KING'S College LONDON

INSTITUTE OF PSYCHIATRY,
PSYCHOLOGY & NEUROSCIENCE

Module:
Techniques in Neuroscience

Week 1:
Understanding the brain: Who we study, how and why?

Dr Frank Hirth

Topic 2:
Model organisms
Part 1 of 3

Topic list

This week, we will be looking at the following topics:

- ***Topic 1: The living brain***
- ***Topic 2: Model organisms***
- Topic 3: Focused journal club

Click **Next** to continue

Introduction

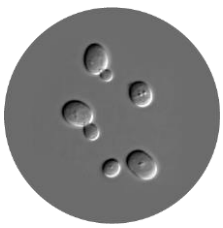
Animal models in neuroscience research

Learning objectives

1. To gain an understanding why animals are used in research, as models and a means to address a scientific question, both holistic and reductionist.
2. To study *in vivo* – as compared to *in vitro* – the causes, mechanisms and pathways from molecule to mind.
3. To understand why studies in a specific animal can have general application and significance because of evolutionary conservation (structural, molecular and functional homology).
4. To gain knowledge and understanding of how animals are used to study the function of genes, proteins, pathways, circuits, brain and behaviour.
5. To gain knowledge and understanding of how functional studies in animals are conducted.
6. To be able to name an example of how research using a specific animal species led to insights of general significance, and to know the limitations of such studies.

Part 1

Why do we use animal models in neuroscience research?



Yeast

Worm

Fruit fly

Zebrafish

Lamprey

Mouse

Main reasons:

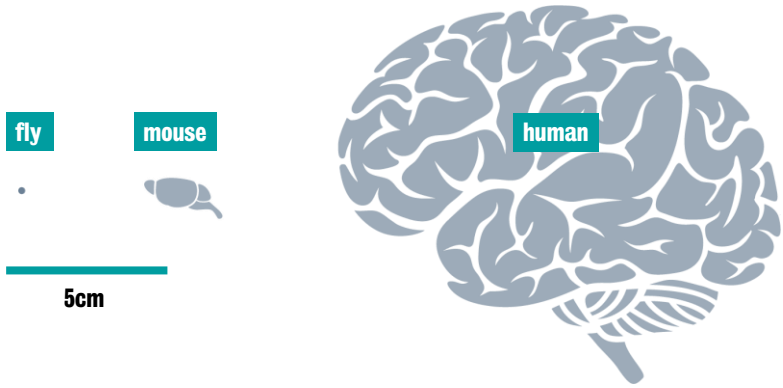
- a means to address a scientific question
- in *vivo*, as compared to *in vitro*

Important to note:
Ethics committee approval and Home Office consent are mandatory requirements for work with vertebrates.

White (2016)

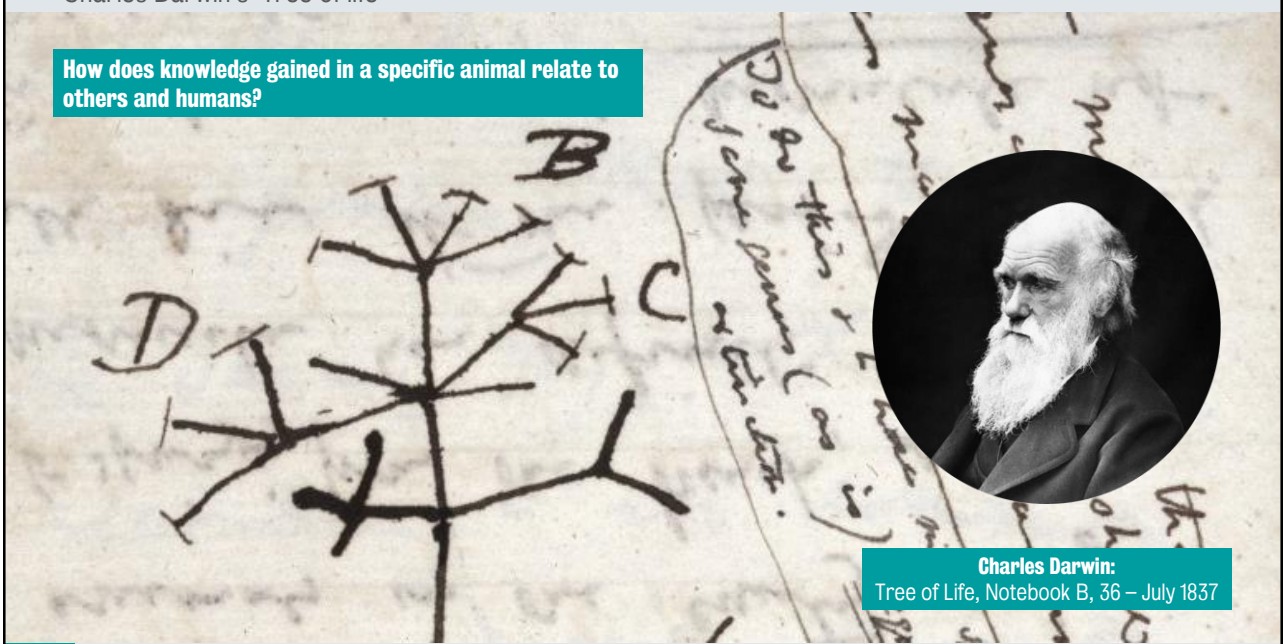
What can we learn from animal models?

Main reason:
understand causes, mechanisms, pathways from molecule to mind



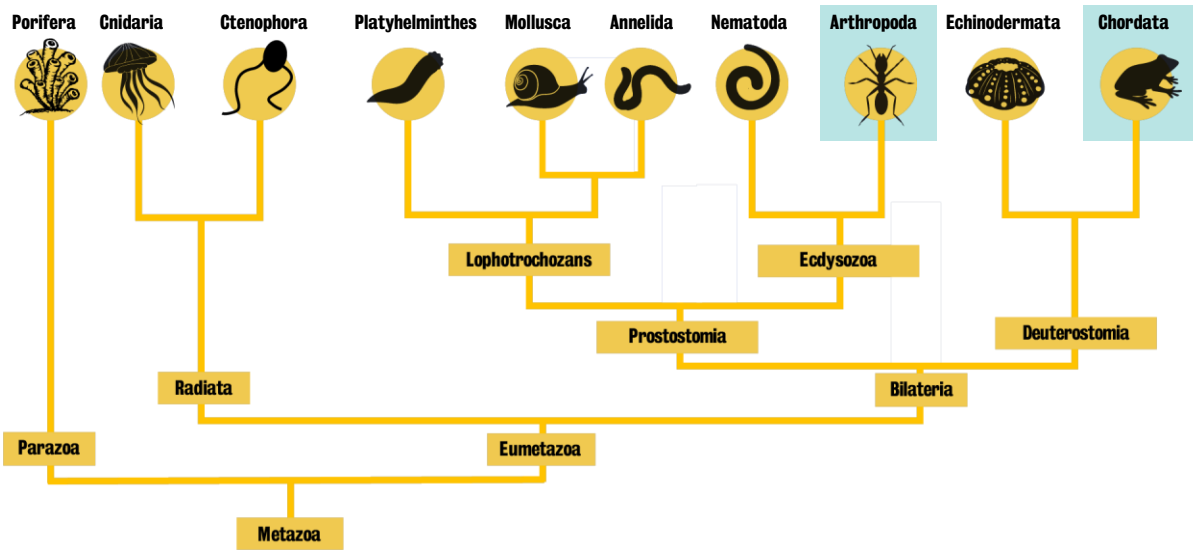
Charles Darwin's 'Tree of life'

How does knowledge gained in a specific animal relate to others and humans?



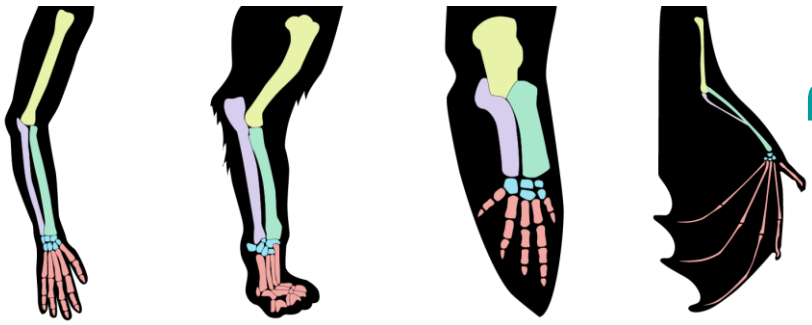
Charles Darwin:
Tree of Life, Notebook B, 36 – July 1837

Phylogenetic tree of animals



Dunn et al. (2014)

The concept of homology: evolutionary conservation



Homologous structures

> "The relative position or connection in homologous parts; they may differ to almost any extent in form and size, and yet remain connected together in the same invariable order."

Darwin, 1876, p. 382

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Dm otd  QRRERTTFTR'AQLDVLEALF'GKTRYPDIFM'
Mm Otx1 QRRERTTFTR'SQLDVLEALF'AKTRYPDIFM'
Mm Otx2 QRRERTTFTR'AQLDVLEALF'AKTRYPDIFM

Dm otd  REEVALKINL'PESRVQVWFK'NRRAKCRQQL'
Mm Otx1 REEVALKINL'PESRVQVWFK'NRRAKCRQQQ'
Mm Otx2 REEVALKINL'PESRVQVWFK'NRRAKCRQQQ'
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Homologous genes/proteins

Sequence identity between orthologous genes/proteins from different species

Darwin (1859)

What can we learn from animal models? (1)

We can gain knowledge and understanding about the function of:

a gene and its encoded protein (and different isoforms)

how specific genes and proteins interact

the signalling pathway and how it works

the formation/ specification of cell types, tissues and organs

the circuits and networks in the nervous system

the above in relation to disease

What can we learn from animal models? (2)

To gain knowledge and understanding, functional studies involve:

mutating, inactivating or overexpressing a gene/protein

finding interacting/ binding partners

screening for enhancers/ suppressors of 'disease gene/protein'

epistasis tests and manipulation of a signalling pathway

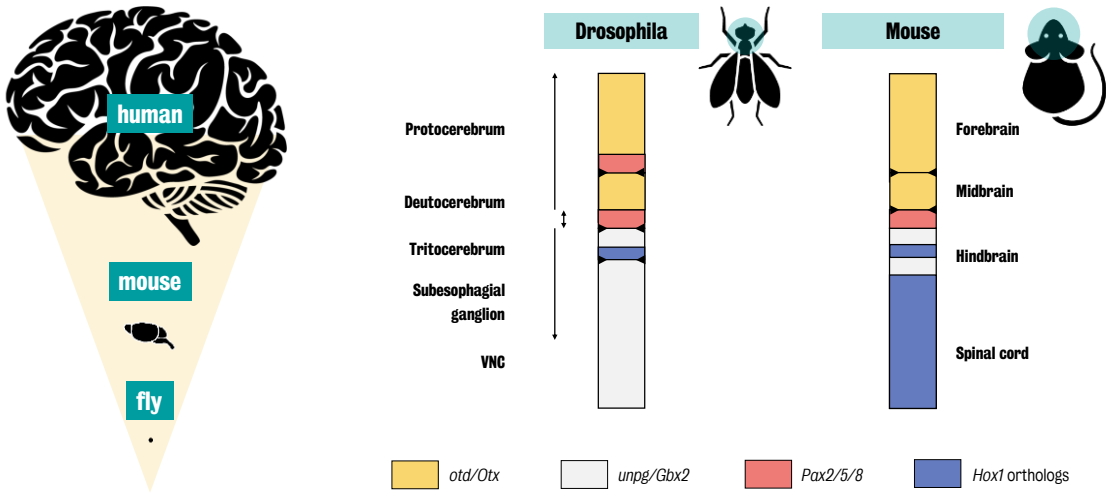
targeted activation/ inactivation of neural circuits

the regulation and function of behaviour

The dysfunction of the above that may underlie disease.

Important to note:
The majority of these studies are not possible in humans except for cell culture or non-invasive studies with written consent.

Conserved genetic programs in insect and mammalian brain development



Hirth & Reichert (1999)

End of part 1