Assessing emotion, learning and memory and social behaviors in rats and mice

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Models of behavioral disease

- Modeling components of a complex disease
- Avoiding over-interpretation
- Understanding the model you use
- Appreciating complexity of animal behavior

Evaluating "higher" brain functions in animals

" I said in my heart with regard to human beings that God is testing them to show that they are but animals. For the fate of humans and the fate of animals is the same…They all have the same breath, and humans have no advantage over the animals…"

Ecclesiastes 3:18-21, NRSV

Approaches

- Knowing the tests for different behavioral domains
  - What tests to use
- Methodological principles
  - How to test
  - How many tests
  - When to test
  - How often to test

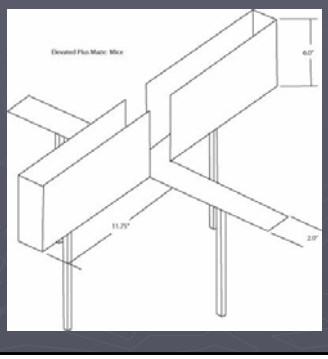
Emotionality

- Fear-related responses
  - Freezing, immobility
  - Startle response
  - Avoidance and escape
  - Autonomic responses
    - Urination and defecation
    - Cardiovascular responses
- Positive reinforcement
  - Drug addiction
  - Intracranial stimulation

Tests for emotionality

- Elevated plus-maze
- Open field test
  - Central activity vs. peripheral activity
  - Freezing, grooming
  - Rearing
- Acoustic startle response
- Exposure to a predator

Elevated plus maze



Open arm entries

Closed arm entries

Time spent in open vs. closed arms

Other behaviors
- **stretching**
- **Head dips**

Acoustic startle response

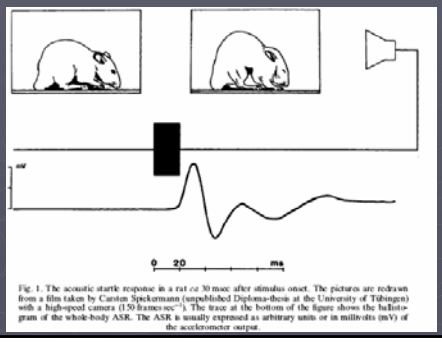
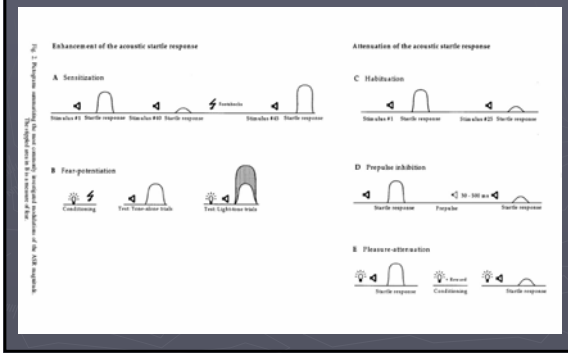


Fig. 1. The acoustic startle response in a rat *ca* 30 msec after stimulus onset. The pictures are redrawn from a film taken by Carsten Spickermann (unpublished Diploma-thesis at the University of Tübingen) with a high-speed camera (150 frames sec^{-1}). The trace at the bottom of the figure shows the ballistogram of the whole-body ASR. The ASR is usually expressed as arbitrary units or in millivolts (mV) of the accelerometer output.

Modification of the startle response



Learning and memory

- Short-term (working) vs. long-term memory
- Long-term memory
  - Explicit memory
    - Episodic (events)
    - Semantic (facts)
  - Implicit
    - Procedural
    - Perceptual-representational

Tests for learning and memory

- Procedural learning in animals
  - Operant conditioning (e.g., a Skinner box)
  - Pavlovian conditioning (e.g., a Shuttle box)

Skinner box

American psychologist B. F. Skinner designed an apparatus, now called a Skinner box.
An animal placed inside the box is rewarded with a small bit of food each time it makes the desired response, such as pressing a lever or pecking a key. A device outside the box records the animal's responses.

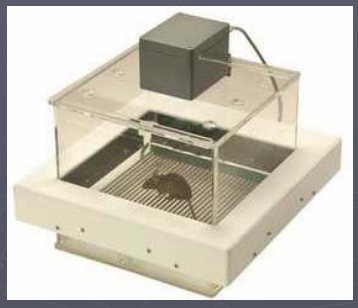
Active and passive avoidance

Pavlovian conditioning

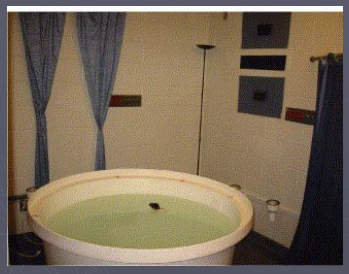
Tests for learning and memory

- Spatial reference hippocampus-dependent memory tests
  - Fear conditioning (context vs. cue-dependence)
  - Morris water maze

Fear conditioning



Morris water maze

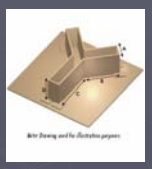


Adapted from Moy et al, 2007

Tests for learning and memory

- Explicit learning in animals
  - Working memory
    - Mazes
      - T; Y; Radial, Barnes
  - Episodic memory
    - Reversal repeated Morris water maze

Mazes



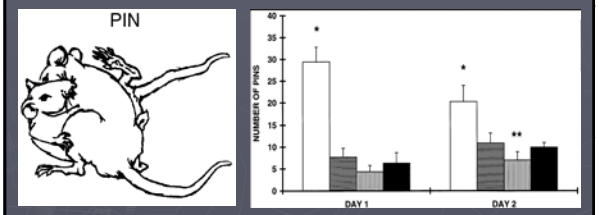
Social behaviors

- Social interaction in young animals
  - Play activity
- Social behaviors in adult animals
  - Non-aggressive interaction
  - Aggressive interaction
  - Sexual behavior

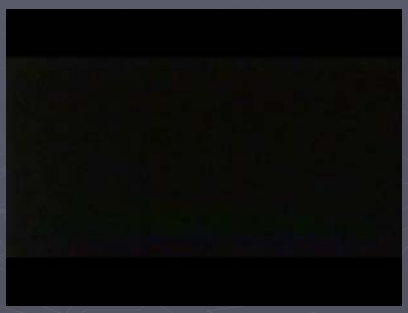
Tests for social activity

- Play behavior and play solicitation behaviors
  - Play wrestling and pinning
  - Darting, pounces; crawl over/under
- Intruder-resident paradigm
  - Measuring inter-male and/or territorial aggression
    - Male mice
  - Social interaction after social deprivation
    - Male and female rats
- Sociability and social preference/recognition tests
  - Time spent in exploring live mouse vs. inanimate object
  - Time spent in exploring familiar vs. novel subject

Play activity



Play behavior in young rats



Sociability and social preference

Adapted from Moy et al, 2007

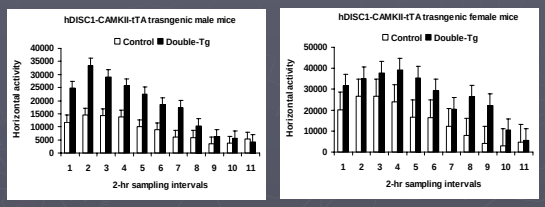
Methodological principles

- Genetic background, strain effect

Methodological principles

- Sex dependence

Male but not female mice exhibit hyperactivity

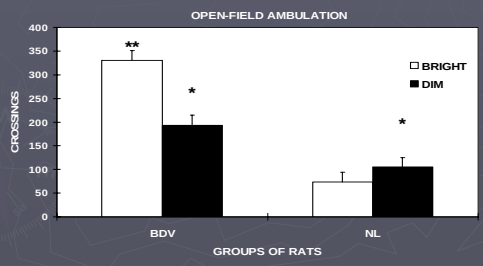


Methodological principles

- Manipulations of the test conditions

Manipulation of the test conditions

Bright vs. dim illumination



Methodological principles

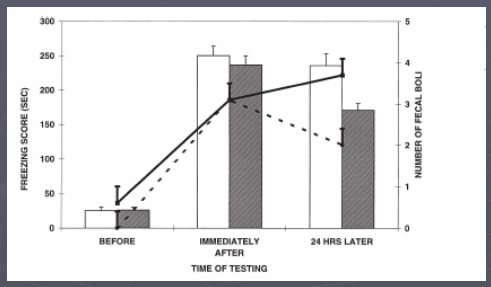
- "Challenging" animals to observe effects

Methodological principles

- Multiple outcome measures
  - Different measures can show inconsistent results
    - overt responses vs. autonomic responses

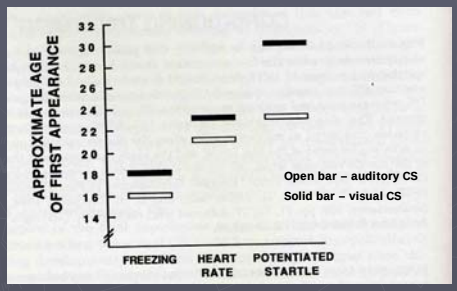
Multiple measures

Context-dependent fear conditioning



Multiple measures

Developmental course of fear-related responses



From Hunt and Campbell, 1997

Methodological principles

- Paradigms based on different motivations
  - Hunger vs. thirst
  - Negative vs. positive reinforcements

Methodological principles

- Paradigms involving different brain systems and functions:
  - Fear of height; predator or pain
  - Learning and memory tests using auditory, visual or olfactory conditioned and unconditioned stimuli
  - Social interaction in familiar and unfamiliar settings
    - Aggressive vs. non-aggressive social behaviors

Methodological principles

Behavioral analysis of developing animals

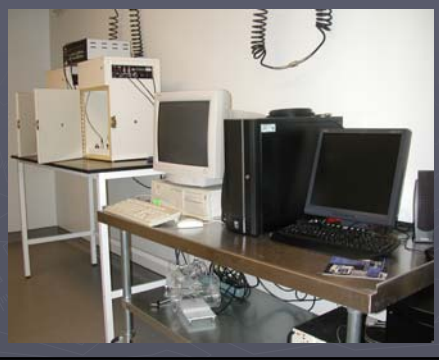
- **Litter as the unit of analysis**
- Standard litter size (four males four females)
- Comparing homogeneous and heterogeneous litters
  - mother can attend treated and untreated pups differently
  - depending on treatment pups respond to the mother differently
- Testing at different times across postnatal development
- Early tests can be more sensitive

The behavioral suite in the BRB

- How you can use it
  - Collaboration, i.e. we will do it for you
    - Grant based
    - Fee based (in progress)
  - Learn and use
    - We will show how
    - We will schedule your activity and use
    - We will help choose a test and analyze your data
      - Collaboration

Activity chambers

Acoustic startle response



Rotarod system

How to find us

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