~~Small~~ Animal Imaging

Clara Aabye Madsen
M.Sc., PhD student

Neurobiology Research Unit
Department of Neurology, Neuroscience Center
Copenhagen University Hospital, Rigshospitalet
Denmark

Neurobiology Research Unit
Rigshospitalet
Copenhagen University Hospital

REGION H Rigshospitalet

UNIVERSITY OF COPENHAGEN
FACULTY OF HEALTH AND MEDICAL SCIENCES

Animal Imaging

Clara Aabye Madsen
M.Sc., PhD student

Neurobiology Research Unit
Department of Neurology, Neuroscience Center
Copenhagen University Hospital, Rigshospitalet
Denmark

Animal Brain Imaging

Clara Aabye Madsen
M.Sc., PhD student

Neurobiology Research Unit
Department of Neurology, Neuroscience Center
Copenhagen University Hospital, Rigshospitalet
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Agenda

- Why do we use animal?
- Introduction to preclinical imaging
- Advantages and disadvantages of using animals

Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

Animals in neuroscience

Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

Why do we use animals in research?

- Basic research
  - Fundamental processes
    - Macroscopic, microscopic, molecular
  - How does the cells, organs, systems work?
  - Healthy animals

Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

Why do we use animals in research?

- Basic research
- Preclinical research
  - Disease etiology, pathogenesis and mechanisms
  - Treatment targets, mode-of-action and efficacy
  - Animal models

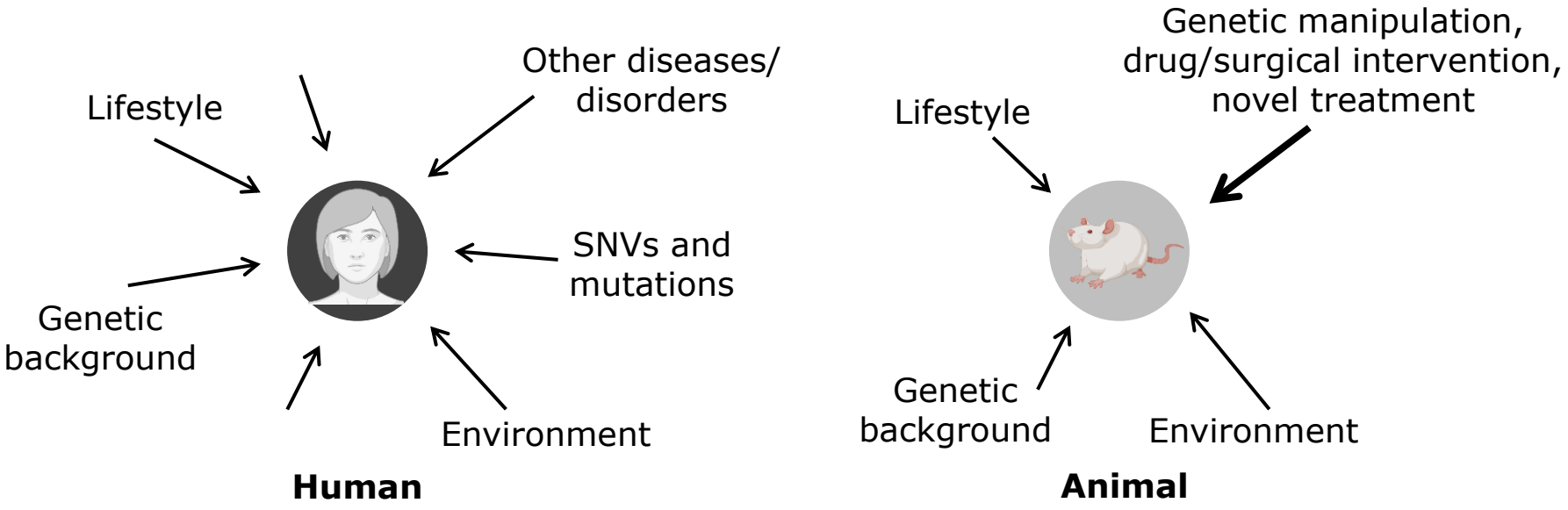
Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

Why do we use animals in research?

- Basic research
- Preclinical research

} Translational

- Why do we still need animals?



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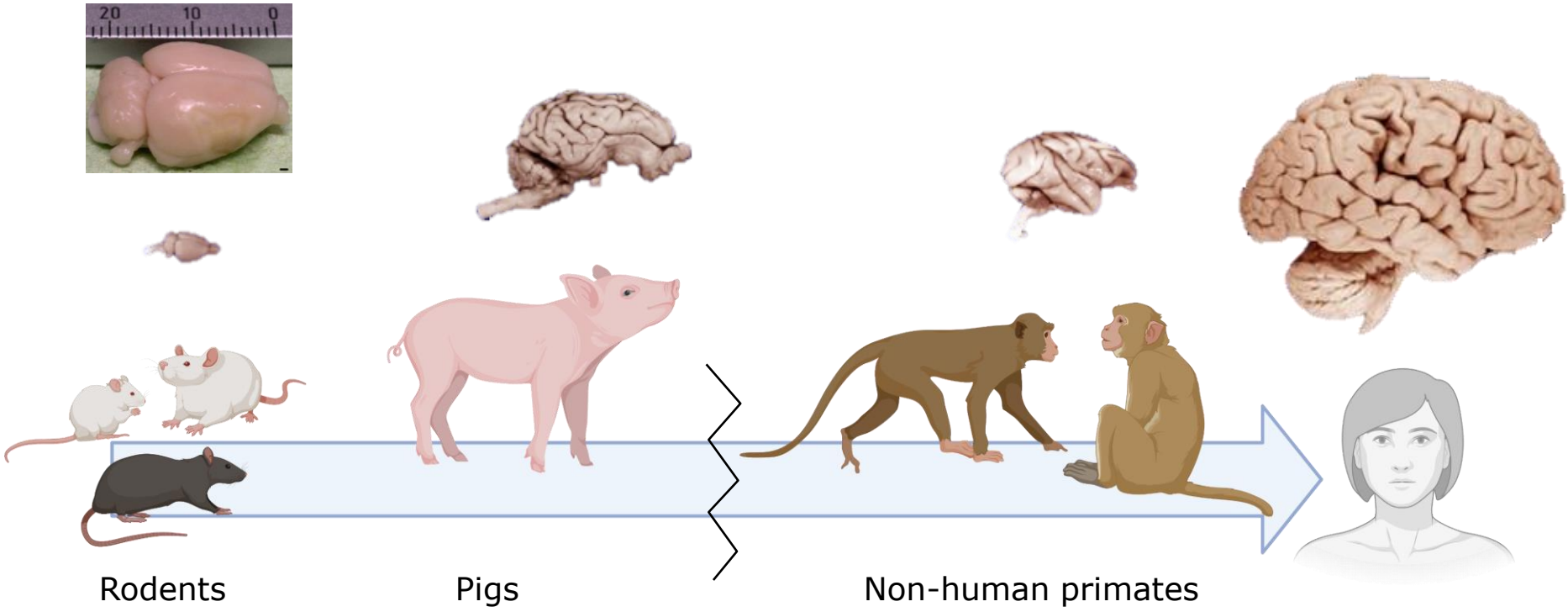
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

Why do we use animals in research?



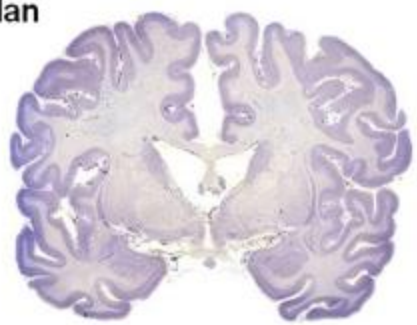
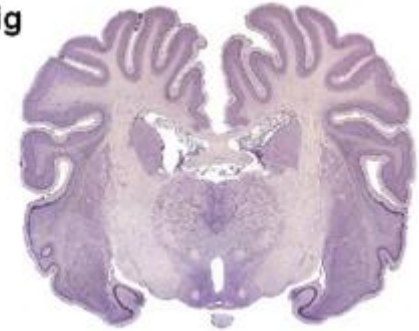
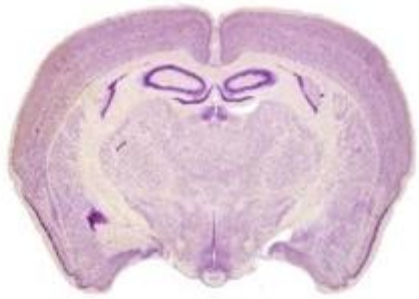
Considerations for choosing an animal species:

1. Translation
2. Ethics and accessibility
3. Budget

Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

Neuroimaging in animals

Table 1 Brain weights and sizes of adult humans, pigs, dogs, cats, rats, and mice

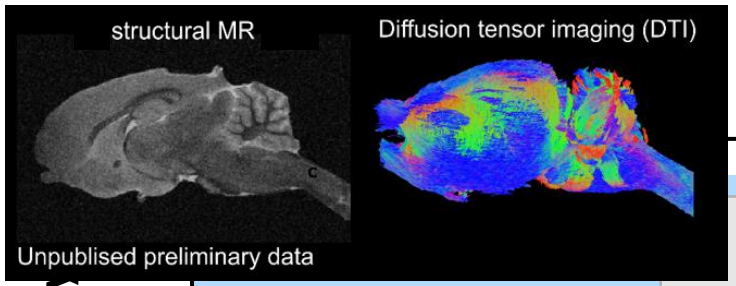
	Species					
	Human	Pig	Dog	Cat	Rat	Mouse
Brain size						
	Man	Pig			Rat	
						
Gyri and sulci	Gyrence-phalic	Gyrence-phalic			Lissence-phalic	

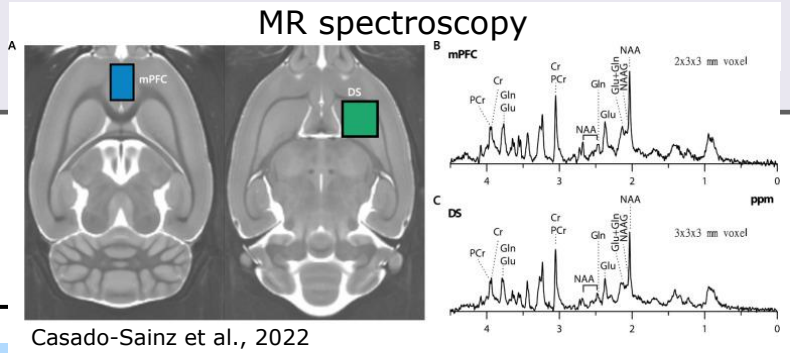
Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

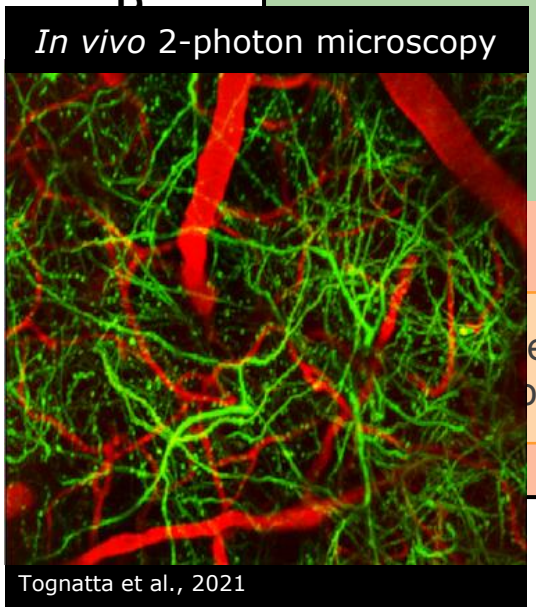
Preclinical imaging

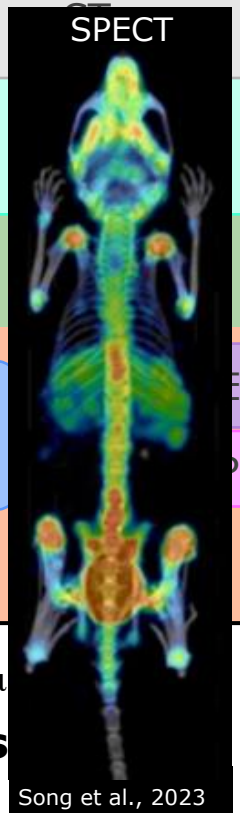
Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

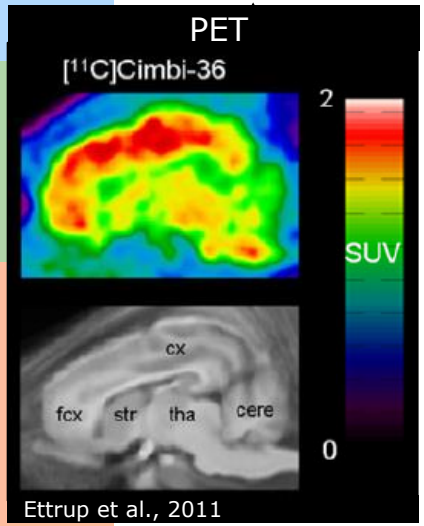
Preclinical imaging











Optical microscopy

10μm

100μ

10mm

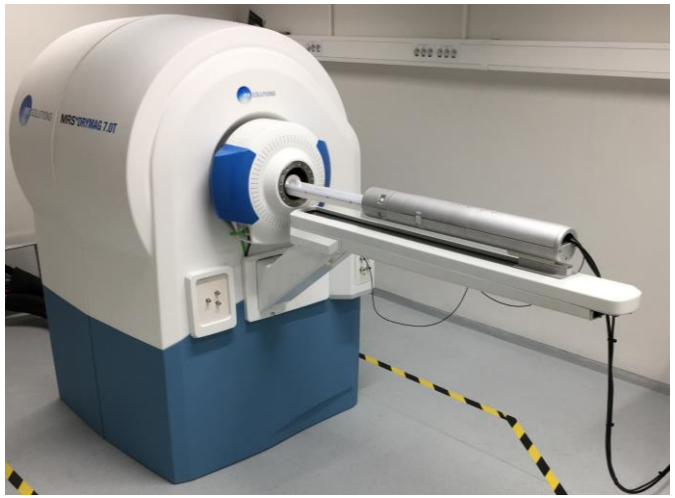
Spatial res

Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

Preclinical scanners

Human scanners

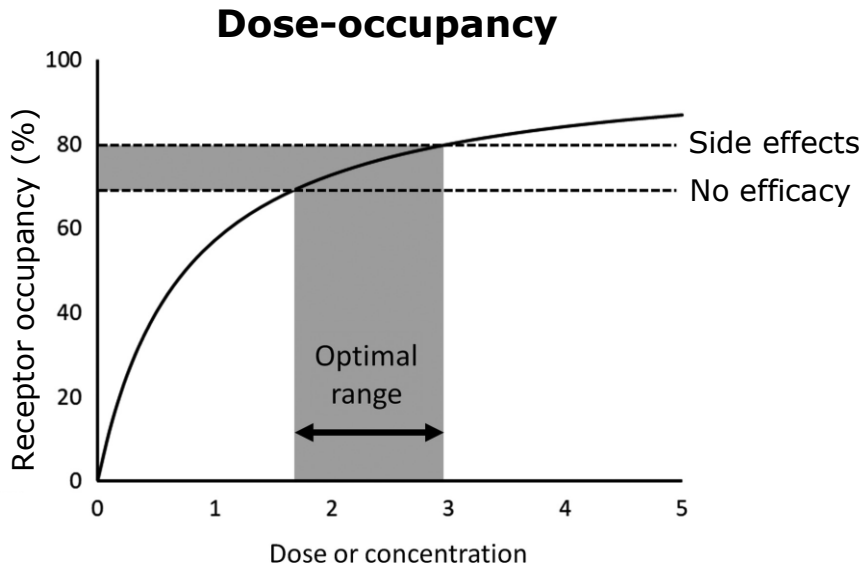
Small animal scanners



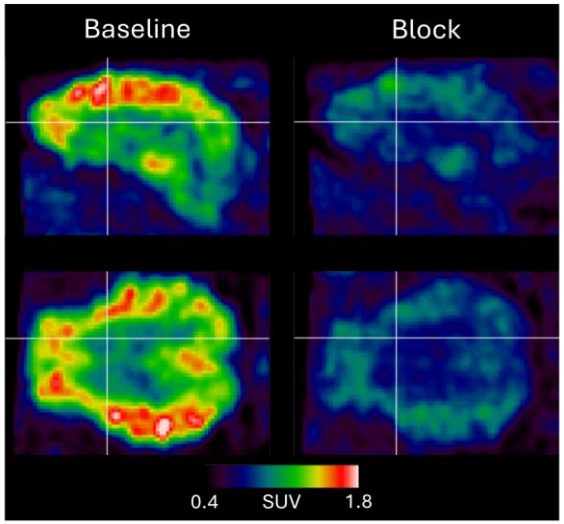
Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

Why do we use animals in brain imaging?

- Basic research
- Preclinical research
  - Disease etiology, pathogenesis and mechanisms
  - Treatment targets, mode-of-action and efficacy
    - PET imaging: Target engagement, BBB penetration, pharmacokinetics



Edited from Arakawa, Takano & Halldin, 2020



Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

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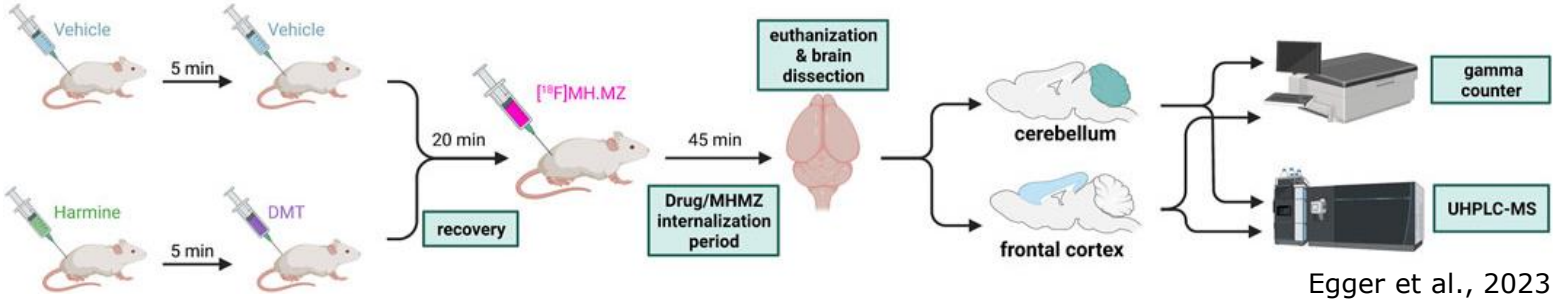
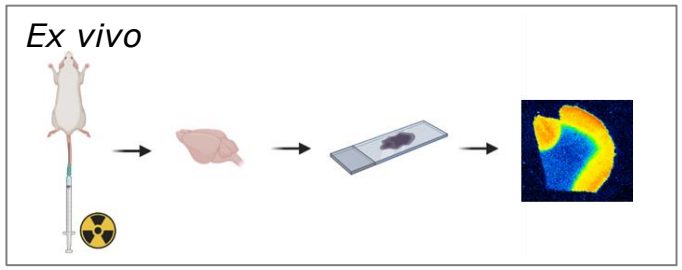
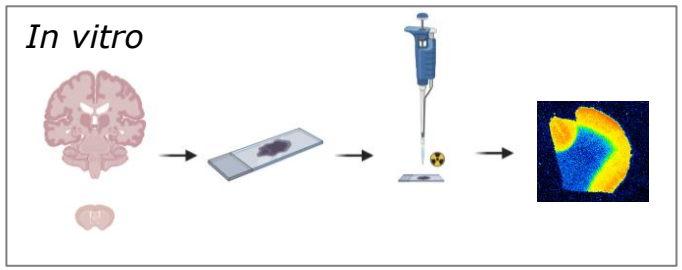
***Ex vivo* occupancy**



Egger et al., 2023

Autoradiography



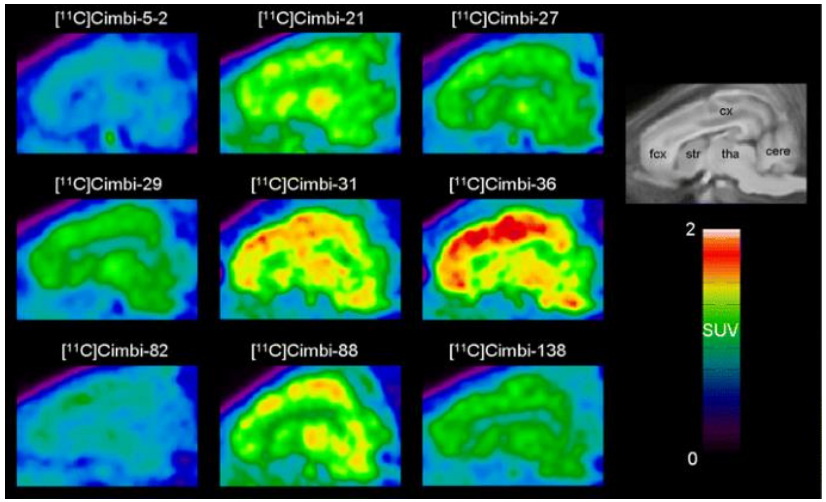


Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

Why do we use animals in brain imaging?

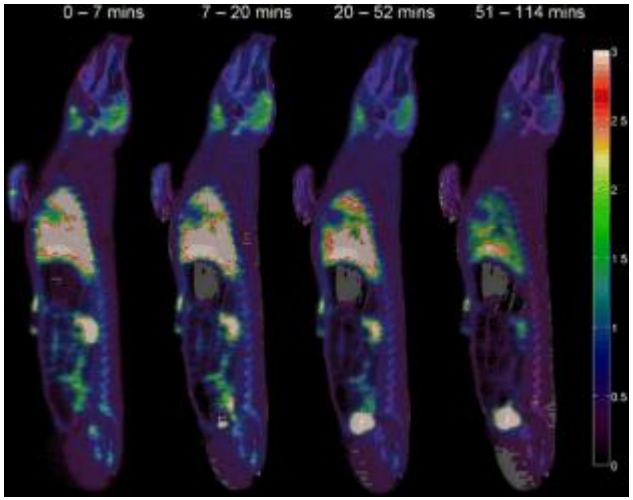
- Basic research
- Preclinical research
- Develop and validate new methods for imaging in humans
  - PET tracer development

BBB penetration, target binding, pharmacokinetics



Ettrup et al., 2011

Biodistribution and dosimetry



Ettrup et al., 2013

Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

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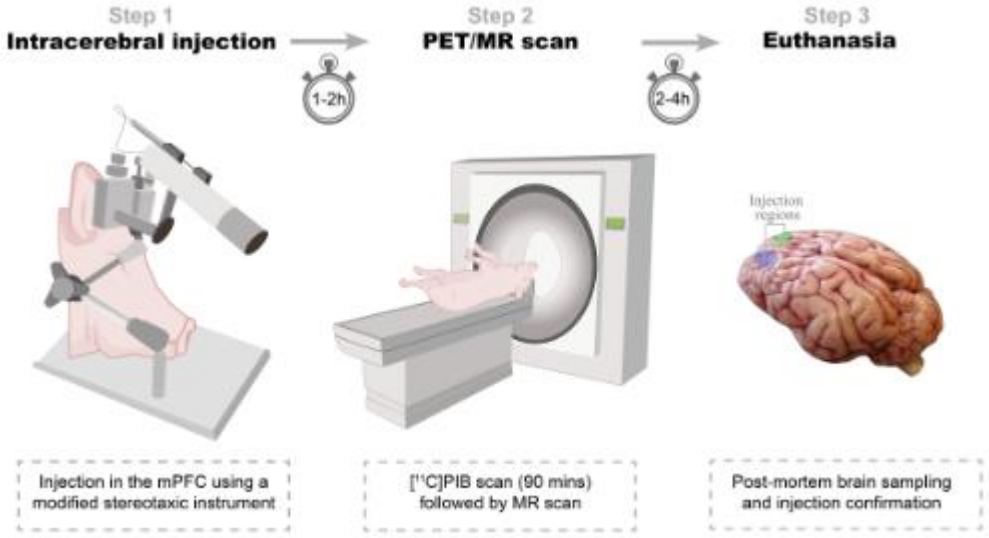
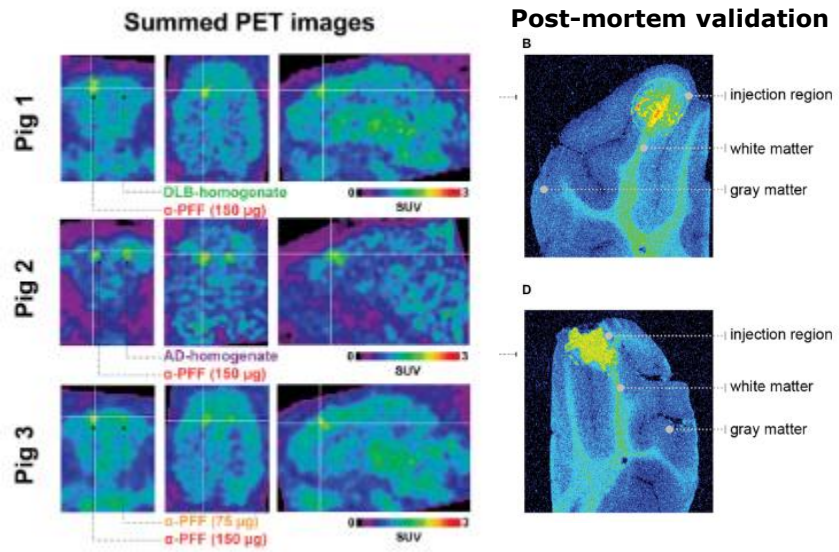


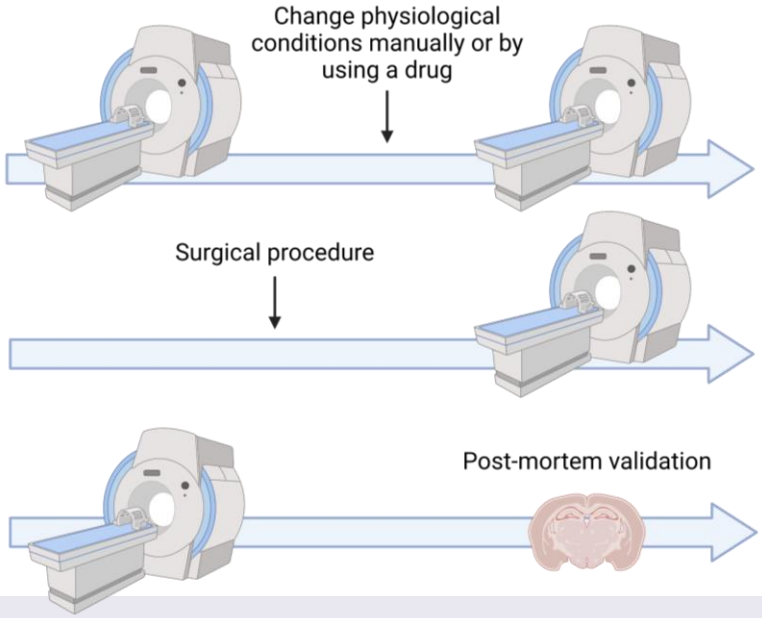


Raval et al., 2022a,b

Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

Why do we use animals in brain imaging?

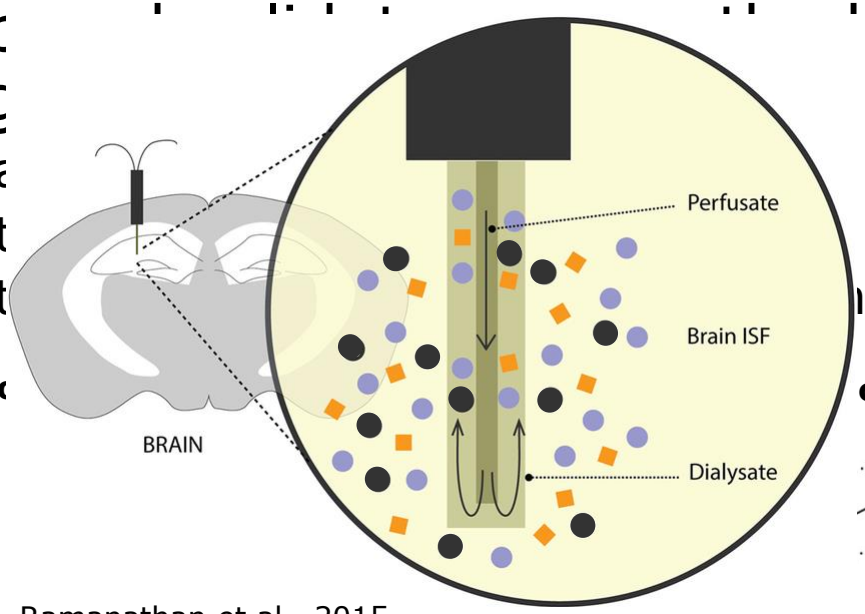
- Basic research
- Preclinical research
- Develop and validate new methods for imaging in humans
  - PET tracer development
  - Validation of MR sequences



Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

Why do we use animals in brain imaging?

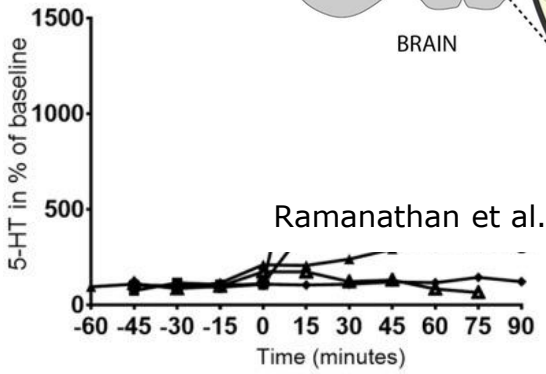
- Basic research
- Preclinical research
- Develop[illegible]'s for imaging
  - PET tra[illegible]
  - Validat[illegible]
  - Validat[illegible]echanisms



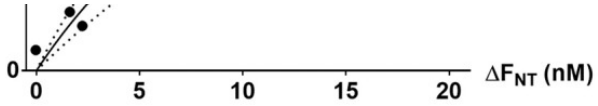
Ramanathan et al., 2015

Micr[illegible]

cy plot



Jørgensen et al., 2016

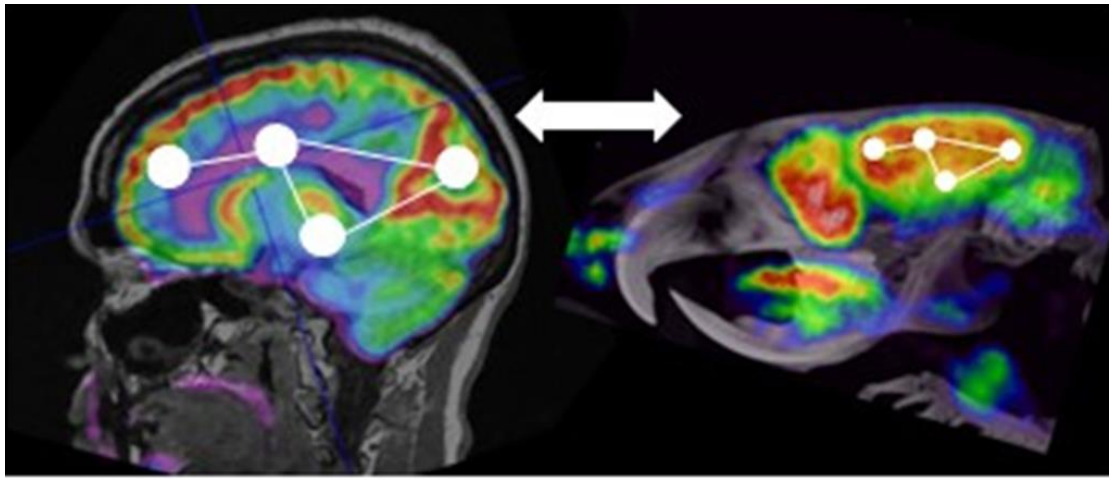


Change in neurotransmitter concentration

Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

Why do we use animals in brain imaging?

- Basic research
- Preclinical research
- Develop and validate new methods for imaging in humans
- Validating animal models



Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

Advantages of using animals for imaging

- High throughput
- Less animals compared to *in vitro*/*ex vivo*
- Genetic manipulation and drug/surgical interventions
- Post-mortem validation
- Less scatter and attenuation
- Higher radiation dose

Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

Disadvantages of preclinical imaging

Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

Anesthesia

- Affect brain metabolism and cerebral blood flow

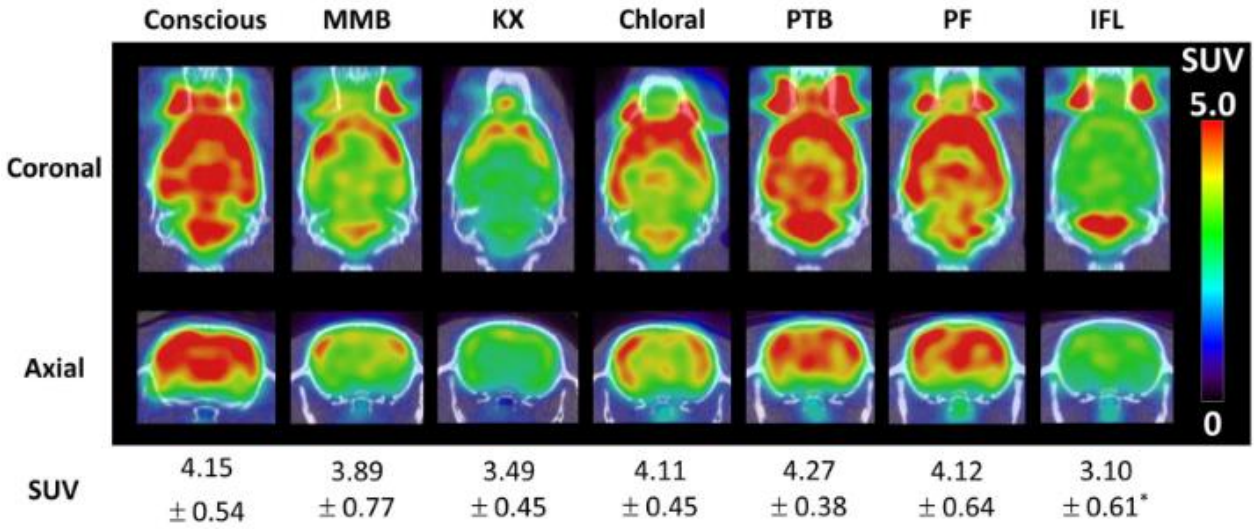


Table 3 Cerebral blood flow (CBF) in conscious and anesthetized rats, determined using [^{125}I]IMP

	CBF (mL/100 g/min)
Conscious	94.7 ± 6.0
MMB	63.8 ± 8.1**
KX	62.5 ± 19.1**
Chloral	104.6 ± 12.9
PTB	49.3 ± 4.9**
PF	52.9 ± 4.4**
IFL	115.6 ± 8.4**

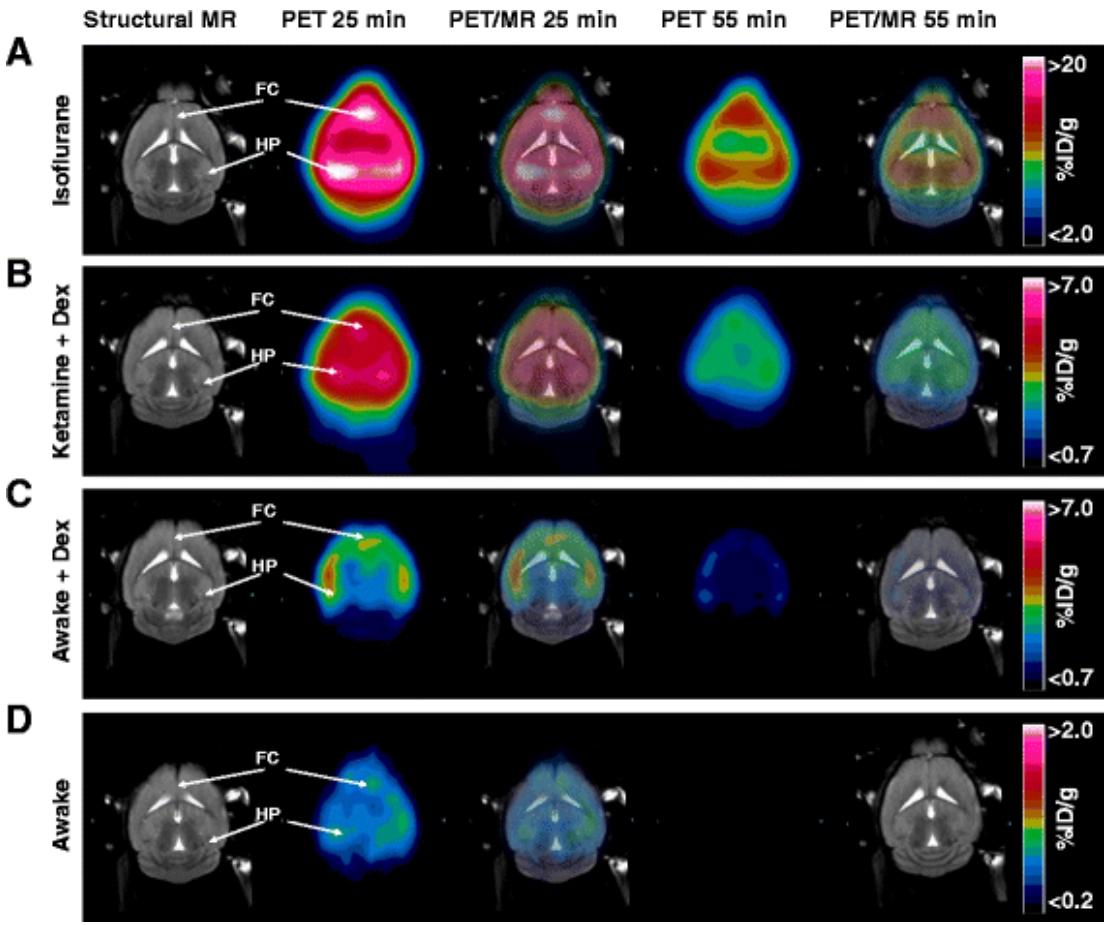
Data are expressed as mean ± SD (n = 6–7). **P < 0.01 compared with conscious rats as determined using ANOVA with Dunnett's multiple comparison test

Suzuki et al., 2021

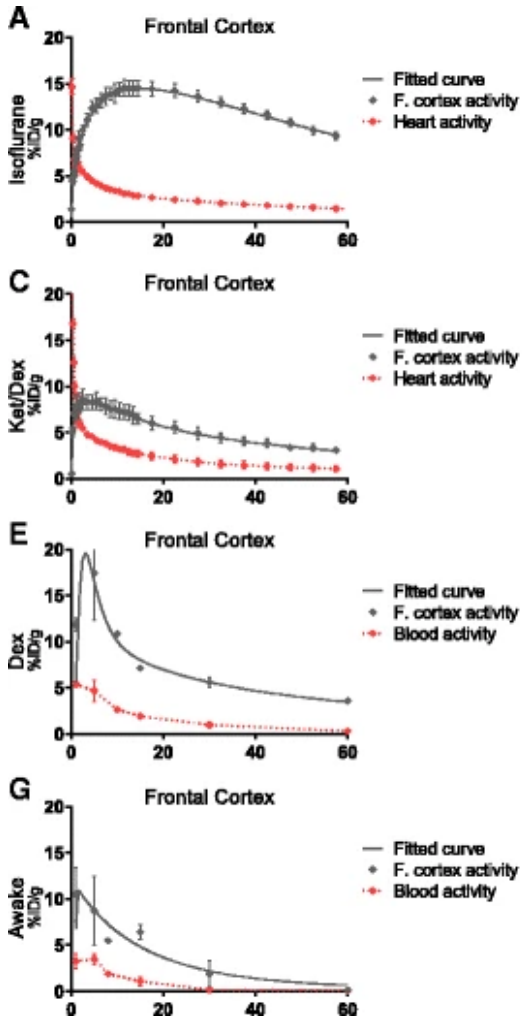
Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

Anesthesia

- Affect pharmacokinetics of PET tracer



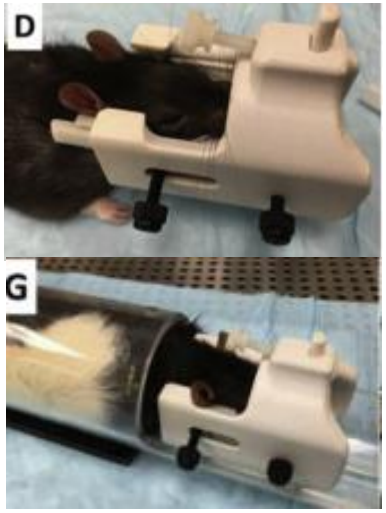
Palner et al., 2016



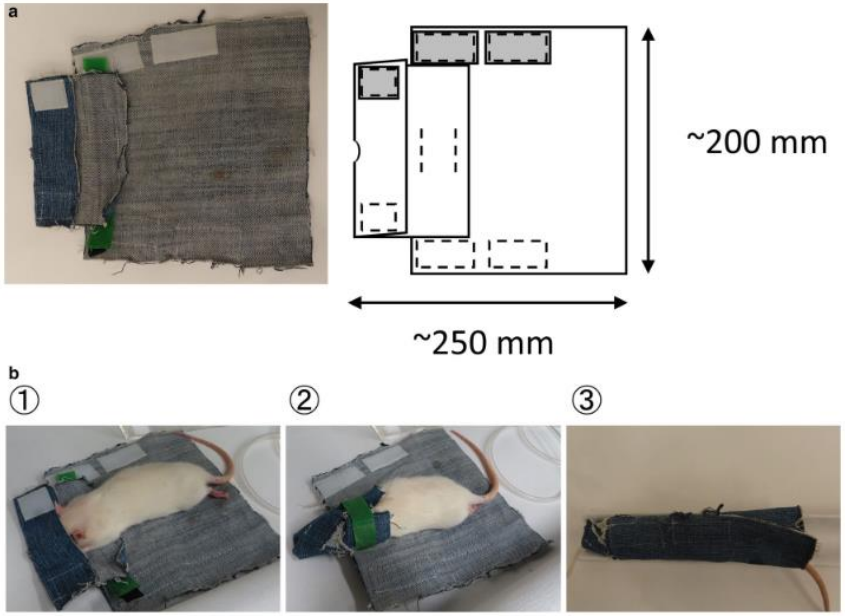
Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

Is anesthesia necessary?

Contrained

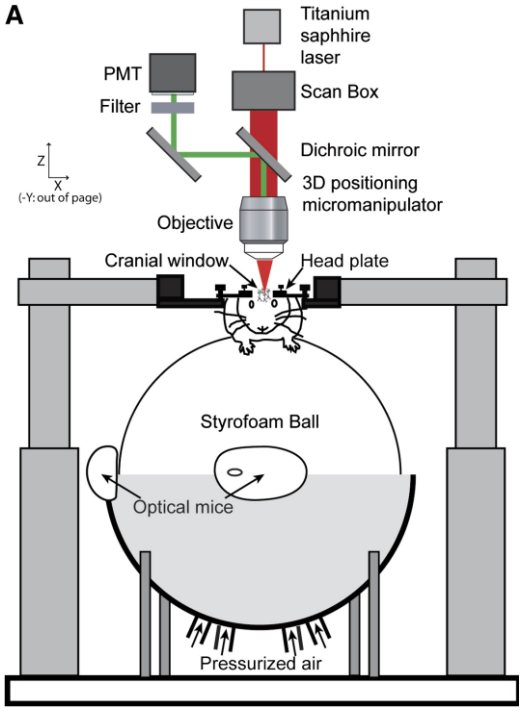


Dopfel & Zhang, 2018



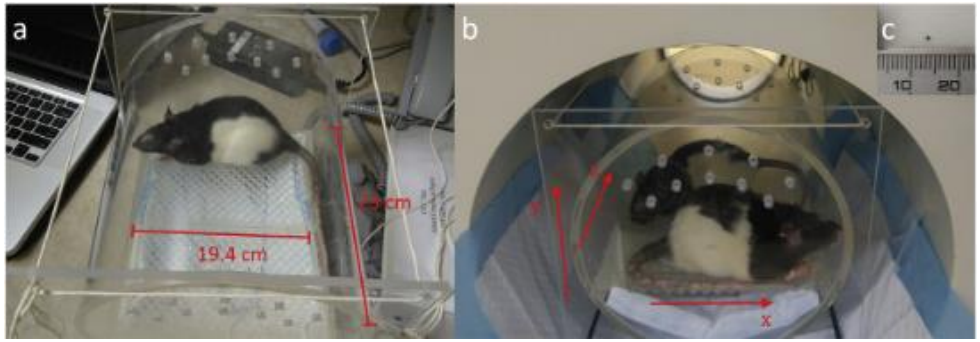
Suzuki et al., 2021

Head-fixed



Dombeck et al., 2007

Freely moving



Miranda et al., 2019

Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

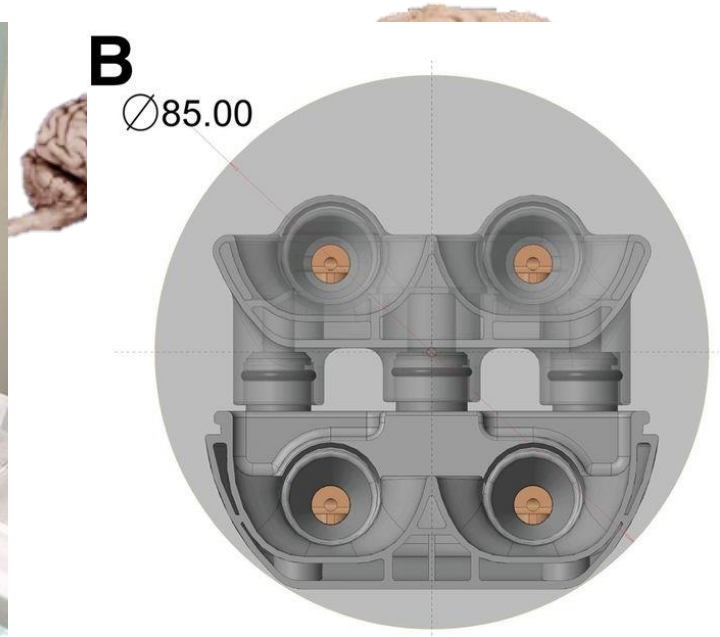
Kinetic modeling

- Large vs small animals
- Input function
  - Arterial vs image-derived
  - Metabolites
- Reference region
- Is quantification necessary?

Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

Spatial resolution

- Human scanner vs small animal scanner
  - Scanning multiple animals at the same time



Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

Unforeseen complications

- Anesthesia
  - Rodents: body temperature, overdose
  - Large animals: change in BP, HR, resp., blood glucose etc.
- Tracer production
- Scanner problems

Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet

Take-home

- Animals have important roles in translational research and preclinical imaging
- There are several advantages and disadvantages when using animals for imaging
  - Advantages: interventions, dose limit, post-mortem
  - Disadvantages: anesthesia, kinetic modelling, resolution

Clara Aabye Madsen
Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet