KING'S College LONDON

INSTITUTE OF PSYCHIATRY, PSYCHOLOGY & NEUROSCIENCE

Module:
Techniques in Neuroscience

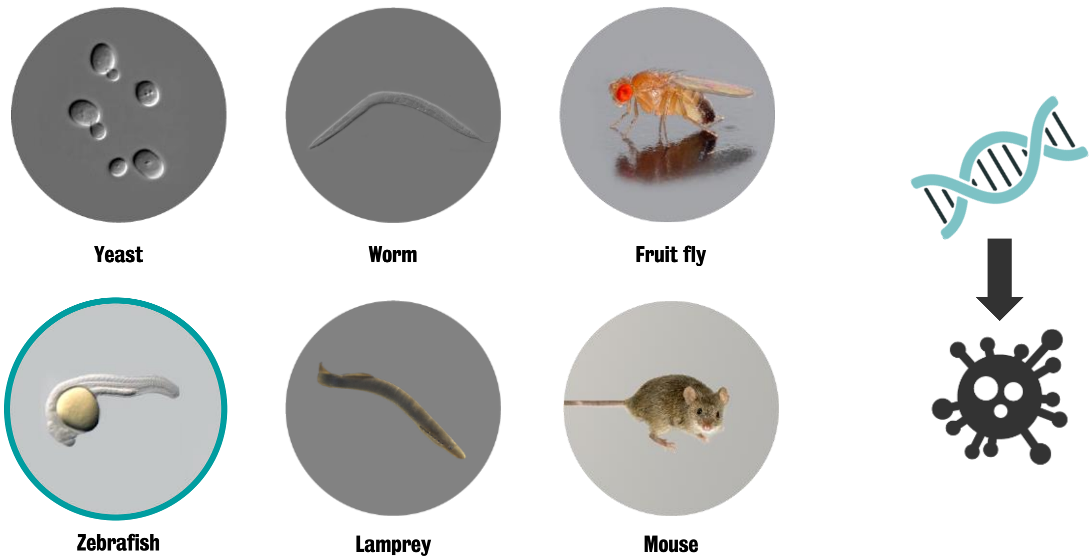
Week 1:
Understanding the brain: Who we study, how and why?

Dr Frank Hirth

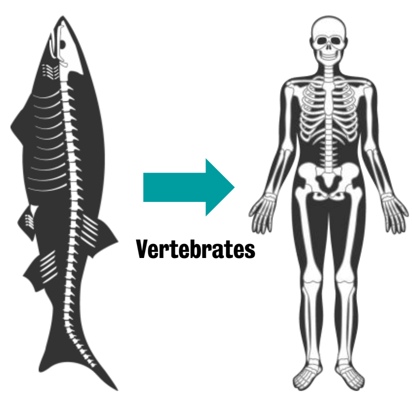
Topic 2:
Model organisms
Part 3 of 3

Part 3

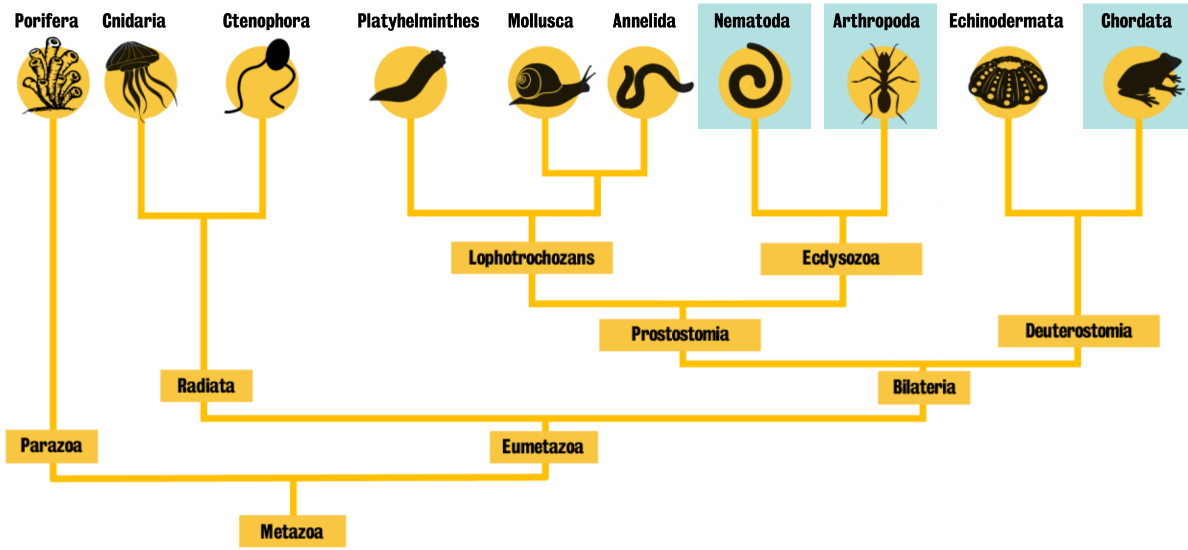
What can we learn from animal models: zebrafish



The zebrafish: *Danio rerio*

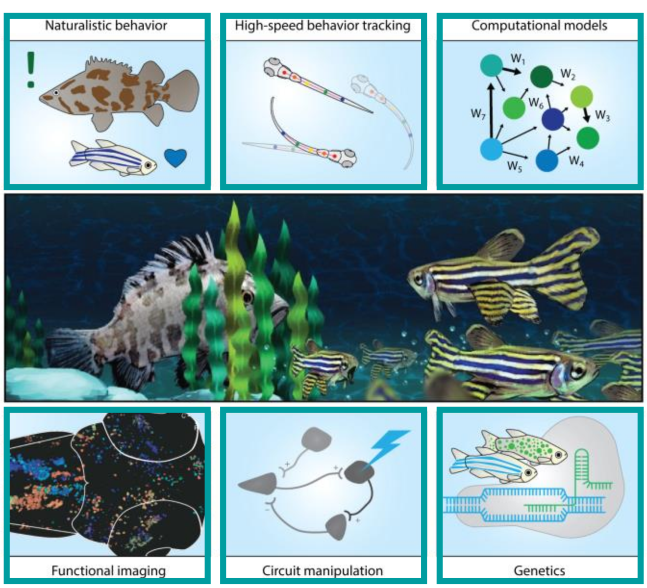


Phylogenetic tree of animals: chordata



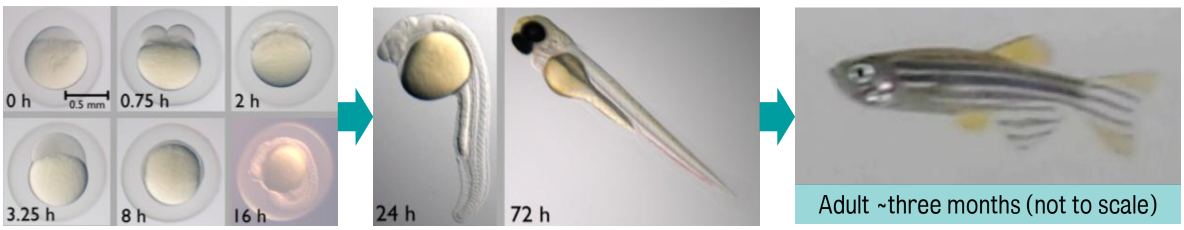
Dunn et al. (2014)

Functional *in vivo* studies in a vertebrate

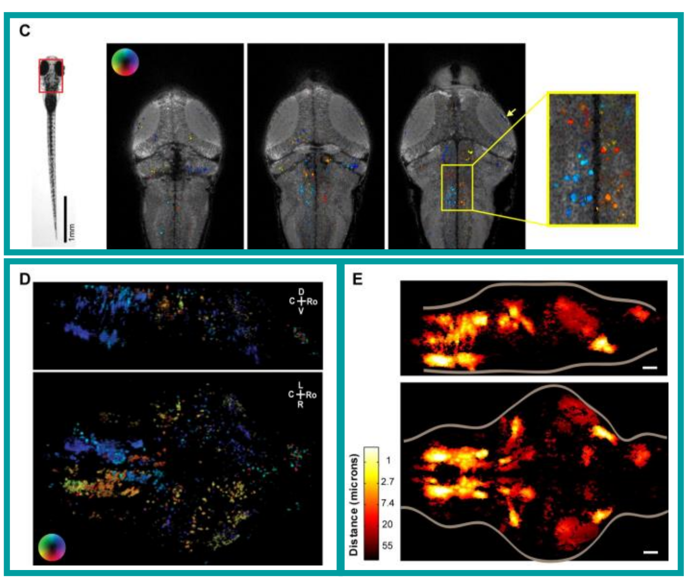


Orger & de Polavieja (2017)

Transparent embryo and a genetically identical offspring



Whole brain imaging of a behaving animal

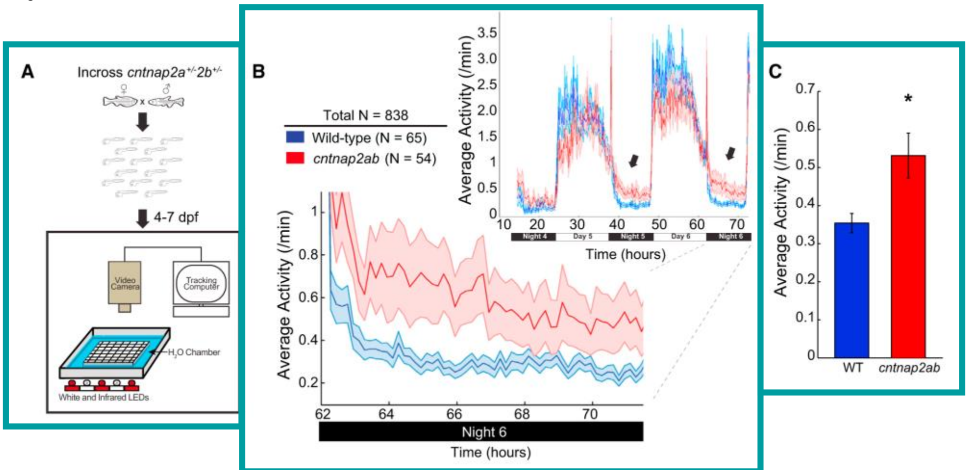


Feierstein et al. (2015)

Mutation of *cntnap2a*: an autism-related gene

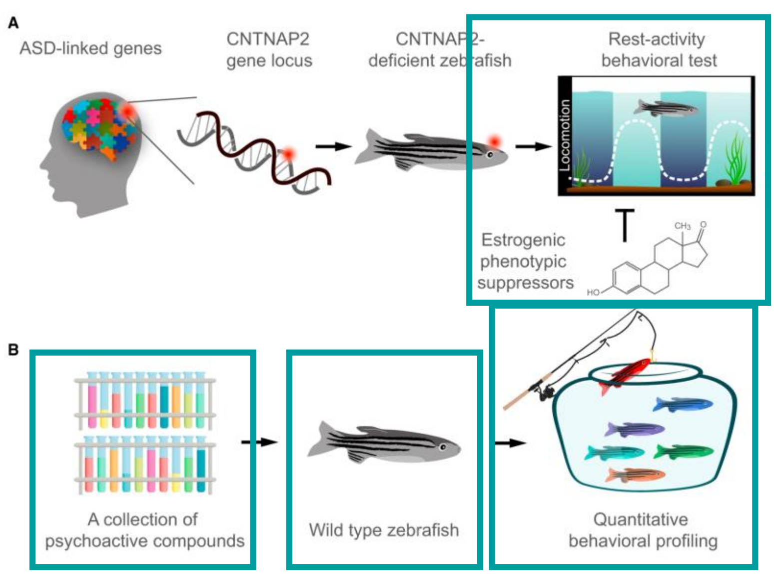
Mutation of cntnap2a found to be related to:

- autism in humans
- hyperactivity



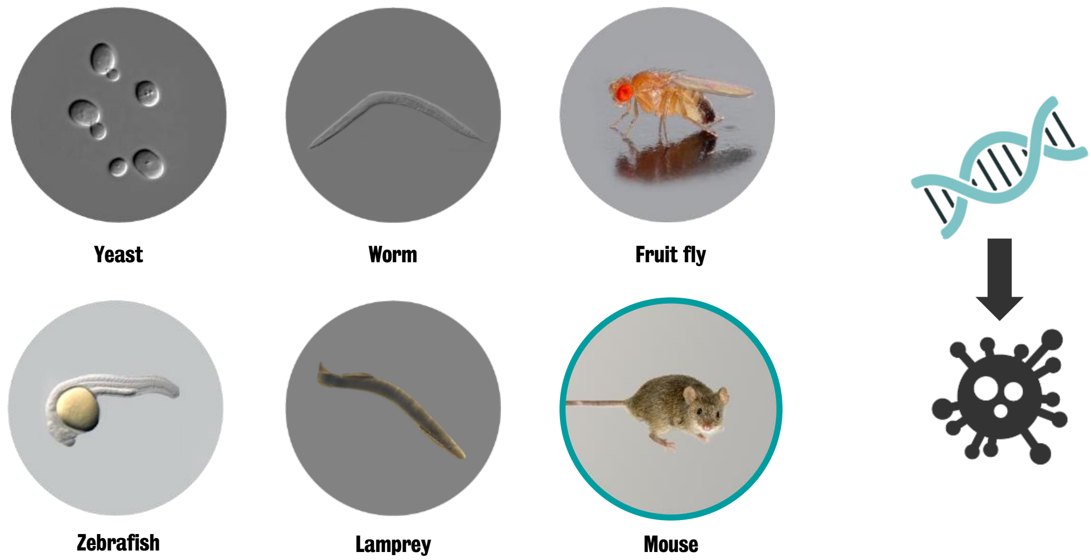
Hoffman et al. (2016)

Phenotypic suppressors of autism gene-related defects



Biran & Levkowitz (2016)

What can we learn from animal models: mouse



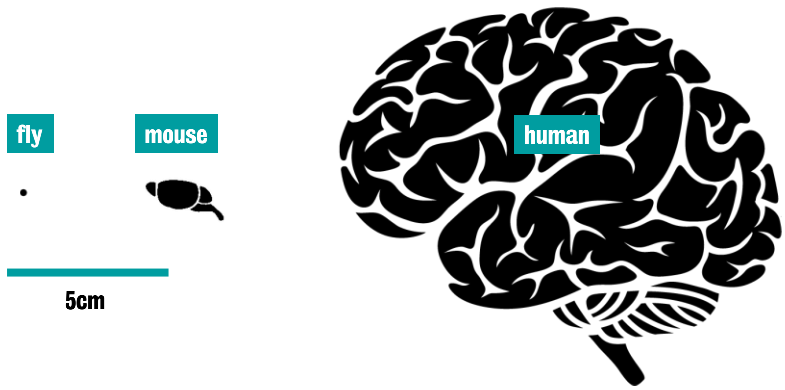
The house mouse: *Mus musculus* (1)

Mammal with social behaviour

90 per cent of genes homologous to human

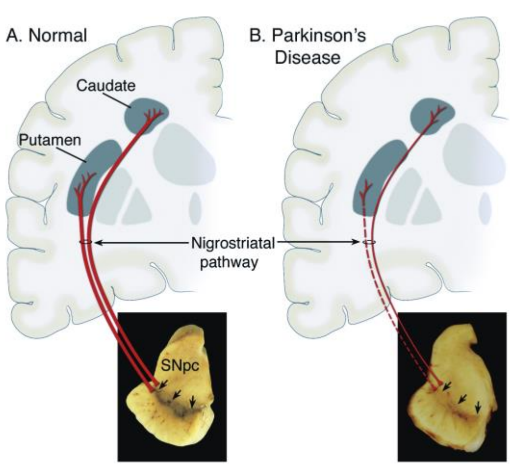
The house mouse: *Mus musculus* (2)

Study:
causes, mechanisms, pathways

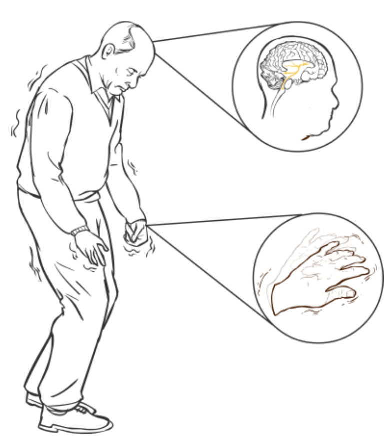


Aim:
to go from molecule to mind

Impact of Parkinson’s disease on body and brain



What happens in the brain:
- loss of nigrostriatal pathway
- degenerative loss of dopaminergic neurons in the SNpc (substantia nigra pars compacta)



What happens in the body:
shuffling, tremor, rigidity and bradykinesia

Dauer & Przedborski (2003)

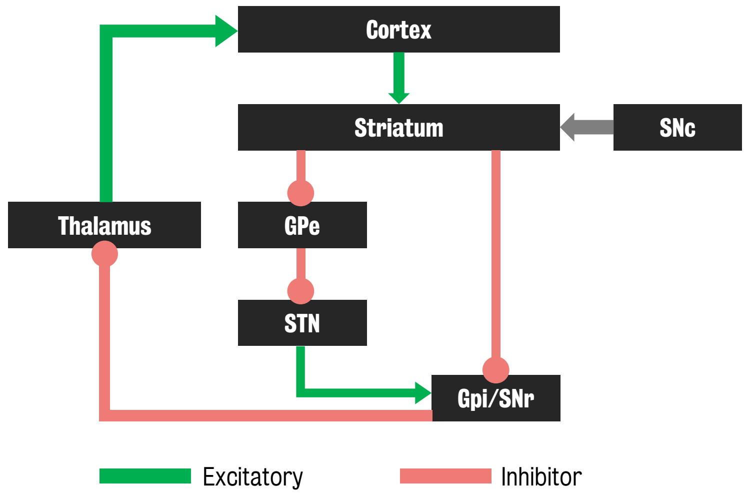
Functional anatomy of the mammalian basal ganglia

Input:
- striatum: caudate and putamen

Intrinsic:
- subthalamic nucleus (STN)
- external segment of globus pallidus (GPe)

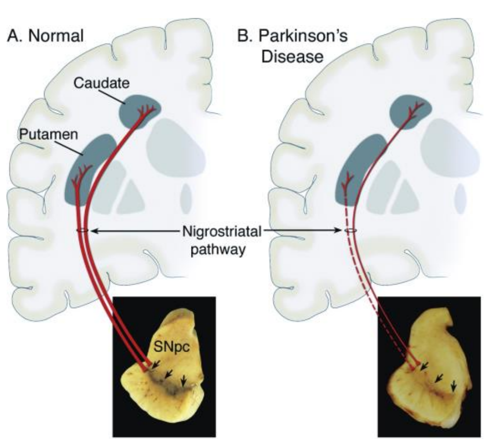
Output:
- substantia nigra pars reticulata (SNr)
- internal segment of globus pallidus (GPi)

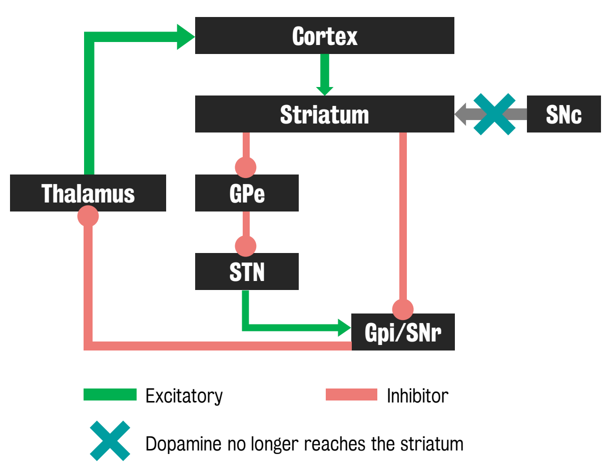
Neuromodulator:
- substantia nigra pars compacta (SNc): dopamine input



Gerfen & Surmeier (2011)

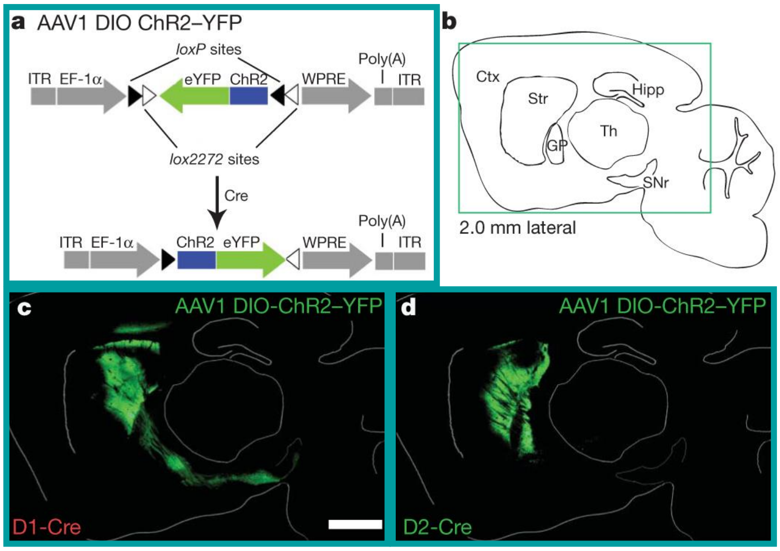
Lack of striatal dopamine innervation





Dauer & Przedborski (2003); Gerfen & Surmeier (2011)

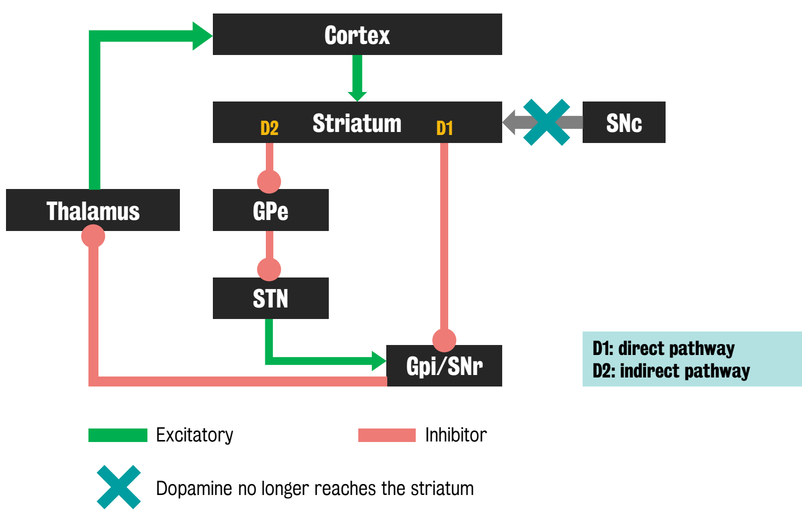
Targeted manipulation of neural circuitry mediating complex behaviour



ChR2: Channelrhodopsin

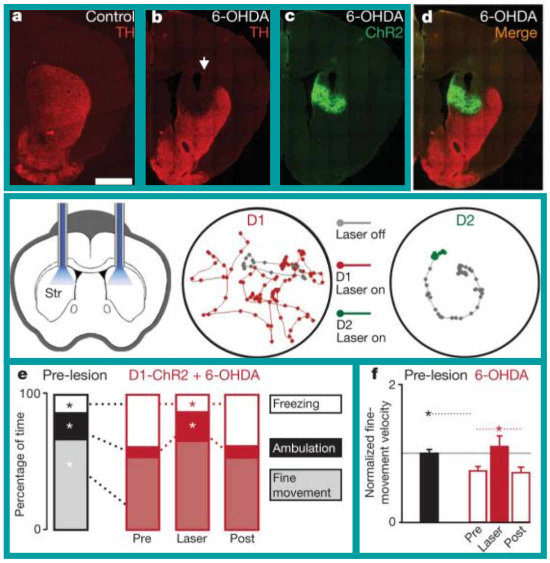
Kravitz et al. (2010); Friend & Kravitz (2014)

Direct and indirect pathways



Gerfen & Surmeier (2011)

Targeted D1 activation can overcome PD-related motor impairment



Study findings:

- D1 and D2 have a crucial role in voluntary movement
- the activation of D1 can overcome a parkinsonian phenotype

Kravitz et al. (2010); Friend & Kravitz (2014)

From gene mutation, inactivation and overexpression to their relation to disease

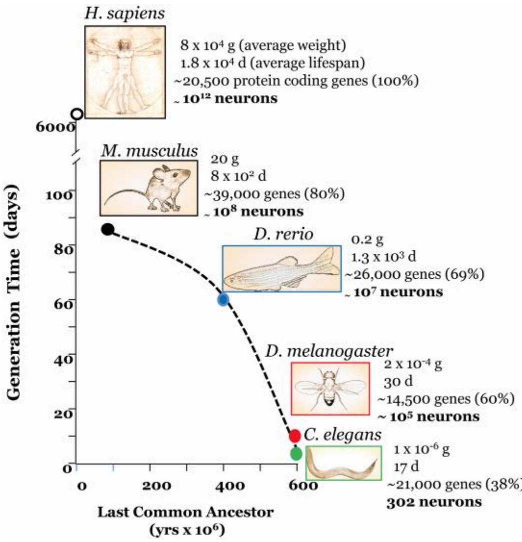
To gain knowledge and understanding, functional studies involve:

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.

Gene evolution and the study of mental health disorders



It is the evolutionary conservation of genes, pathways and their dysfunctions that gives great power to animal models in the study of mental health disorders.

White (2016)

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End of topic