PATHOPHYSIOLOGY OF LEARNING AND MEMORY

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Learning

= a change of behaviour based on previous experience, an entry to memory

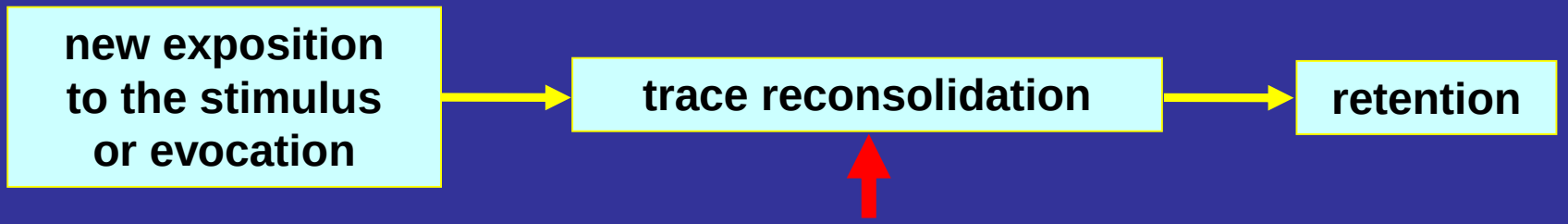
Memory

= storage of information for further utilization

Process of memory

1) creation of the memory trace
2) consolidation of the memory trace
3) retention
4) evocation - evocation based on stimuli (reminder)
   - recall
   - recognition

„warming“ of the trace: extends retention, decreases probability of forgetting



Processes of trace consolidation and reconsolidation are sensitive to disruptive effects.

brain commotion, electroshock, hypoglycaemia, hypothermia, intoxication (alcohol)

In the phase of retention the memory trace is more stable. → amnesia

Non-associative learning

= no association of two or more stimuli, only reactivity to one stimulus changes

1) **habituation**
2) **sensitization**

Associative learning

= association of two or more stimuli acting in narrow time relation

1) **classical conditioning**
2) **operant conditioning**
3) **game**
4) **emulation**
5) **insight**
6) **imprinting**

Classification of memory according to persistance

1) **short-term**
   - seconds - minutes
   - restricted capacity, older information are overlapped with new one
   - information is then shifted into medium-term memory or forgotten
2) **medium-term**
   - minutes - hours
   - important information shifted into long-term memory, other forgotten
3) **long-term**
   - hours, days, years, permanently

Working memory – information is stored until it is used, then it is forgotten, belongs to medium-term memory

Declarative memory

- information can be expressed verbally or as visual image
- evocation is wilful

1) semantic – abstract information
2) episodic - events
(3) recognition – recognition of objects)

Non-declarative memory

- information can not be expressed verbally
- evocation is unaware

1) motor patterns
2) conditioned reflexes
3) perceptive a cognitive patterns

Structures involved in processes of learning and memory

1) **Hippocampus** - necessary for declarative memory
   - emotional component and motivation in the learning process

1) **Associative cortical areas**
2) **Septum**
3) **Corpus amygdaloideum** - emotional memory
4) **Entorhinal cortex**
5) **Cerebellum** - motor learning, role in other types of learning
6) **Striatum** - motor learning

Injury and changes of these regions -structural, metabolic, changes of neuromediator systems (namely acetylcholine, glutamate, dopamine, noradrenalin)

→ Learning and memory defects

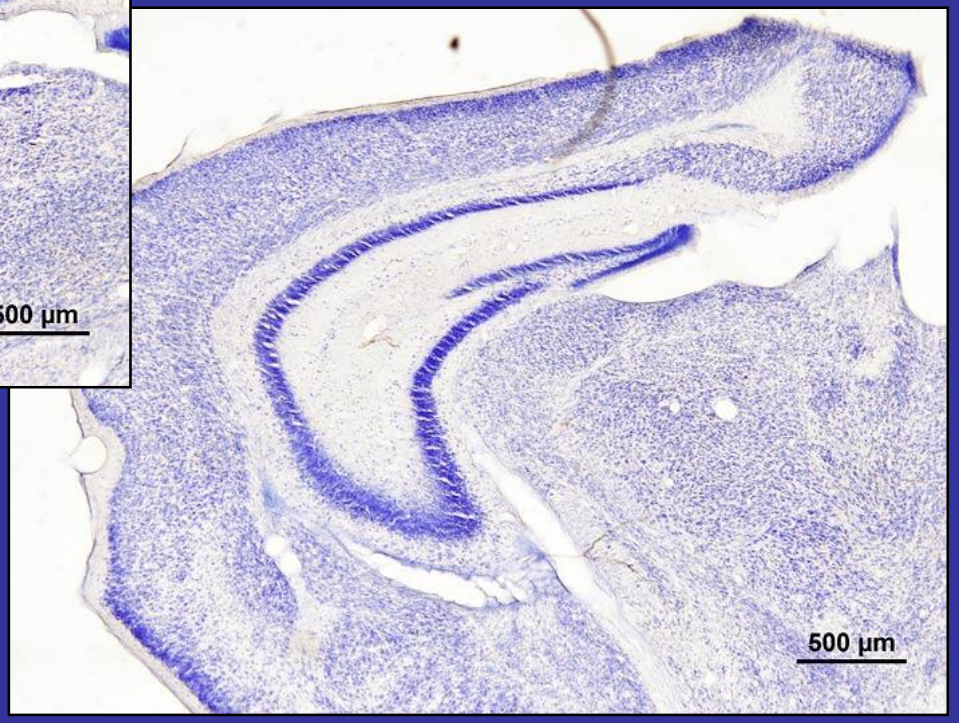
Learning and memory can be also influenced by changes of **attention, motivation and emotions, sensory systems.**

Learned behaviour depends also function of motor system.

HIPPOCAMPUS

mouse hippocampus

Histological structure of the hippocampus

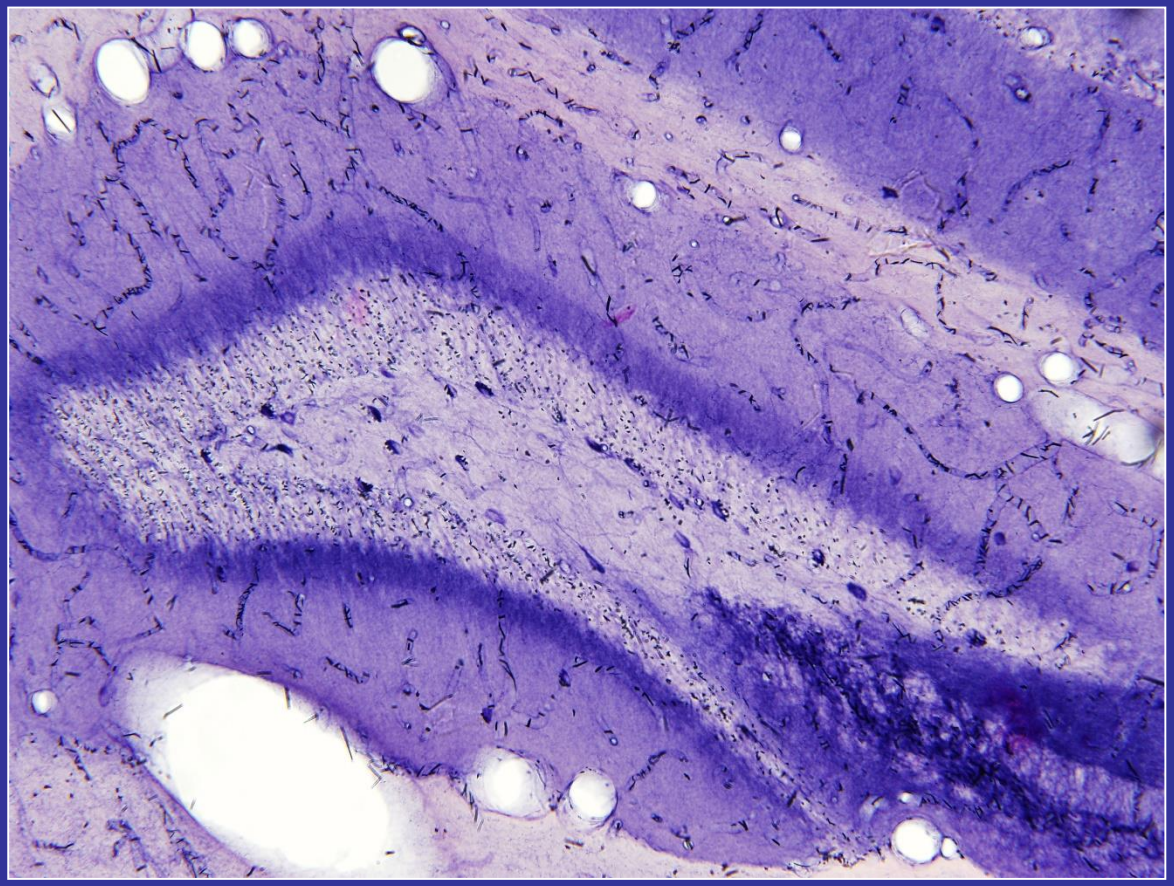


Mouse hippocampus

Nissl staining

NOS activity in the hippocampus

NADPH-diaphorase



MEMORY DISORDERS

- **Amnesia** = complete loss of memory
  - retrograde = loss of information acquired before the genesis of the amnesia
  - anterograde = defect of storing new information
- **Hypomnesia** = decrease of memory capacity
- **Hypermnesia** = excessive and inadequate remembering of some facts
- **Paramnesia** = distortion of stored information, the patient is confident that it is correct
- **Memory delusion** = conviction about reality of an event, which did not happen, a kind of paramnesia
- **Ekmnesia** = inaccurate time localisation of an event (which is memorized correctly)

DISORDERS OF MIND AND INTELLIGENCE

- **Dementia** – acquired disorder of cognitive functions, including memory
  - Alzheimer‘s disease, vascular dementia, alcoholic dementia

  Pick‘s disease, Parkinson‘s disease, Huntington‘s chorea, infections, brain tumours, hydrocephalus, brain trauma, endocrinopathy

  X temporary (reversible) disorders of cognitive functions (e.g. circulatory decompensation, dehydratation, hypothyroidism)

- **Mental retardation** – developmental disorder of cognitive functions
  - slight – independence, possibility of simple job
  - middle – partial independence
  - severe – limited self-service, speech limited to single words
  - deep – inability of self-service, inability to speak

1. SPATIAL LEARNING

Methods of spatial navigation:

- Allothesis - navigation according to landmarks
  - vision, olfaction, hearing, touch
- Idiothesis - current position linked to starting point of the movement
  - proprioception, vestibulum
  - casual correction with allothesis is necessary

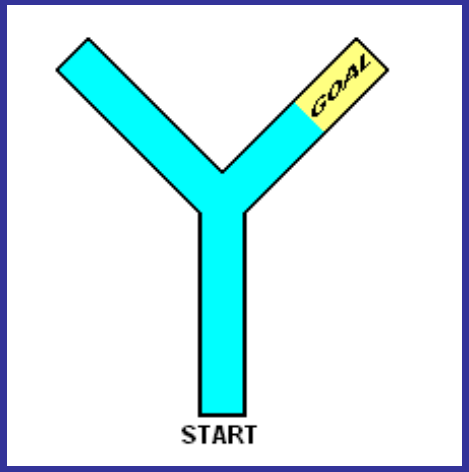
Spatial memory is deteriorated soon in dementias.

→ Spatial orientation and memory tests are used for early detection of Alzheimer‘s disease

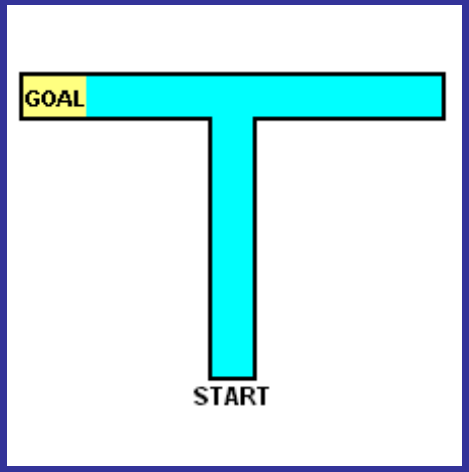
Experimental methods of spatial learning investigation:

- Morris water maze
- radial maze
- Y-maze
- T-maze
- open field with avoidance of certain area
  (possibility of circular arena rotation)

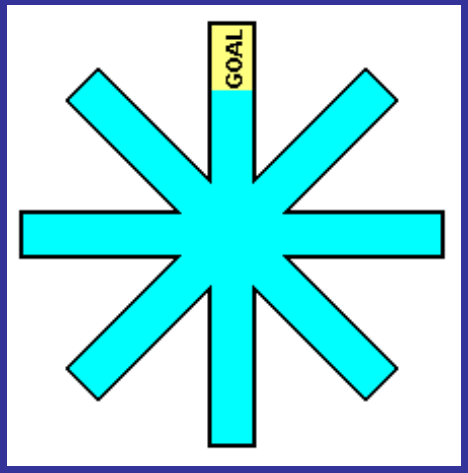
TYPES OF MAZES



Y-maze



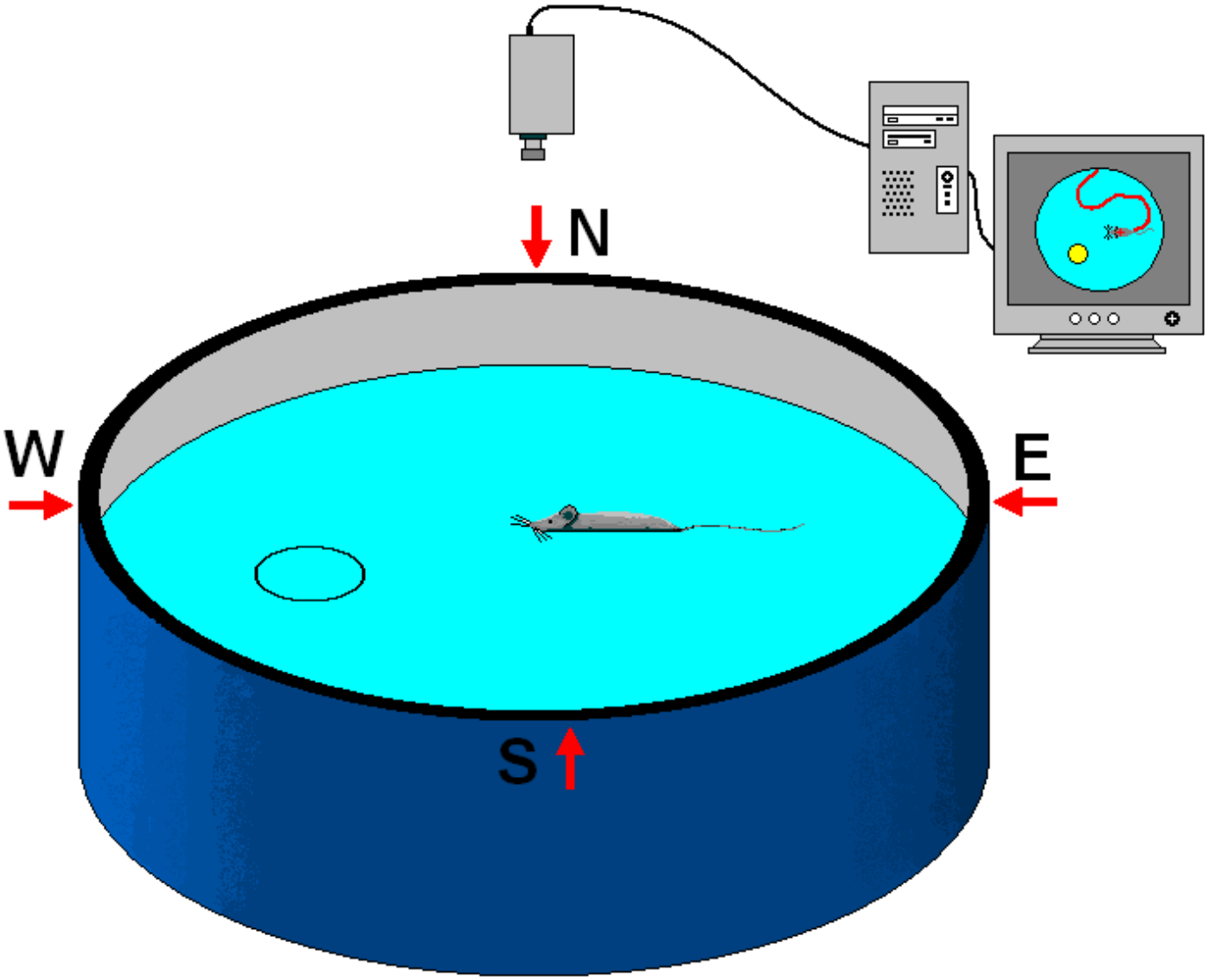
T-maze



radial maze

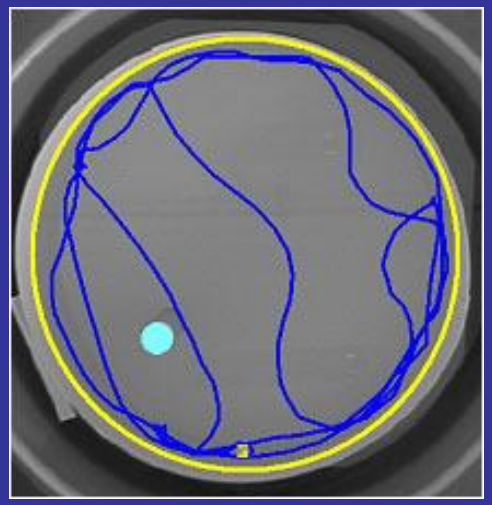
Morris water maze

Morris water maze

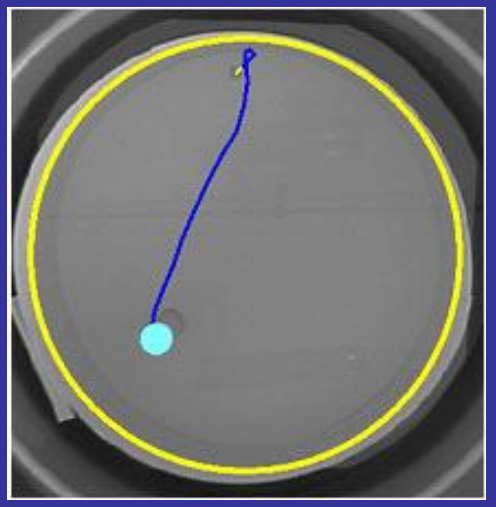


Typical trajectories in the Morris water maze

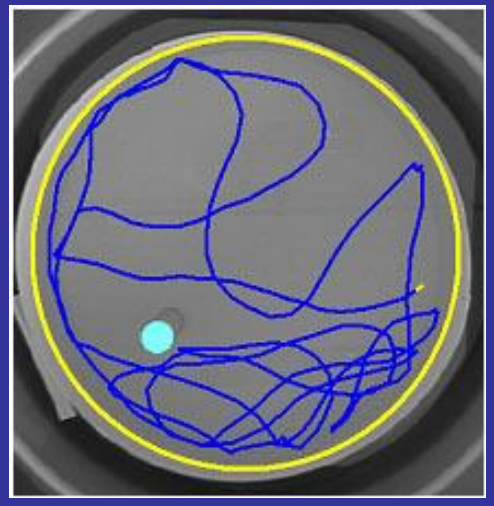
untrained wild type mouse



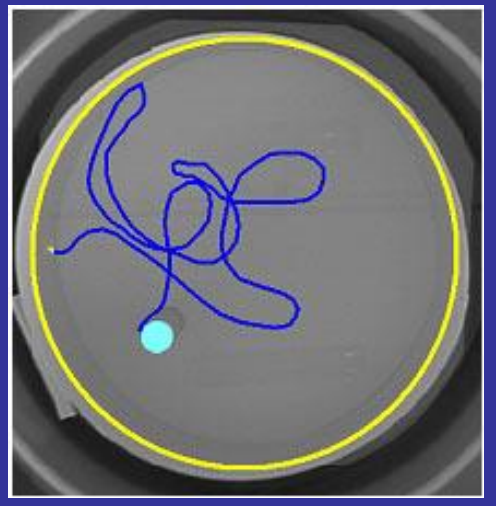
wild type mouse after 5 days of training



untrained Lurcher mutant mouse

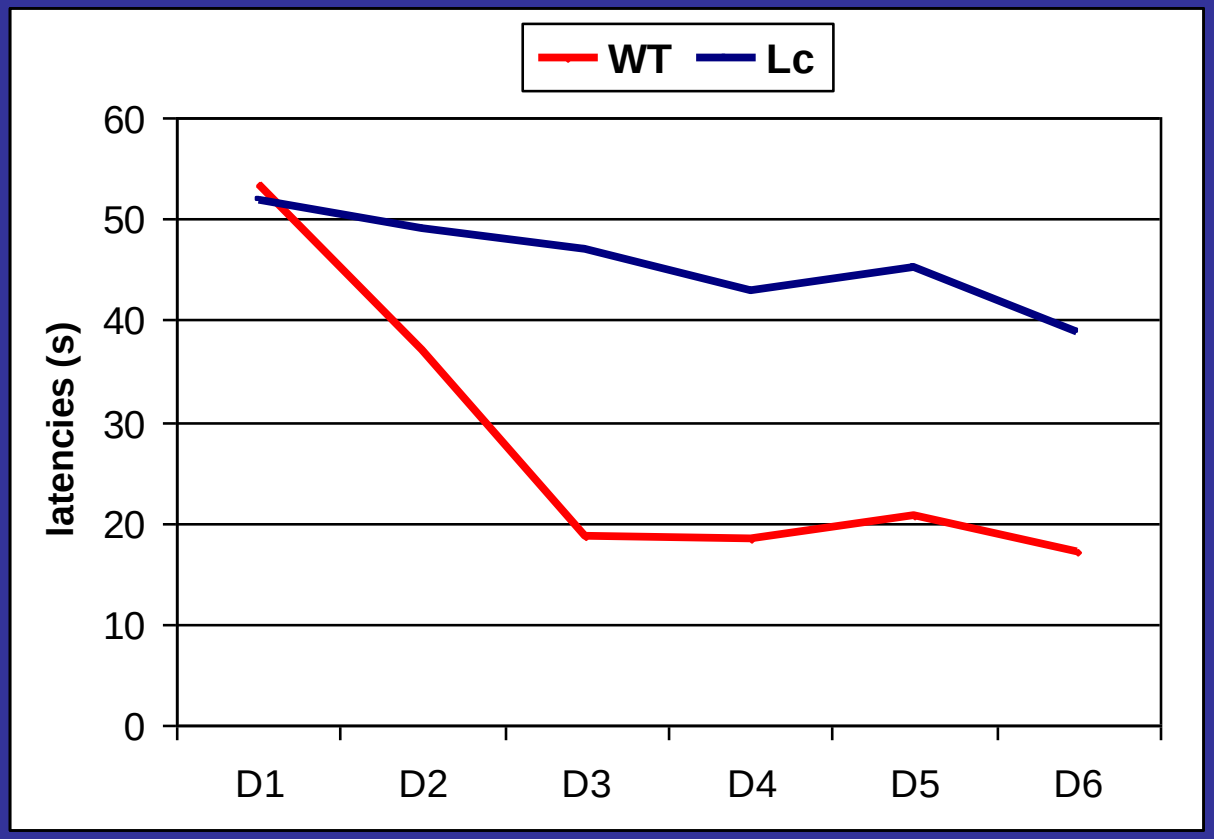


Lurcher mutant mouse after 5 days of training



LEARNING CURVE

Development of latencies in the Morris water maze during repetitive trial in normal mice (wild type = WT) and mice with a cognitive deficit (Lurcher mutant mice = Lc):

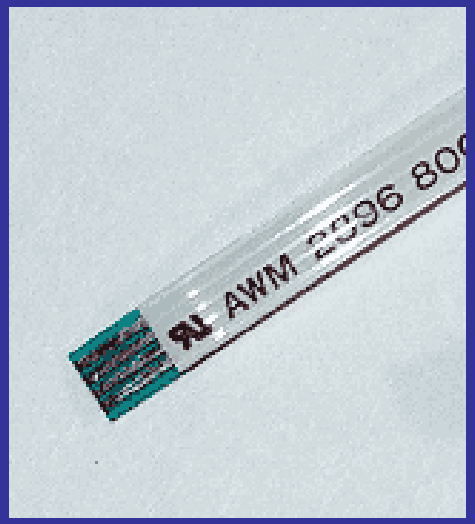


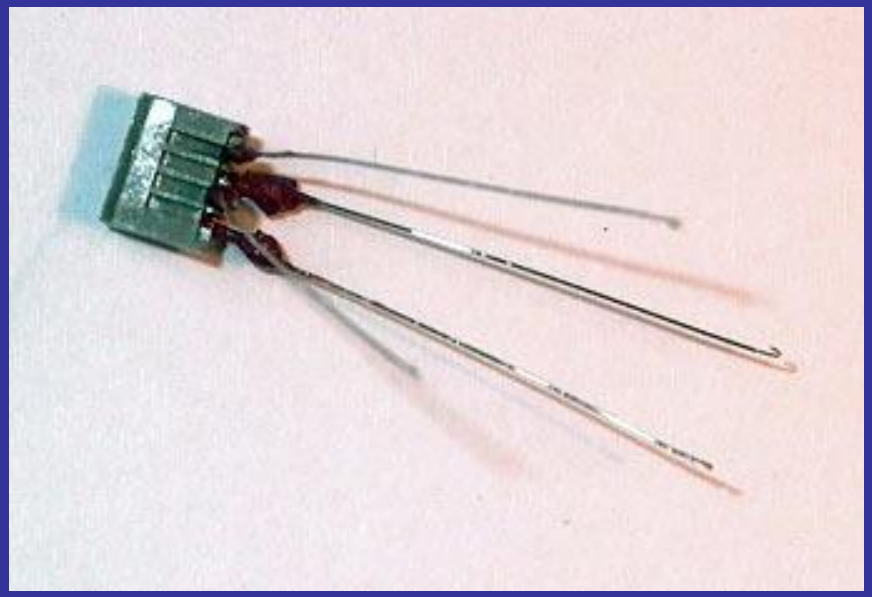
2. CLASSICAL CONDITIONING

Model experiment:
- conditioning of corneal reflex (eye blink conditioning)

<u>Unconditioned stimulus:</u>
electrical impulse to orbital area, air puff

<u>Conditioned stimulus:</u>
sound, weak electrical impulse to orbital area


AWM

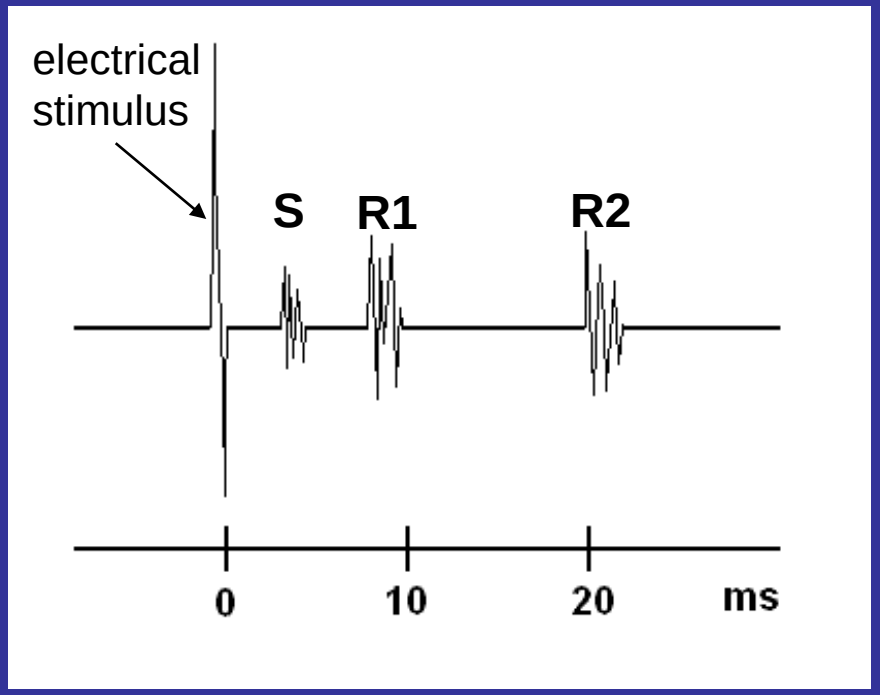


Reflex circuit of corneal reflex:

- nerve endings of the n. trigeminus (n. V.) in cornea and orbital area – n. V. – nuclei of the n. V. and n. facialis (n. VII.) – n. VII. – musculus orbicularis oculi

Structure of reflex response to irritation of the m. orbicularis oculi:

- EMG of the m. orbicularis oculi

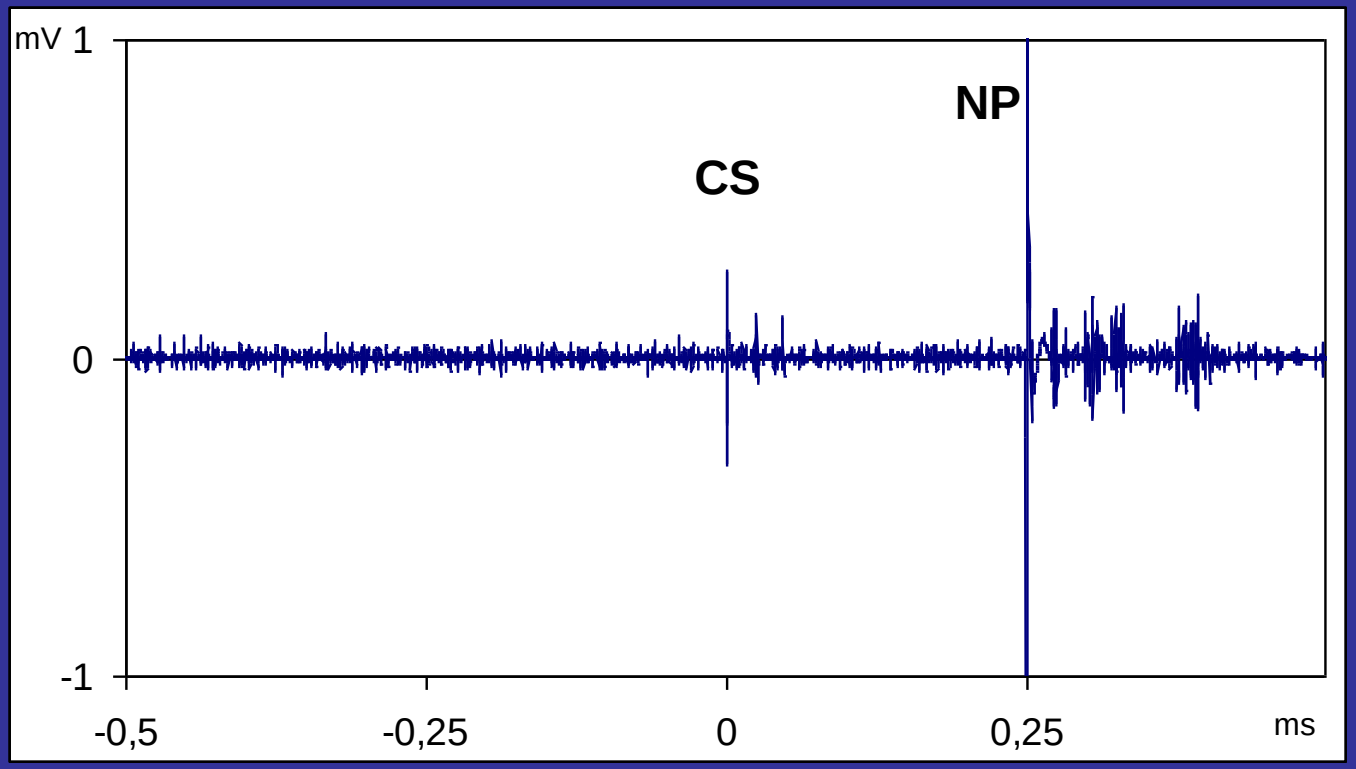


S = synaptic response
latency of 4 ms
- evoked directly by irritation of the n. facialis or muscle

R1 = the 1st reflex response
latency of 8 ms
- reaction to irritation of ending of the n. trigeminus

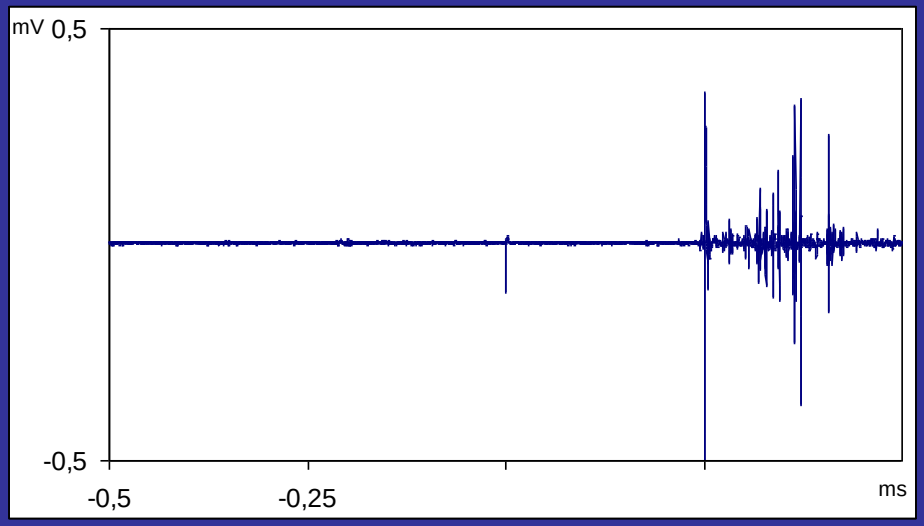
R2 = the 2nd reflexí response
latency of 20 ms
- in the reflex circuit are inserted interneurons → longer latency

EMG of the m. orbicularis oculi – reaction to electrical stimulus

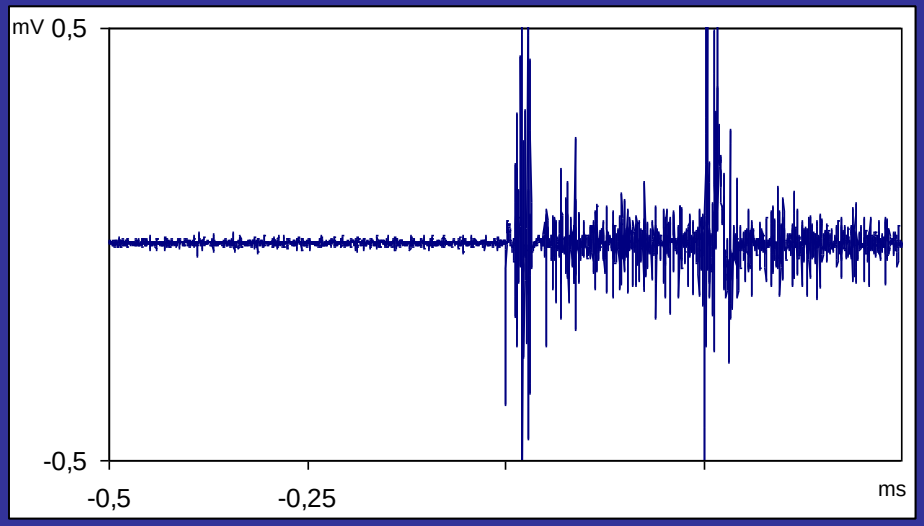


CS = conditioned stimulus
US = unconditioned stimulus

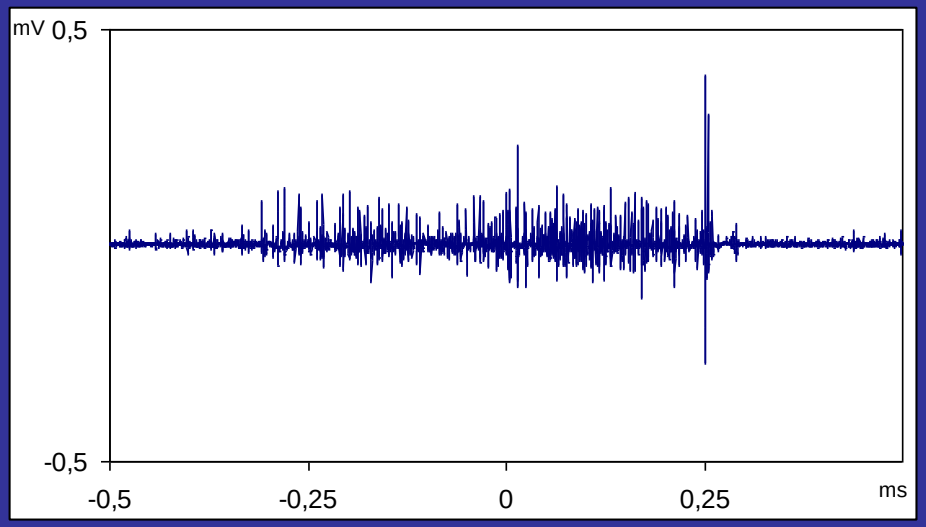
Examples of EMG records of the m. orbicularis oculi during classical conditioning of the eyelid response:



untrained individual



trained individual

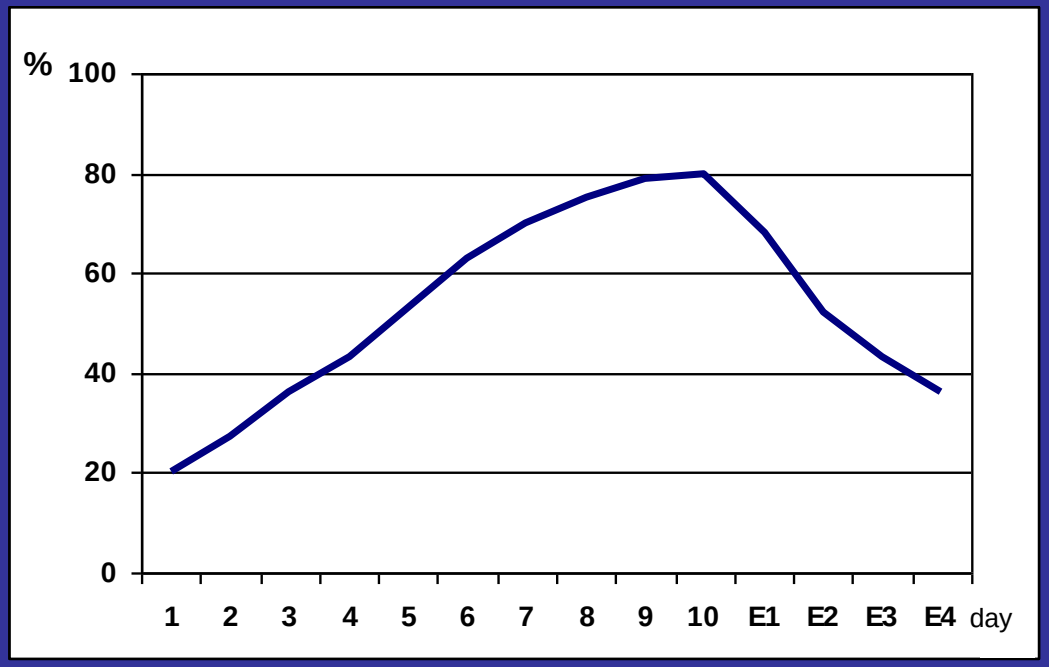


unusable record

Evaluation of classical conditioning test

A couple of stimuli is applied several times a day for several consecutive days. An indicator of learning ability is relative incidence of trials, in which conditioned response occurred, in individual days of the experiment or increase of reaction intensity expressed as area under the curve of absolute value of the EMG record in the interval since 50 ms after conditioned stimulus application until the unconditioned stimulus.

Learning curve:



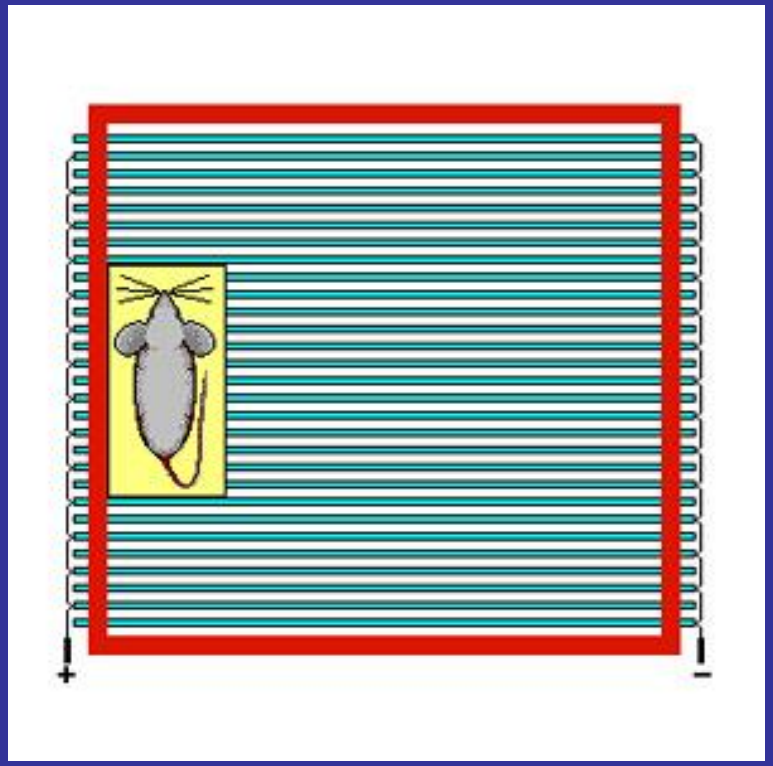
E1-4 = extinction – applied only the conditioned stimulus, the reflex extinct

3. AVOIDANCE

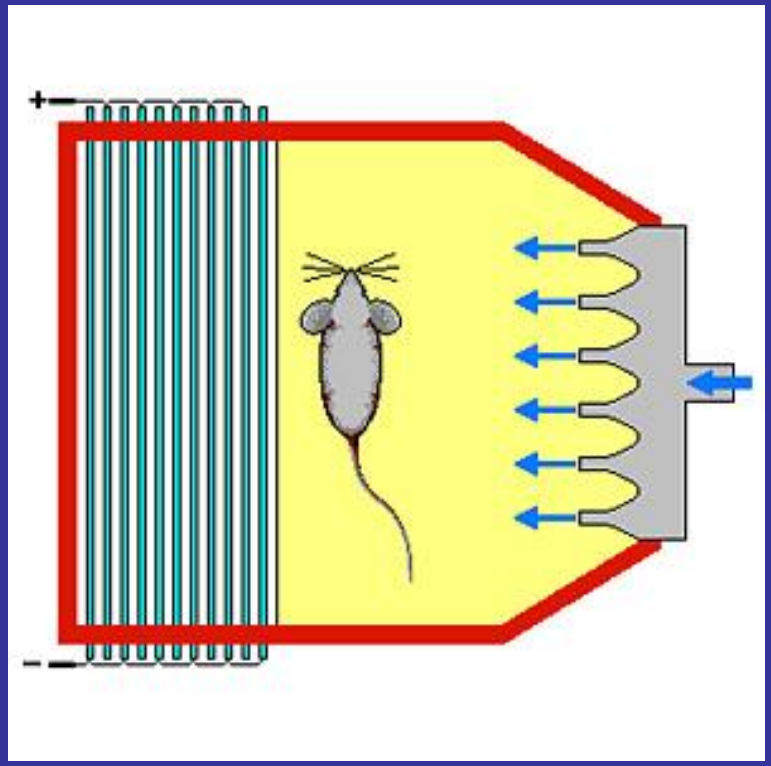
- active – the individual learns to do something to avoid an unpleasant stimulus
- passive – the individual learns to avoid some area or activity, which is followed by an unpleasant stimulus

Examples of passive avoidance:

„step through“



„step down“



ACTIVE AVOIDANCE

- painful stimulus: electrical current in the metal floor

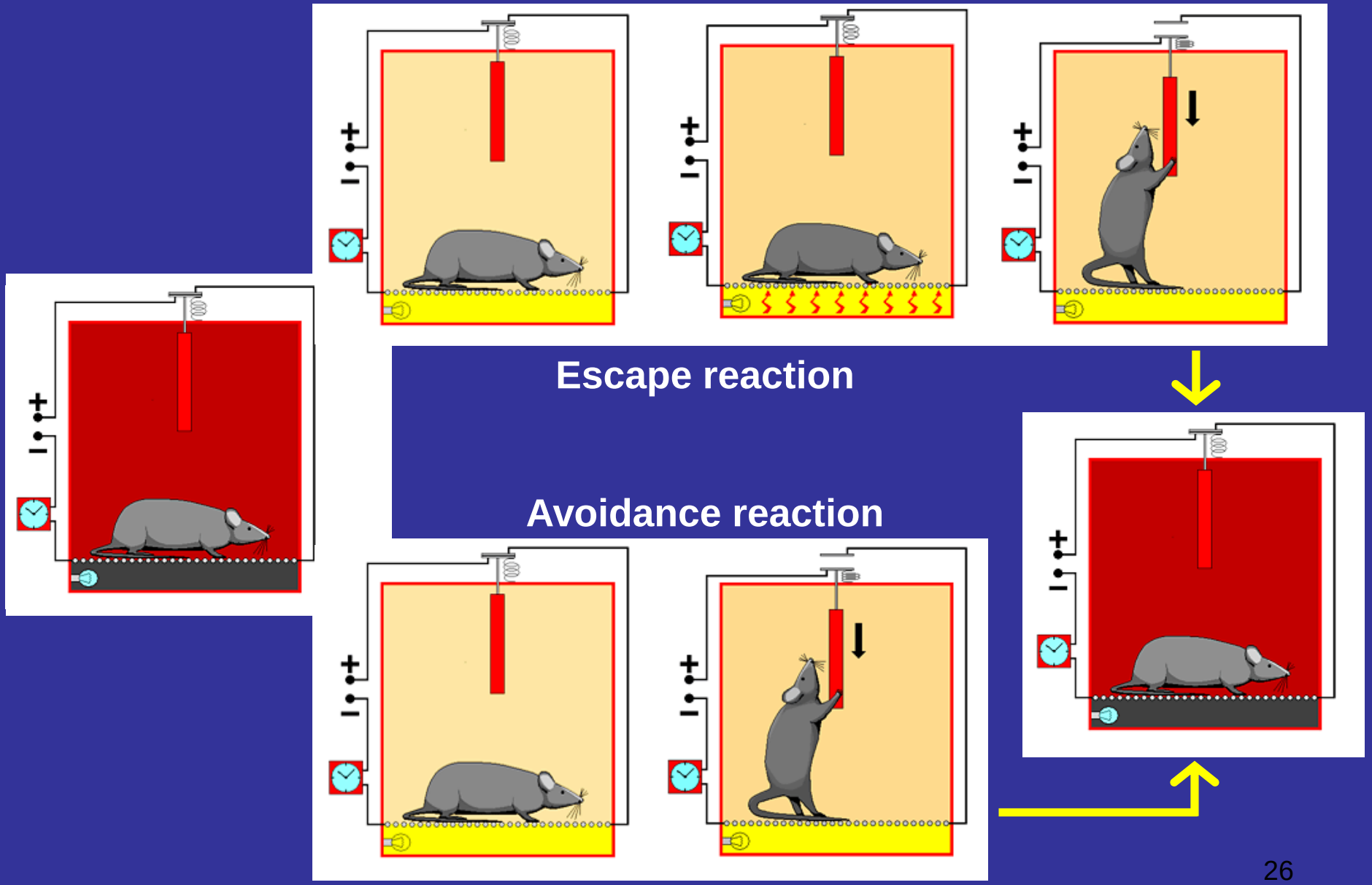
- conditioned stimulus: light – precedes to the painful stimulus

Escape reaction = switching off electrical current after beginning of the painful stimulation

Avoidance reaction = switching off electrical current before beginning of the painful stimulation (in the interval between switching light on and switching current on) by pulling the lever

Indicator of learning ability in the number of trial repetition necessary for creation of avoidance reaction.

Active avoidance



THE END