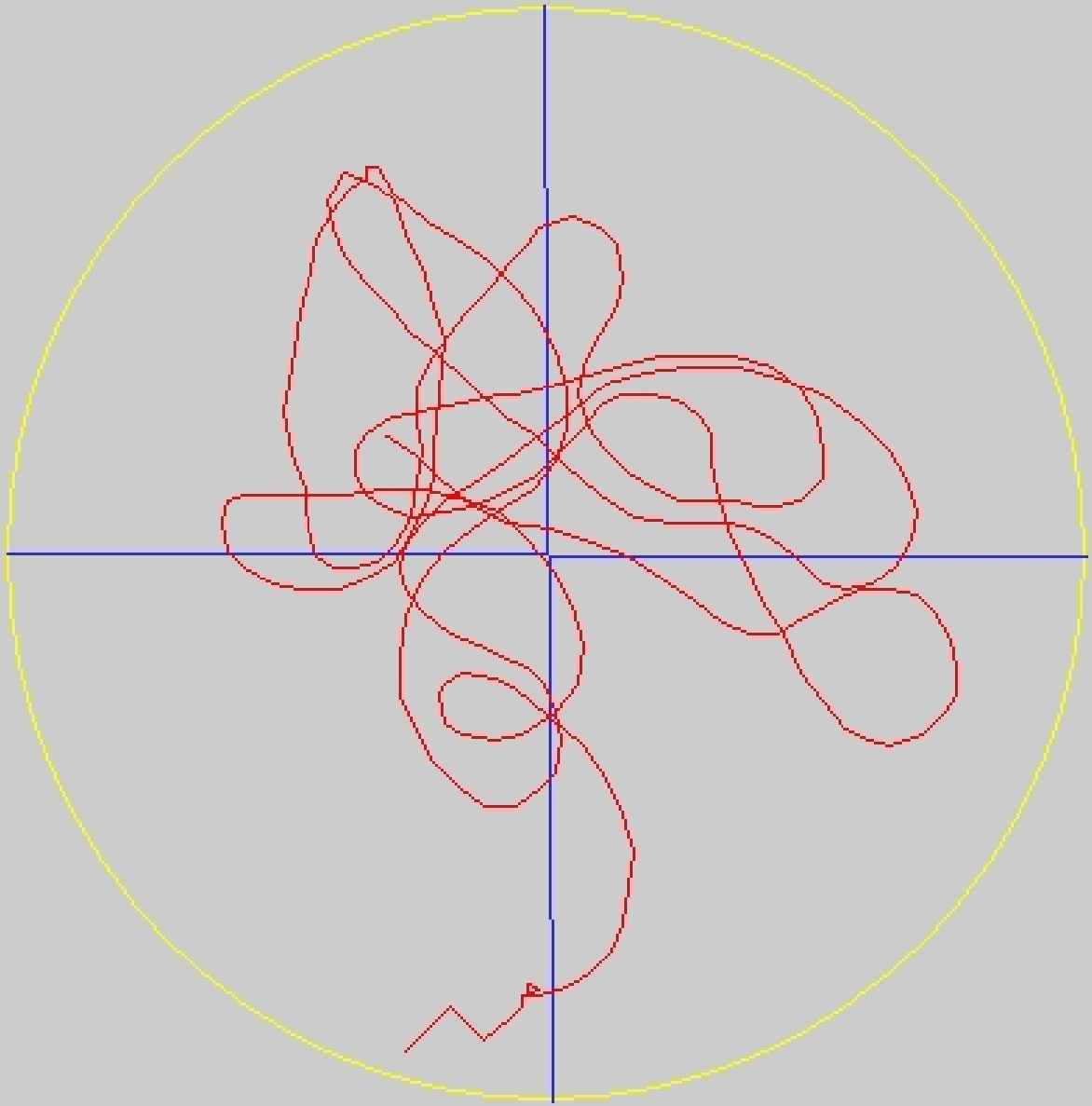
  Learning and memory

    Morris Water maze







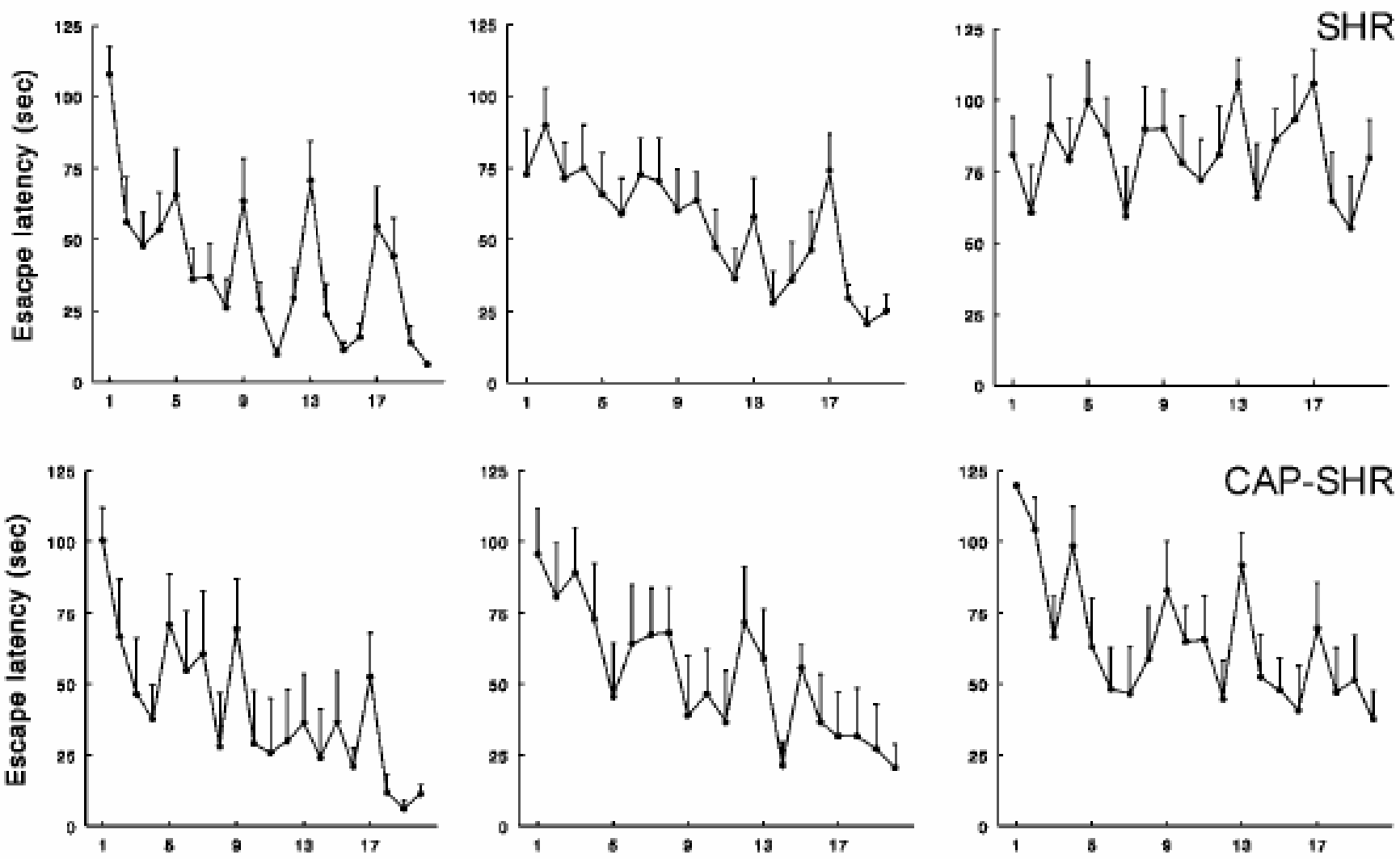


Which is smarter

- Latency to platform
- Distance to platform
- Role of Motor function
- Role of Motivation

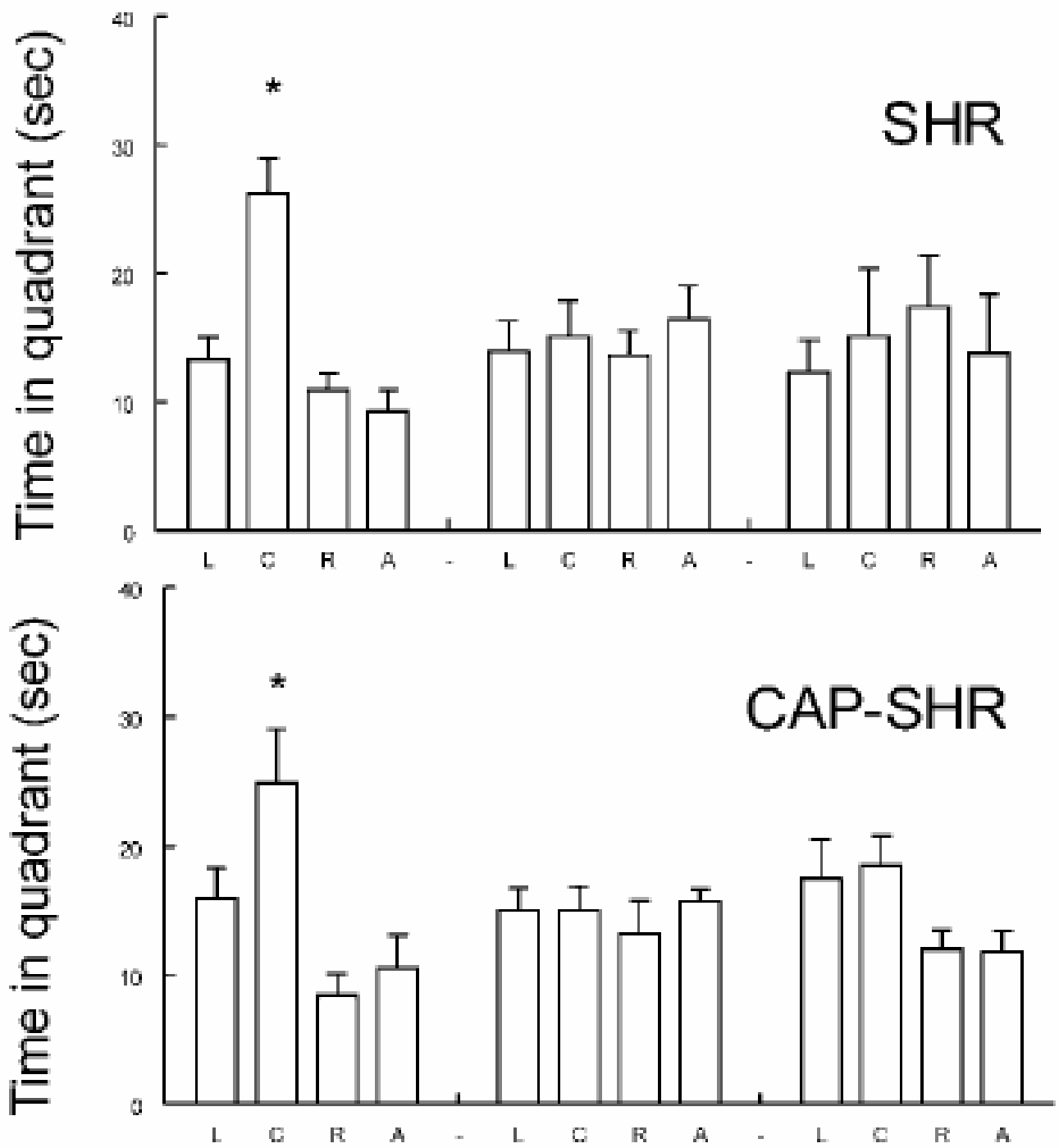
- What are the rodents seeking?

Reacquisition task

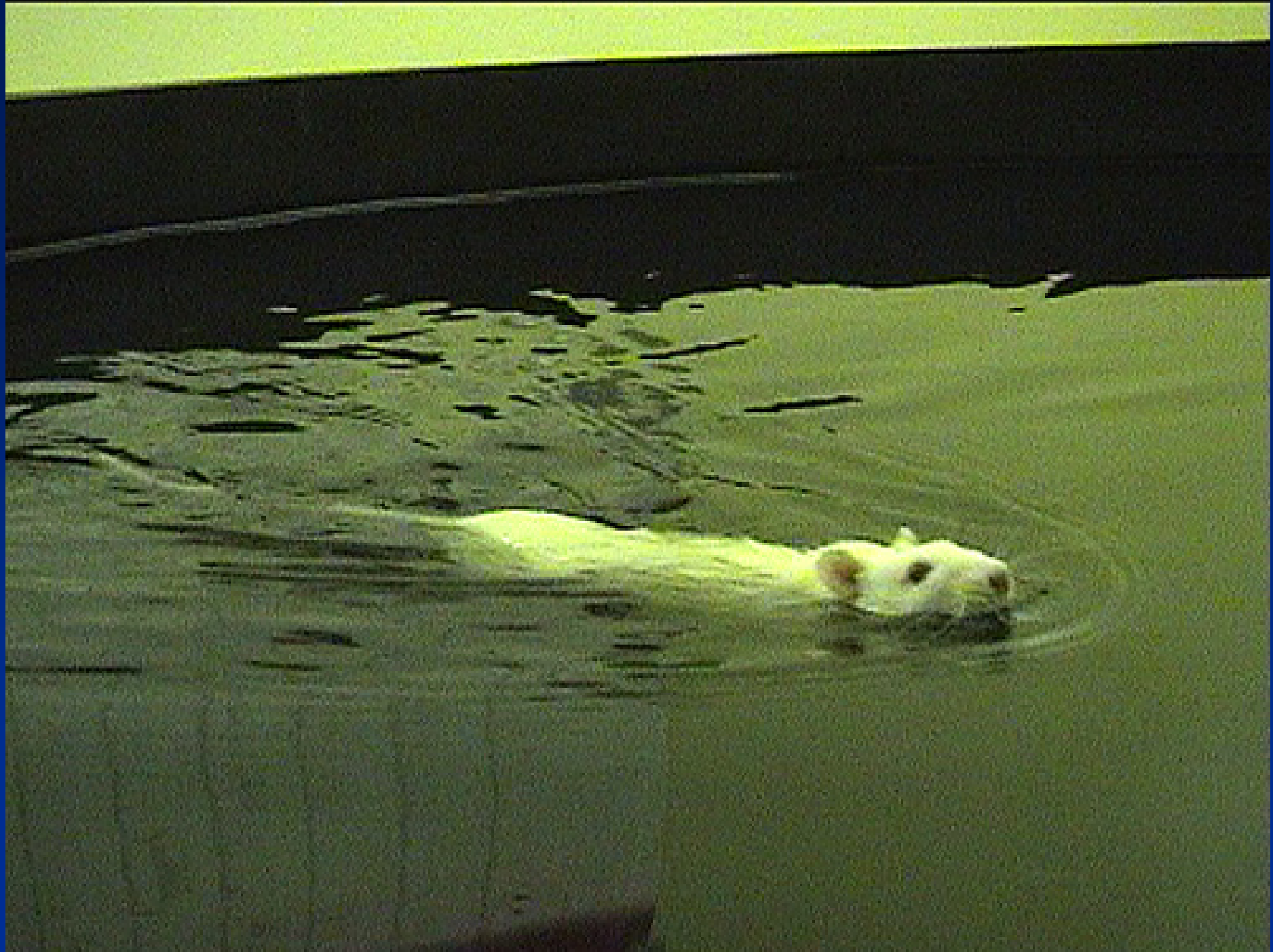


3 months 12 months 18 months

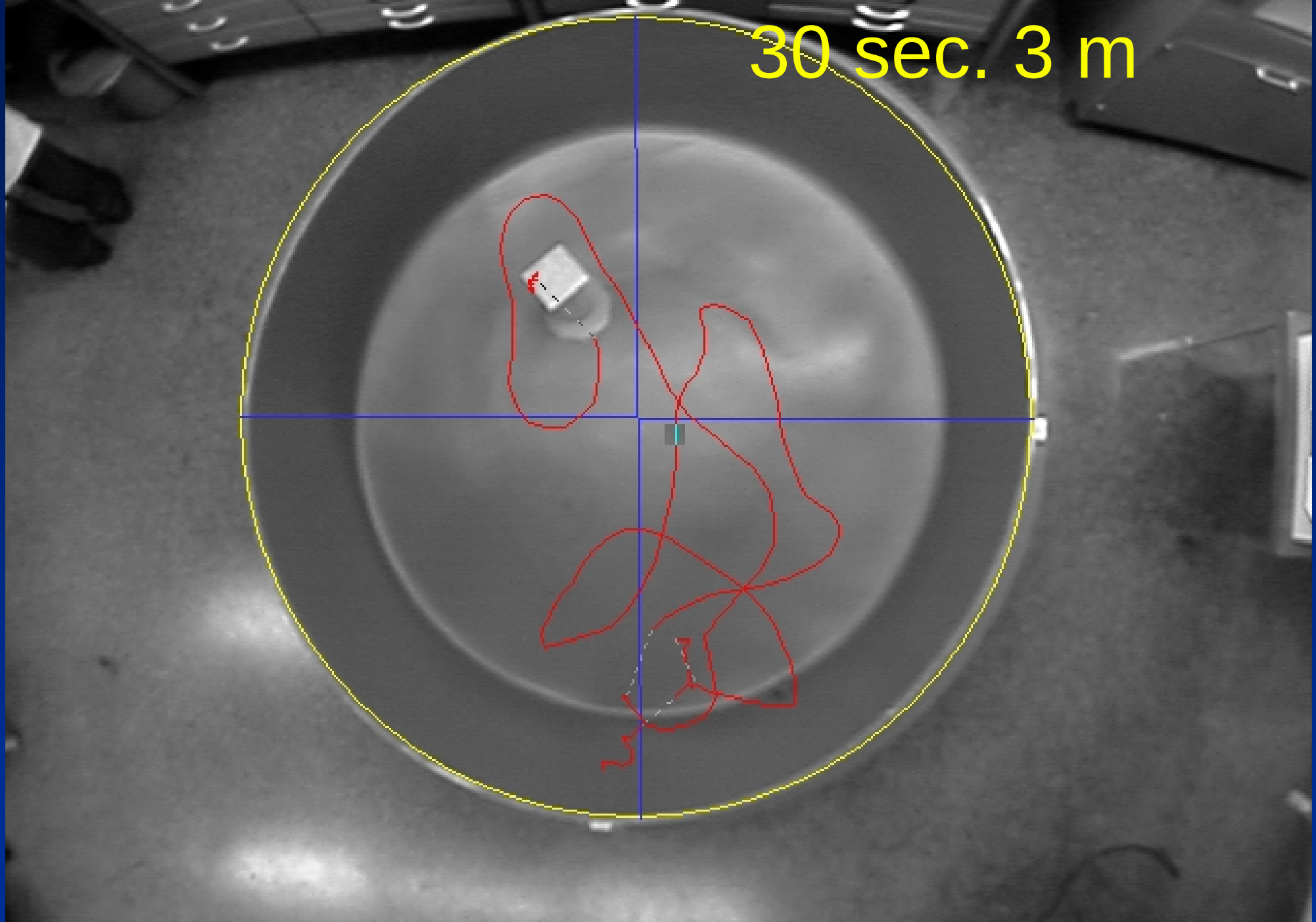
Probe trial

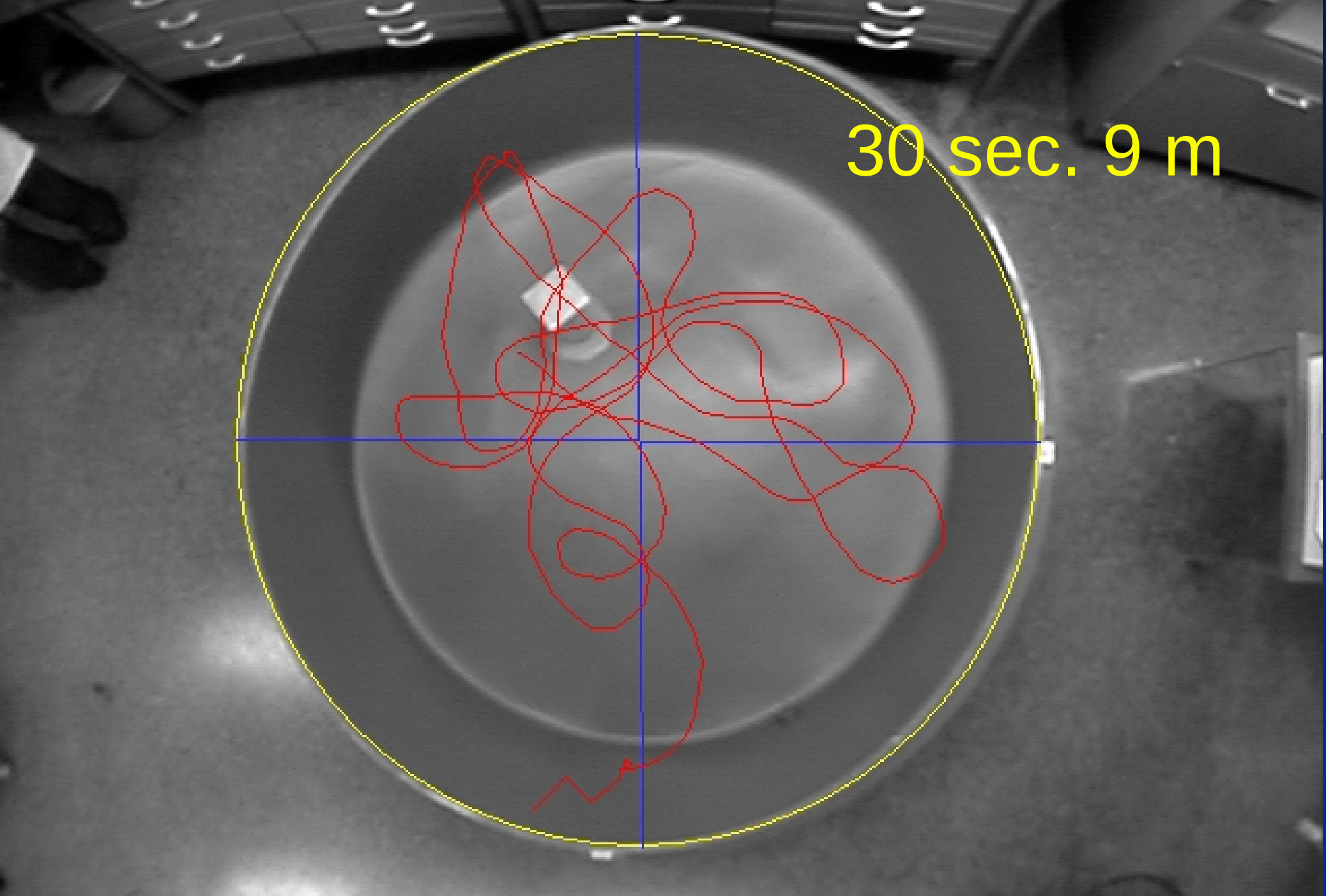

Time in quadrant (sec)
40
30
20
10
0
*
SHR
L C R A - L C R A - L C R A
Time in quadrant (sec)
40
30
20
10
0
*
CAP-SHR
L C R A - L C R A - L C R A

The interpretation of the data is all important



Note: many rats like to dive under water for 30’’ at a time

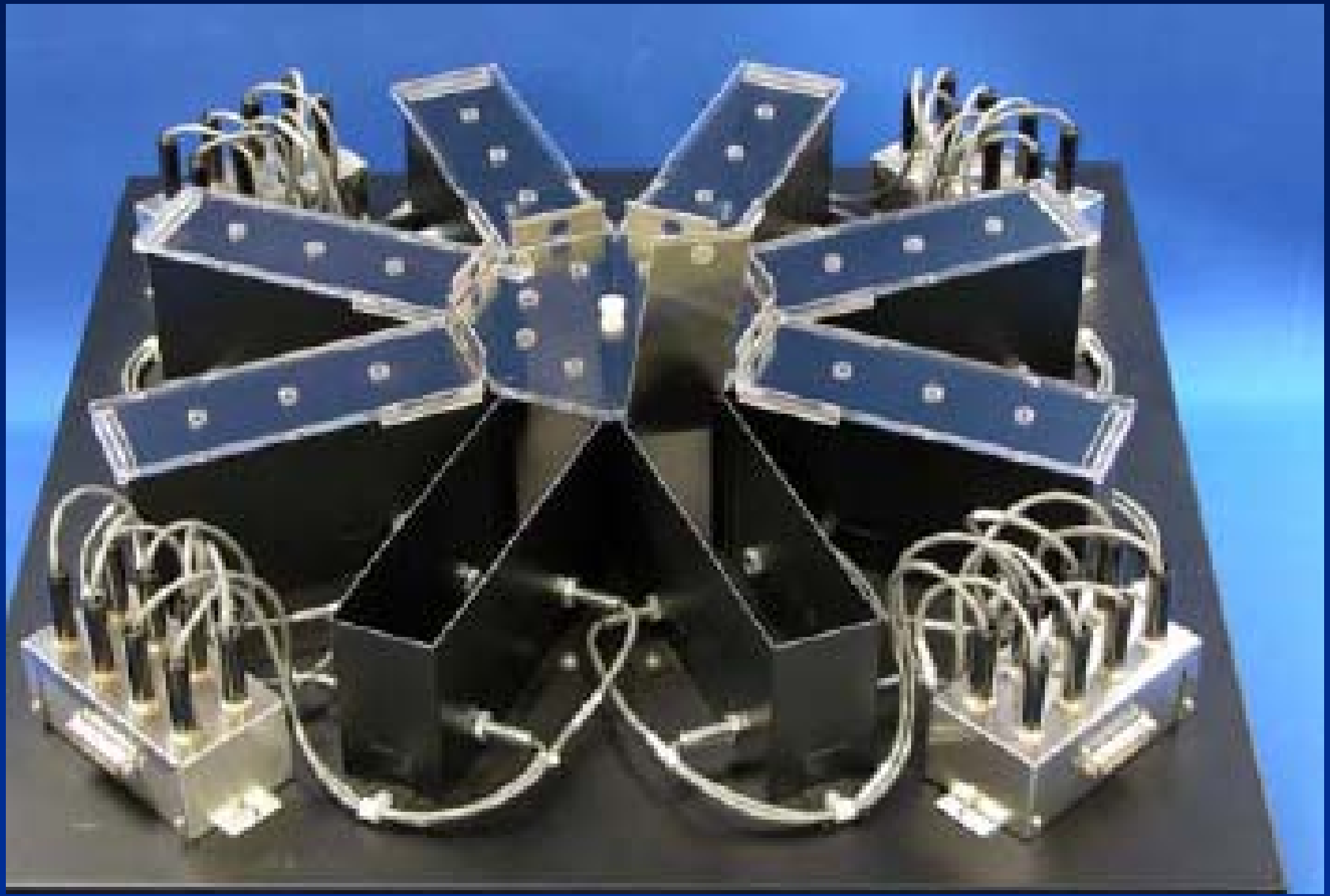

30 sec. 3 m


30 sec. 9 m

A couple of lessons

- Rats like water better than mice.
- When rats and mice get fat, they can float.
  - Thus motivation changes with age.

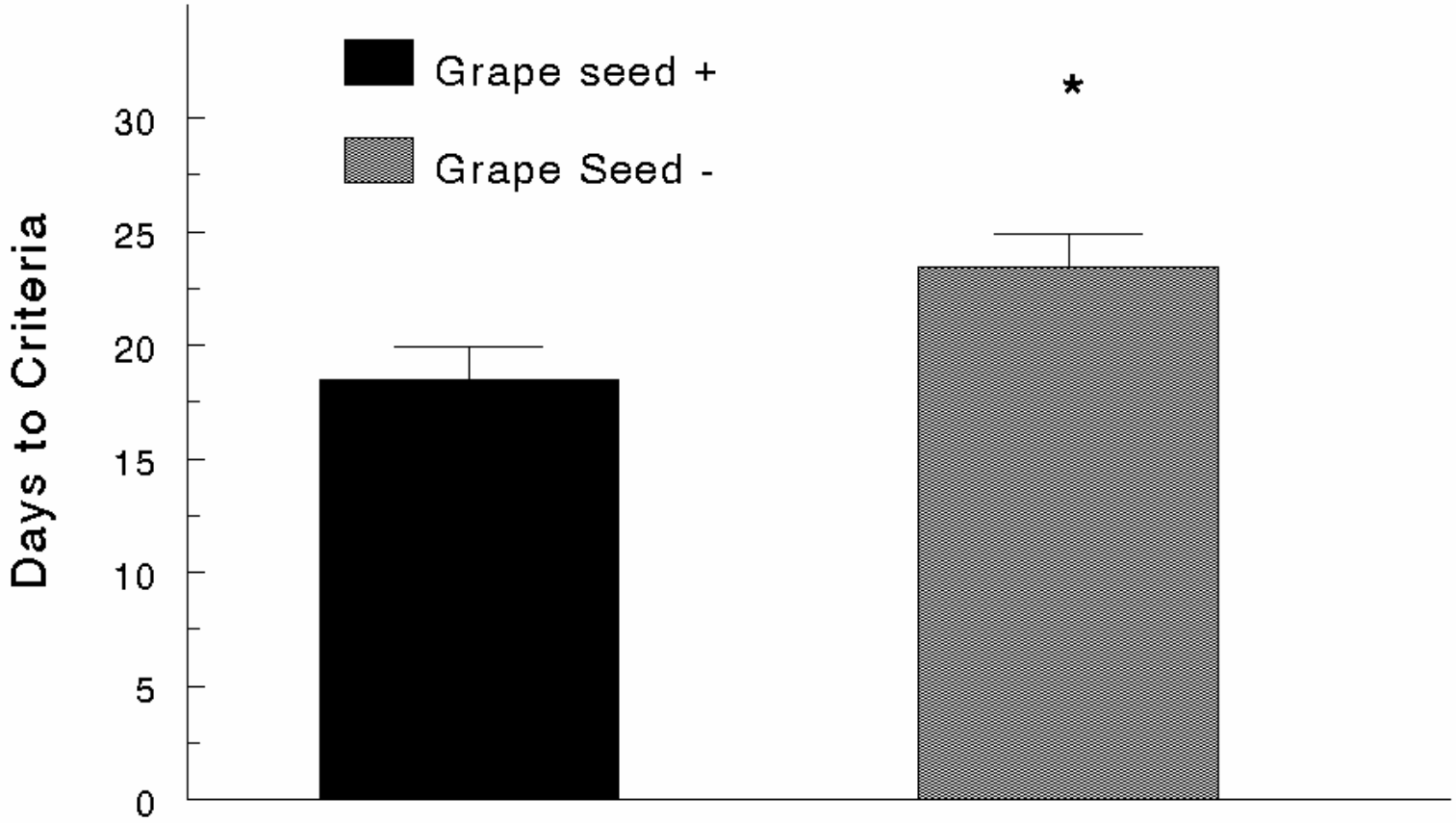
Dry mazes



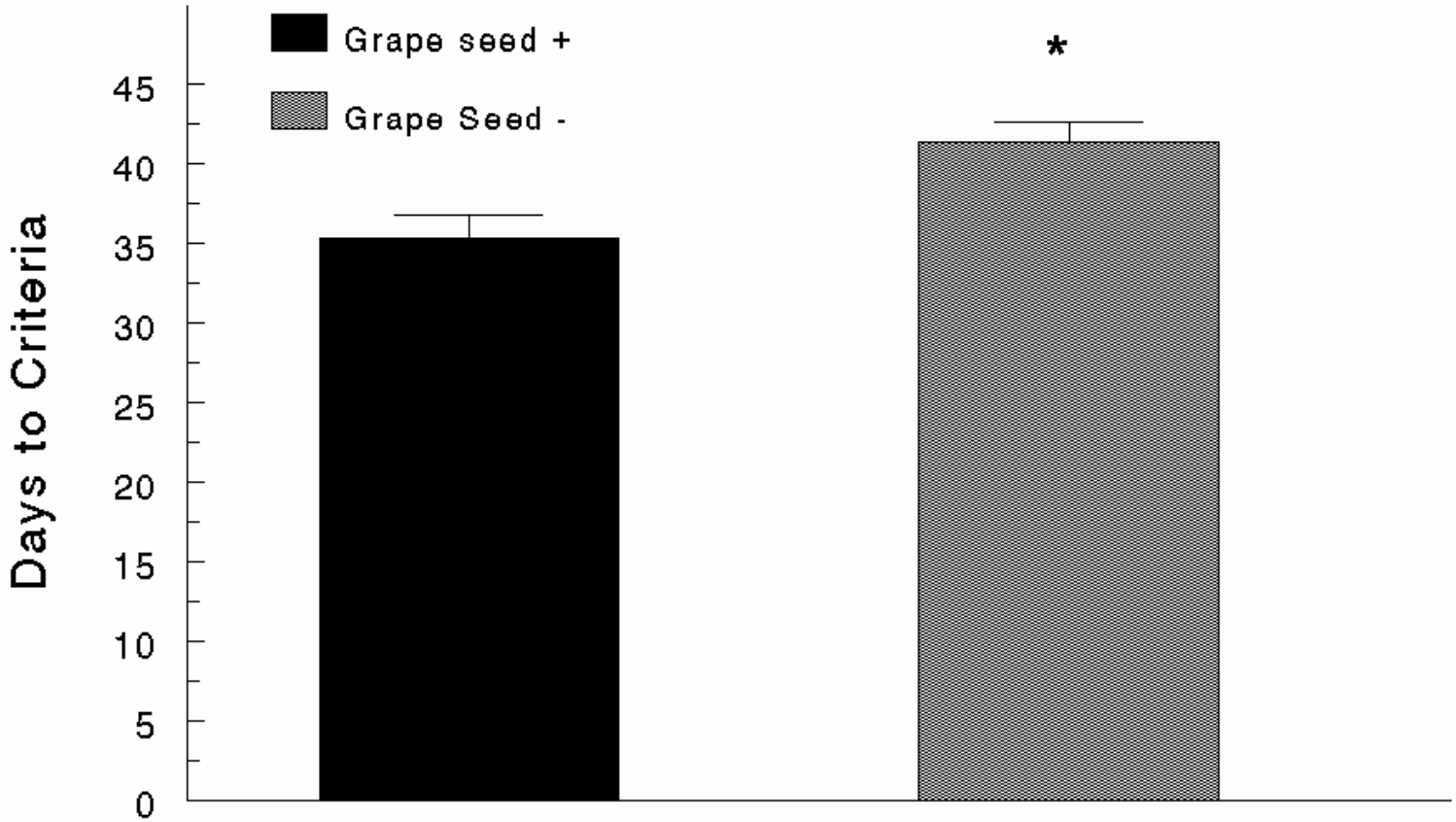
Learning and memory

- Eight arm radial maze task
- Two arms are unbaited
- Completion criterion is to get 5 out of first 6 choices correct on 4 consecutive days
- Working memory error is same day re-entry into a previously visited arm
- Reference memory error is entry into an unbaited arm

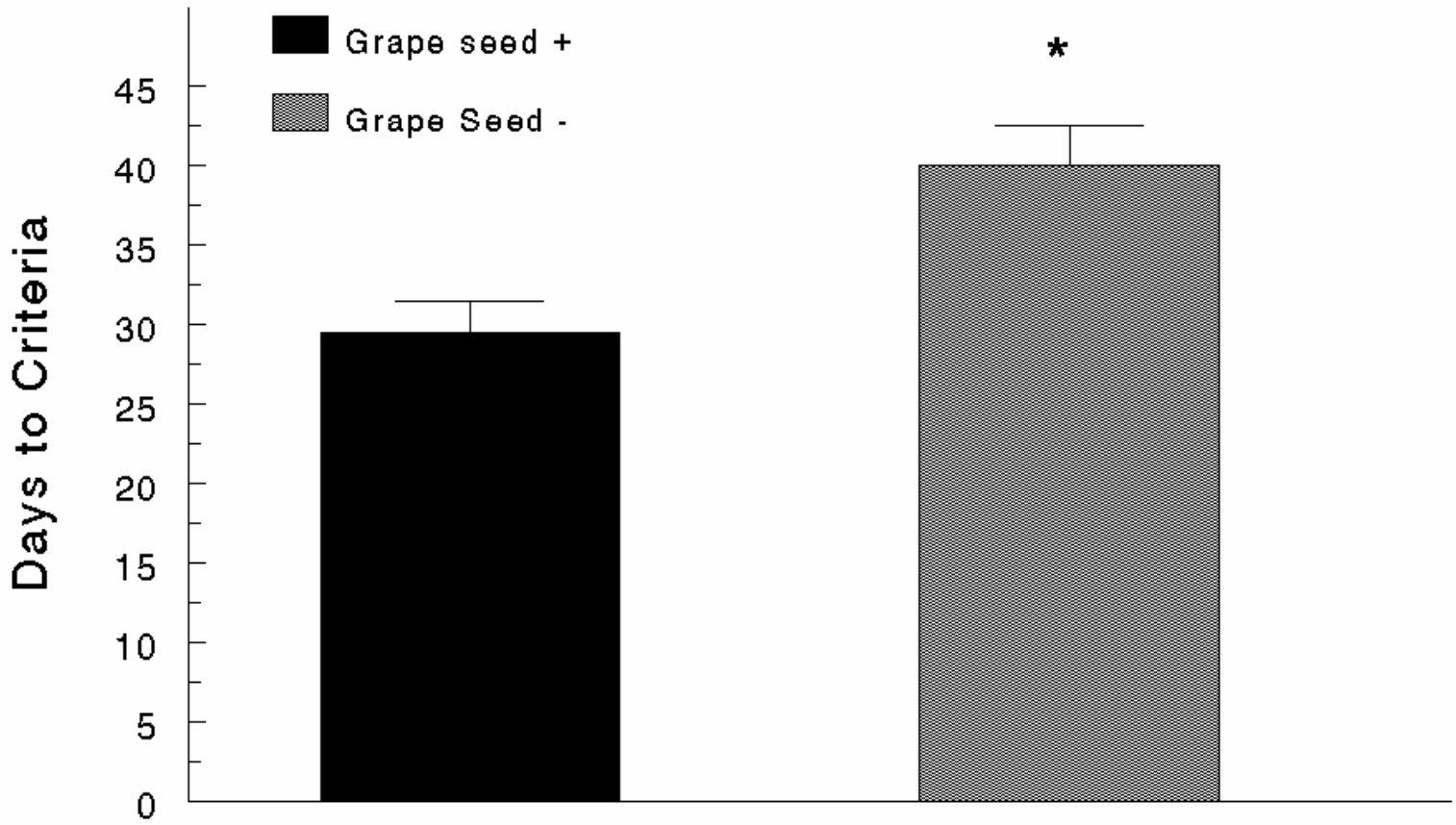
Mean Completion Times



Working Memory Errors



Reference Memory Errors



Radial dry maze

- Both mice and rats learn it well
- Relatively easy to interpret
- Can manipulate the difficulty by delay

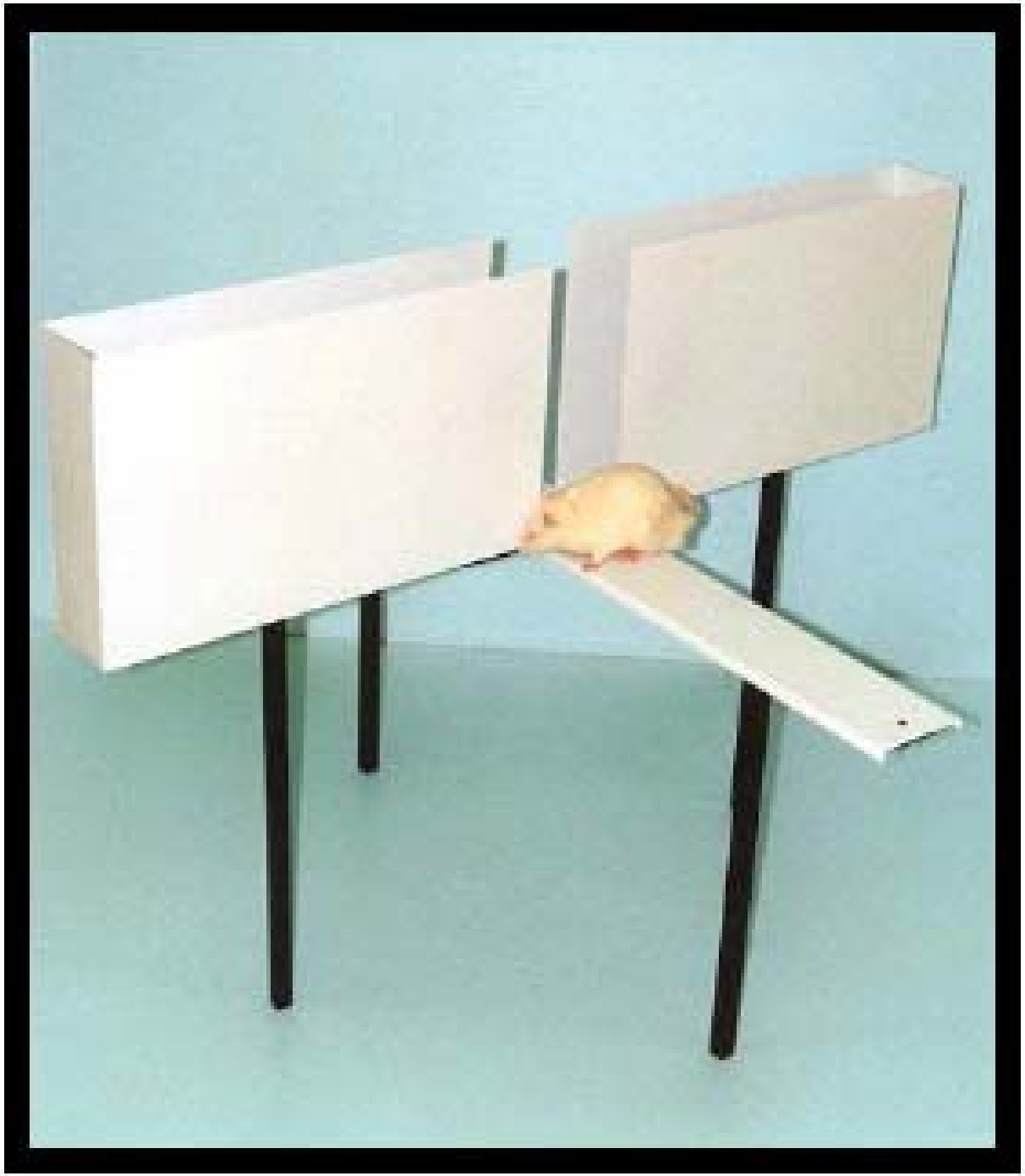
- But
- It takes forever
- Motivation induced by diet restriction

FearFactor

Elevated plus maze

Motivation well controlled but it is negative US

Fear-induced memory related to the amygdala but positive stimuli are more related to the hippocampus.



1. Choose method wisely
2. Ensure that motor/sensory dysfunction does not underlie the differences observed
3. Choose the best test time
4. Choose a task that will discriminate (cost benefit)