Evaluation of learning and memory: From *C. elegans* to primate experiments

Mieke Verslegers

mversleg@sckcen.be
General overview

- Introduction
- Why use animal models to study cognition?
- Examples of animal models
- Conclusion
Introduction

Why use animal models to study cognition?

Examples of animal models

Conclusion
Cognition

Prefrontal cortex: Higher cognitive functions

Hippocampus: Learning & memory

Introduction
Stem cells and our memory

- Generation of new hippocampal neurons driven by emotional input, e.g. fear → helps us to remember fear and how to react
- Which other brain areas/neurotransmitters/cell types are responsible for learning & memory?
- Which genes/proteins help to regulate these responses?
General overview

- Introduction
- Why use animal models to study cognition?
- Examples of animal models
- Conclusion
Why use animal models to study cognition?

- Manipulation of animal’s behavior & environment
- Invasive procedures to the brain & the body
- Genetic engineering
- Short life-span

- Extrapolation to human
- Limited number of tests for complex cognitive behavior
Why use animal models to study cognition?

- **Areas of cognitive research:**
  - Addiction
  - Maternal deprivation
  - Emotion
  - **Learning & memory**
  - Sociability & fear
  - ....
General overview

- Introduction
- Why use animal models to study cognition?
- Examples of animal models
- Conclusion
Examples of animal models

Invertebrate research

- Learning behavior in the marine mollusc *Aplysia*
  - Link with behavioral and synaptic changes
  - Discovery of a role for certain proteins such as cAMP, CREB, ...

- Learning behavior in the nematode *C. elegans*
  - Remarkable behavioral plasticity

- Genetic dissection of learning in the fruit fly *Drosophila melanogaster*
  - First learning mutant and associative learning assay
Caenorhabditis elegans

- Fully characterized nervous system
  - 302 neurons
- Short- and long-term habituation
- Context-dependent memory

Sasakura, 2013, Frontiers in neural circuits
Examples of animal models

**Invertebrate research**

- Learning behavior in the marine **mollusc** *Aplysia*
  - Link with behavioral and synaptic changes
  - Discovery of a role for certain proteins such as cAMP, CREB,...

- Learning behavior in the **nematode** *C. elegans*
  - Remarkable behavioral plasticity

- Genetic dissection of learning in the **fruit fly** *Drosophila melanogaster*
  - First learning mutant and associative learning assay
Drosophila melanogaster

- Drosophila Alzheimer’s disease model available
  - Proteolysis of amyloid precursor protein (APP) → orthologues of APP in the fruit fly (Appl) and formation of amyloid β plaques
  - Models that express human AD genes → revealing underlying mechanisms and high-throughput screening of therapeutic components

- Visual place learning:
  - Preference for 25°C → learn to reach area based on visual cues

Ofstad, 2011, Nature letters
Examples of animal models

**Vertebrate research**

- **Zebrafish** *Danio rerio*

- **Rodents**
  - By far the most extensively studied organism (90%)

- **Cats**
  - Visual deprivation experiments
  - Binocular vision → judgement of distance

- **Non-human primates**
  - Non-invasive
  - Higher cognitive functions
Zebrafish

- Well-known model for vertebrate development
- Increasingly acknowledged as a model to study brain mechanisms
- Easily bred in great numbers and rapid development

- Highly developed spatial navigation & memory skills
- Frontal cortex and hippocampus not so evident
Aquatic T-maze
- Attention
- Memory
- Reinforcement

→ Color discrimination

Habituation test
- Exploration of new (colored) stimulus behind a ‘door’

Rotating drum
- Visually guided escape taxis

→ Hiding of the fish behind the central pole

Place preference
- Conditioned appetitive stimuli

→ Paired toxicant exposure
Examples of animal models

Vertebrate research

- Zebrafish *Danio rerio*

- Rodents
  - By far the most extensively studied organism (90%)

- Cats
  - Visual deprivation experiments
  - Binocular vision → judgement of distance

- Non-human primates
  - Non-invasive
  - Higher cognitive functions
Non-human primates

- 5% of all cognitive studies
  - Higher cognitive functions
  - Point fixation

**Stimulus-response association task**
Recording of eye saccades

Horwitz, 2004, Neuroscience letters
Non-human primates

- 5% of all cognitive studies
  - Higher cognitive functions
  - Complex memory tests

Fuster, 1971, Science
MacIntosh, 2014, PlosOne

Evaluation of region-specific brain activity
Non-human primates

- 5% of all cognitive studies
  - Higher cognitive functions
  - Complex memory tests
General overview

- Introduction

- Why use animal models to study cognition?

- Which animal models are most suited to study cognition?

- Conclusion
Conclusion

- 1960’s to today: high increase in animal cognitive studies

- No in vitro alternatives possible

- Different animal models available
  - The best option is highly dependent on the research question

- Clinical relevance in neurological disorders (e.g. Alzheimer’s, mental illness) and our ageing population
It says here goldfish only have a three second memory.

Yeah, I read that in New Scientist last week.