Principais características e comportamento das espécies convencionais de laboratório

Ciência de Animais de Laboratório - VPT2203

Fatores que Influenciam na Qualidade e no Bem-Estar do Animal

Odores

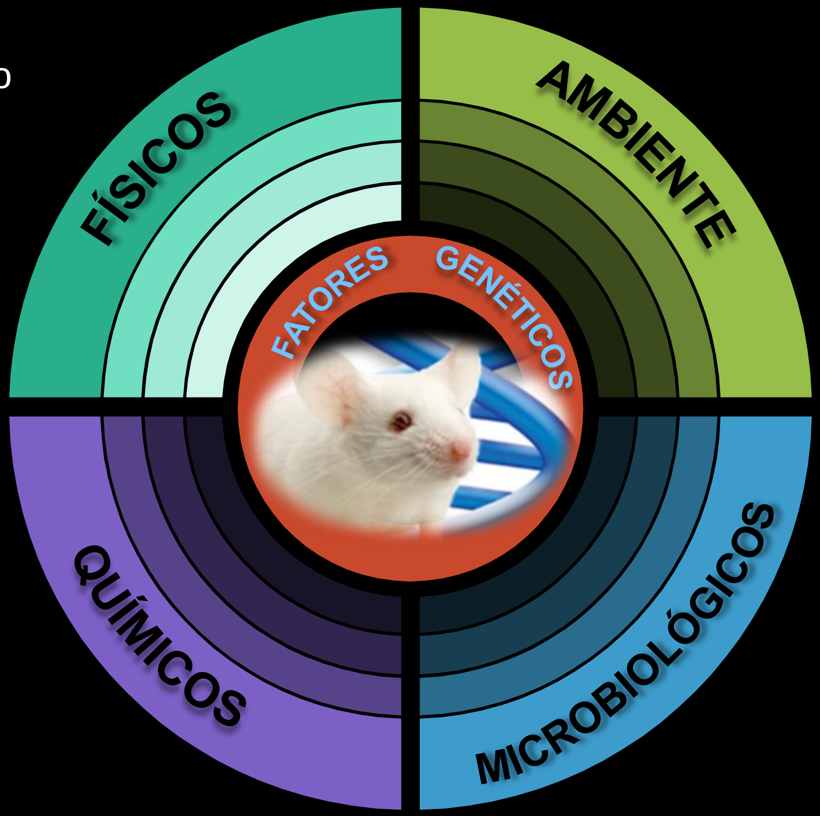
Físicos

- Iluminação
- Vibração
- Ruídos

Ambiente

- Macro / microambiente
- População por gaiola
- Temperatura
- Umidade
- Qualidade do ar
- Enriquecimento ambiental
- Forração das gaiolas

Alimentação



Químicos

- Produtos químicos
- Desinfetantes
- Inseticidas
- Amônia / CO_2

Microbiológicos

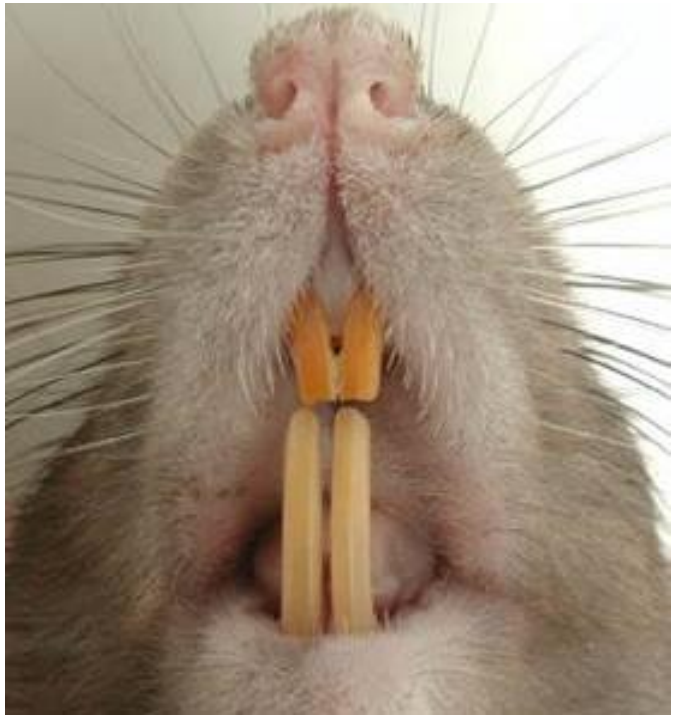
- Patógenos
- Higienização
- Esterilização
- Microbiota

Procedimentos experimentais

Espécies convencionais de laboratório

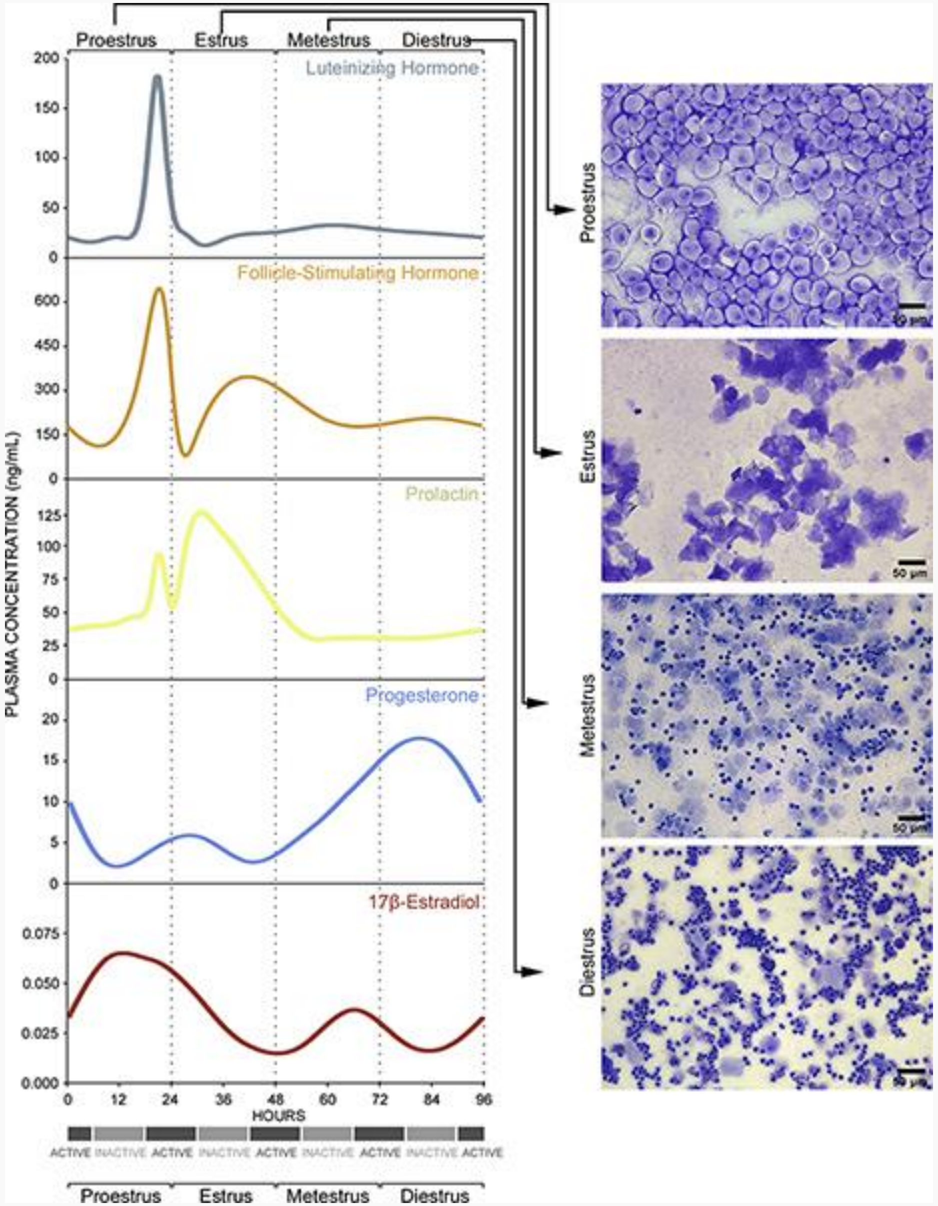
- Classe: Mammalia
  - Ordem: *Rodentia*
    Família: *Muridae*
    - *Rattus norvegicus* 
    - *Mus musculus* 
  - Ordem: *Rodentia*
    Família: *Cricetidae*
    - *Mesocricetus auratus* 
  - Ordem: *Rodentia*
    Família: *Cavidae*
    - *Cavia porcellus* 
  - Ordem: *Lagomorpha*
    Família: *Leporidae*
    - *Oryctolagus cuniculus* 

Roedores X Lagomorfos

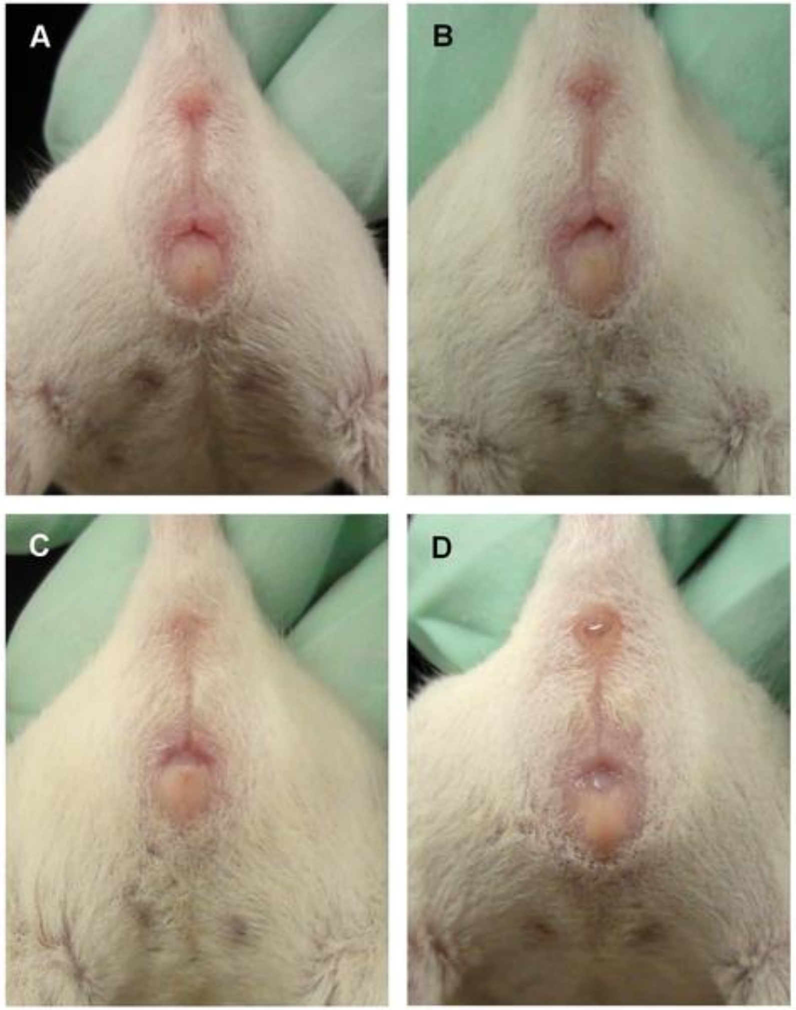



Parâmetros reprodutivos

	Camundongo	Rato	Hamster	Cobaia	Coelho
Puberdade	28 a 48 dias	50 a 60 dias	30 a 50 dias	60 a 90 dias	150 a 180 dias
1º Estro	40 dias	45 dias	40 dias	60 dias	Ovulação induzida – 10 horas após a cópula
Ciclo estral	4-5 dias	4-5 dias	4-5 dias	17 dias	16 dias
Cio pós parto	24h após o parto	24h após o parto	24h após o parto	60 dias	
Acasalamento	50 a 60 dias	60 a 90 dias	> 50 dias	> 60 dias	> 180 dias
Gestação	18 a 21 dias	19 a 22 dias	16 dias	59 a 72 dias	30 a 32 dias
Desmame	21 a 28 dias	21 dias	21 dias	21 dias	30 a 38 dias
Tamanho da ninhada	4 a 12	4 a 12	6 a 16	2 a 5	6 a 8
Peso ao nascer	1 a 1,5 g	4 a 6 g	3 g	70 a 100 g	60 a 80 g
Peso ao desmame	12 a 15 g	30 a 40 g	25 a 30 g	150 a 200 g	800 a 1200 g
Vida reprodutiva	8 a 10 meses	8 a 10 meses	8 a 10 meses	3 anos	3 a 4 anos



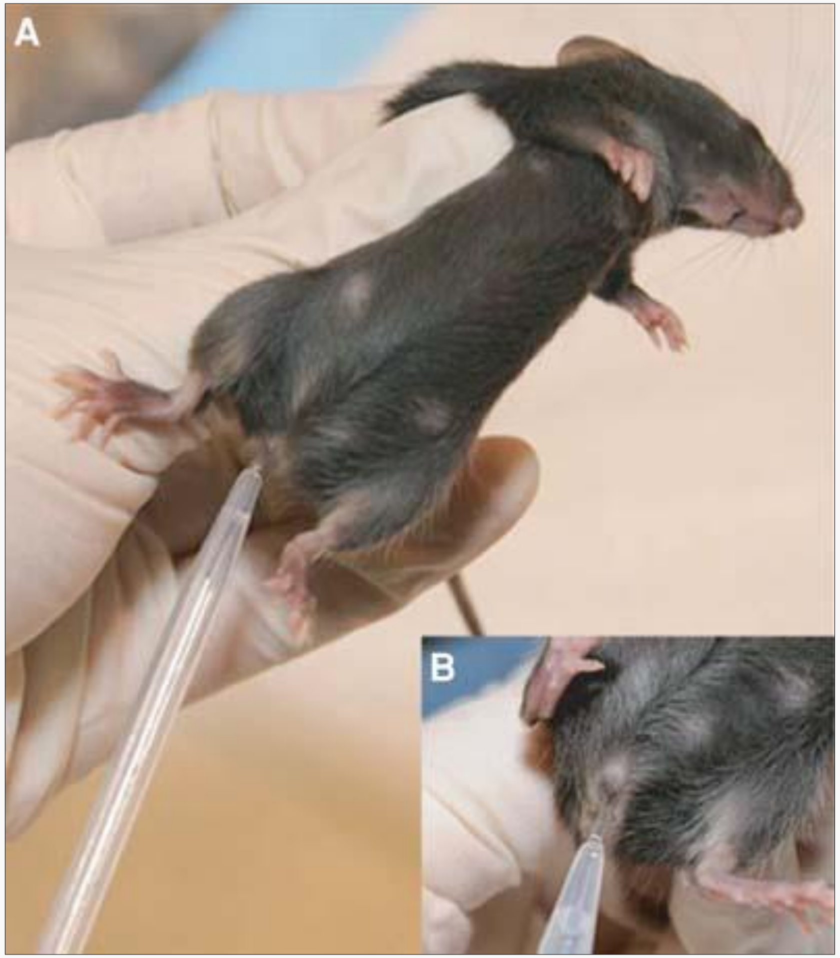
McLean AC, Valenzuela N, Fai S, Bennett SA. Performing vaginal lavage, crystal violet staining, and vaginal cytological evaluation for mouse estrous cycle staging identification. *J Vis Exp*. 2012;(67):e4389. Published 2012 Sep 15. doi:10.3791/4389

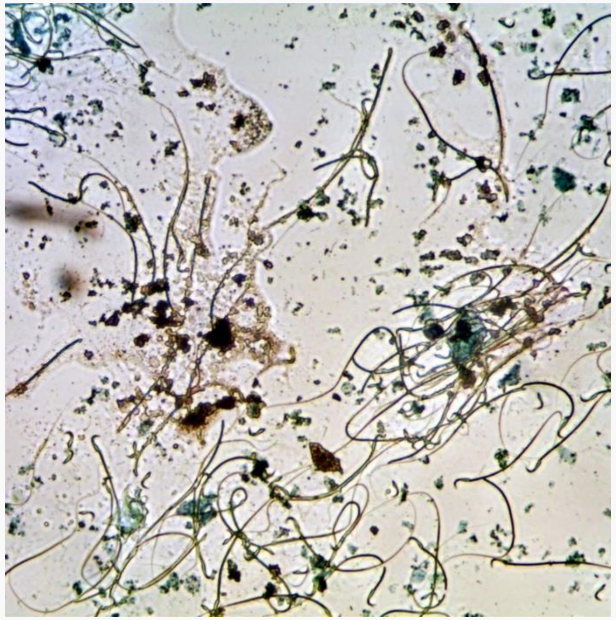


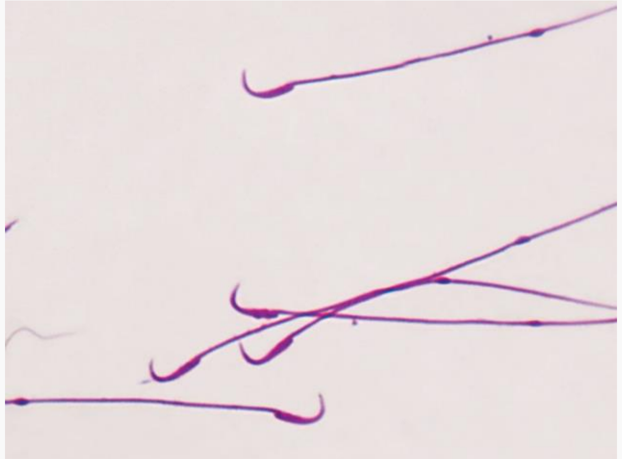
Byers SL, Wiles MV, Dunn SL, Taft RA (2012) Mouse Estrous Cycle Identification Tool and Images. PLOS ONE 7(4): e35538. https://doi.org/10.1371/journal.pone.0035538
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0035538

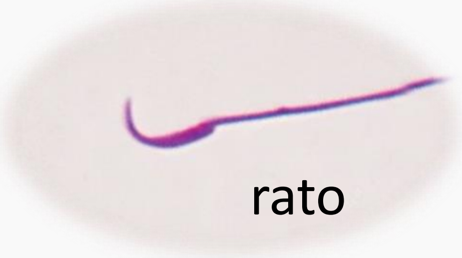
Acasalamento:
tampão “plug” vaginal

Citologia Vaginal

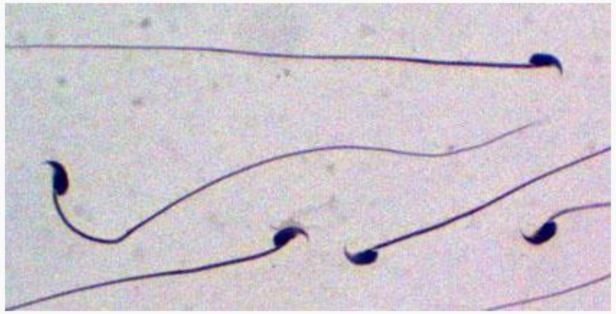








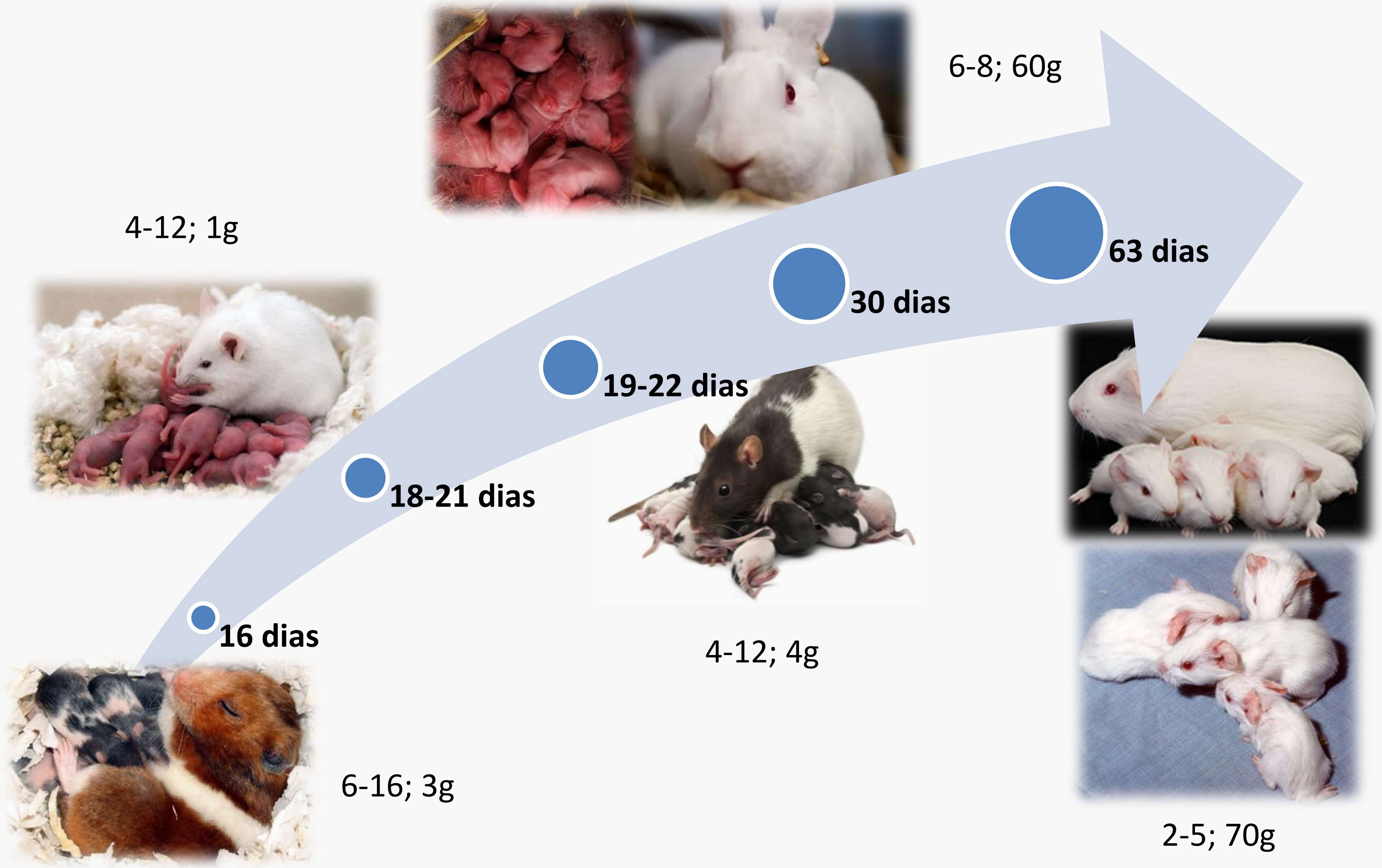
rato



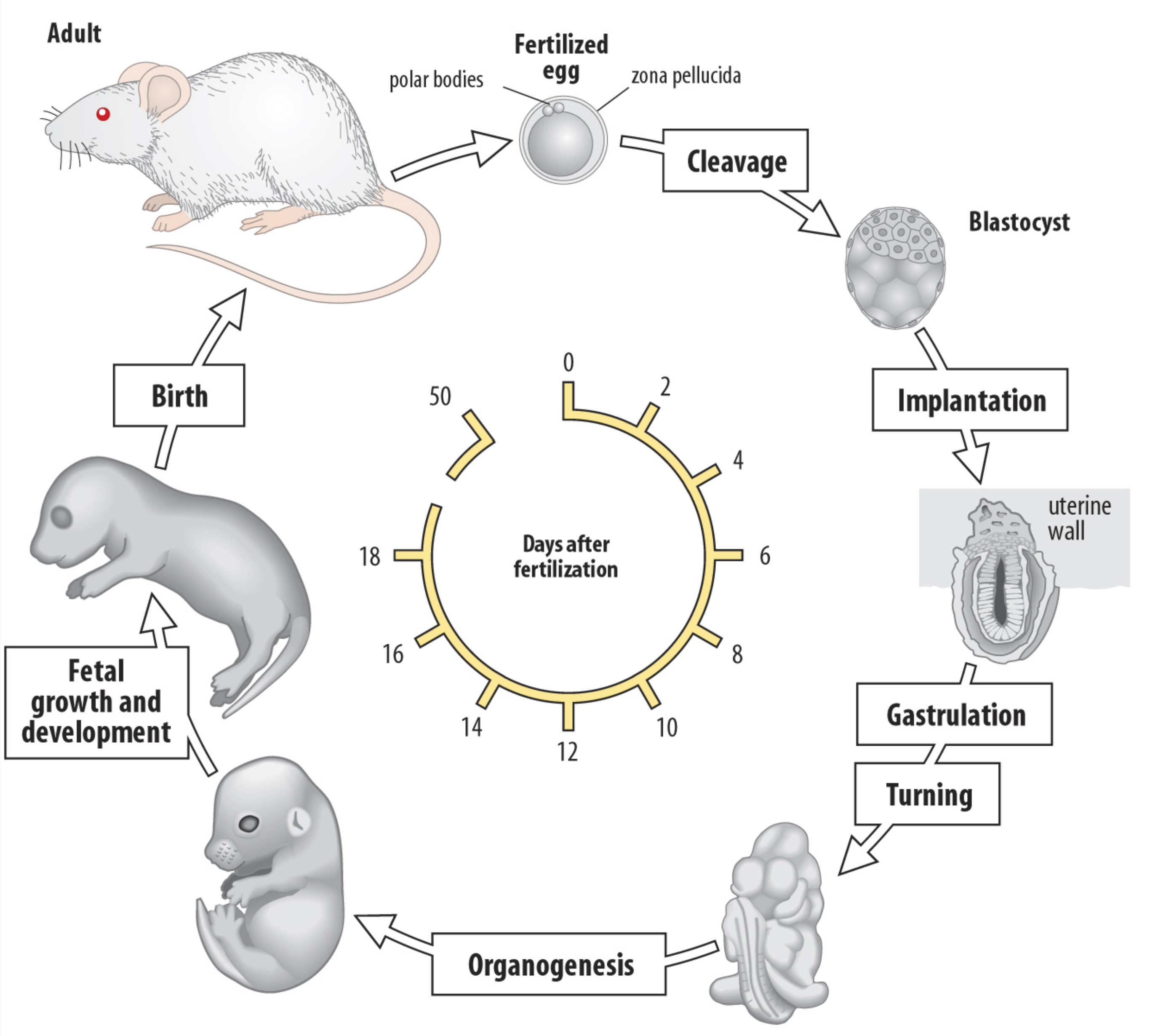
camundongo

Gestação

Período de gestação



Ciclo reprodutivo



Período de lactação

800 a 1200 g

12 a 15 g

30 a 40 g

30-38 dias (4-5 semanas)

21 dias (3 semanas)

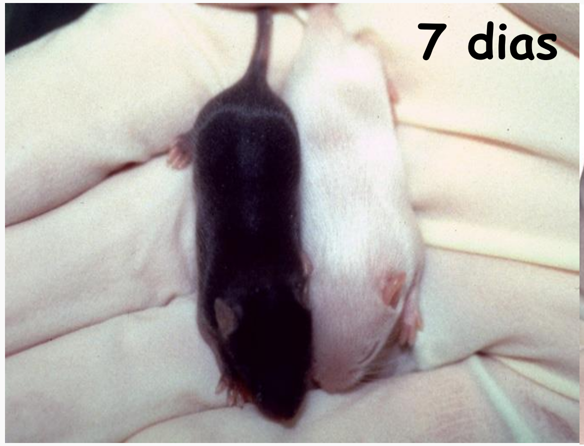
150 a 200 g

25 a 30 g

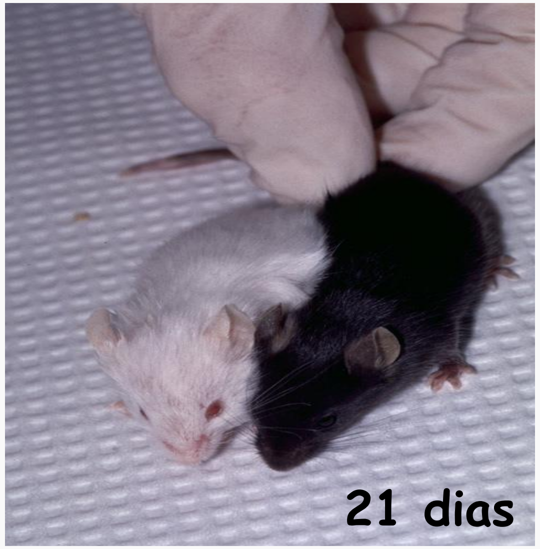
Desenvolvimento dos filhotes

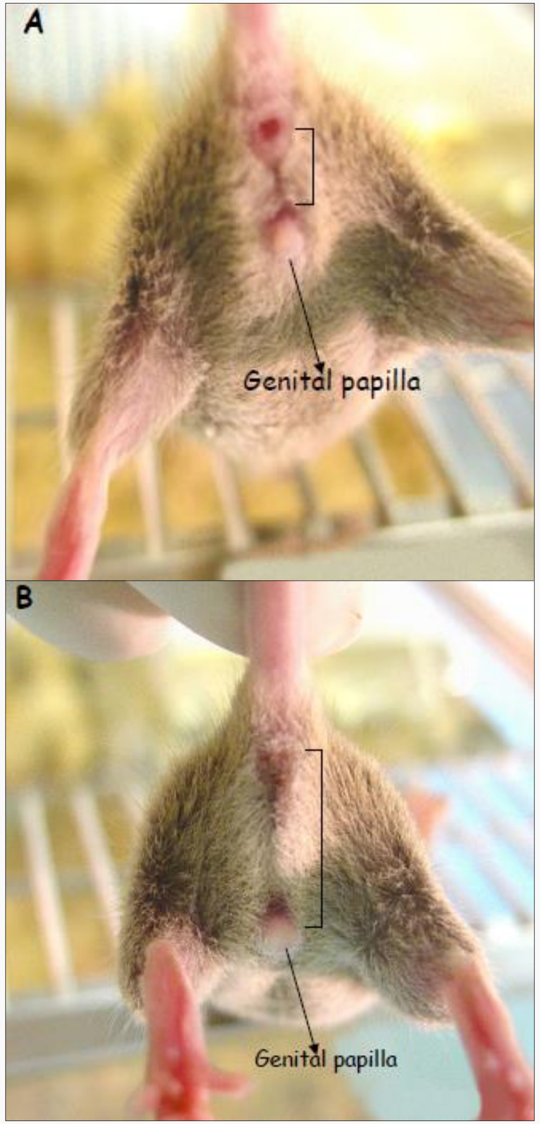
Desenvolvimento dos filhotes

Desenvolvimento dos filhotes



Desenvolvimento dos filhotes





Desenvolvimento dos filhotes

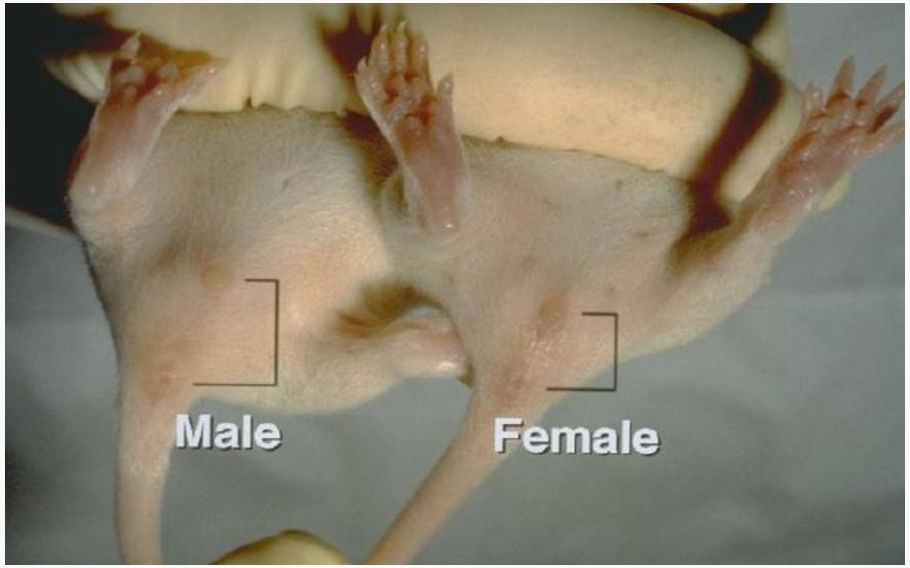
1 dia

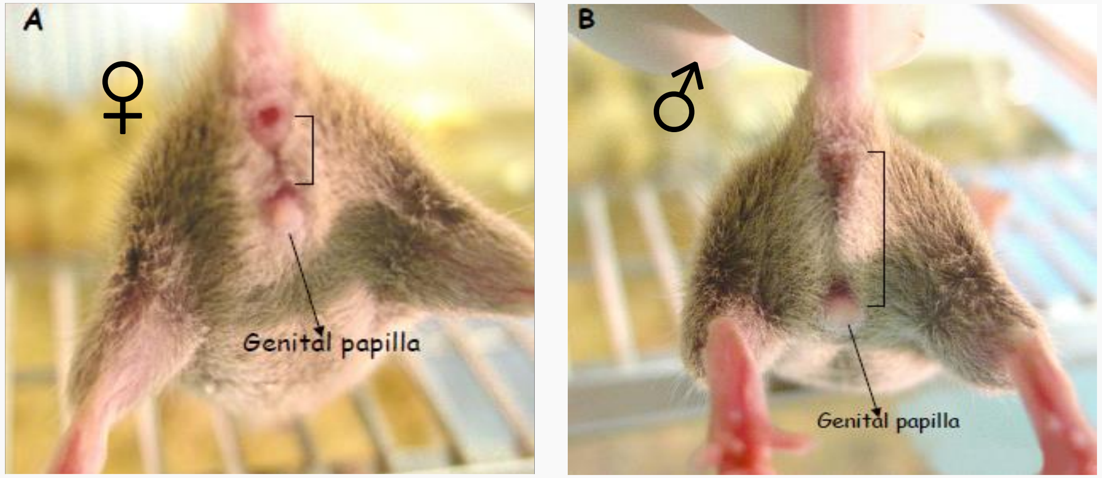
5 dias

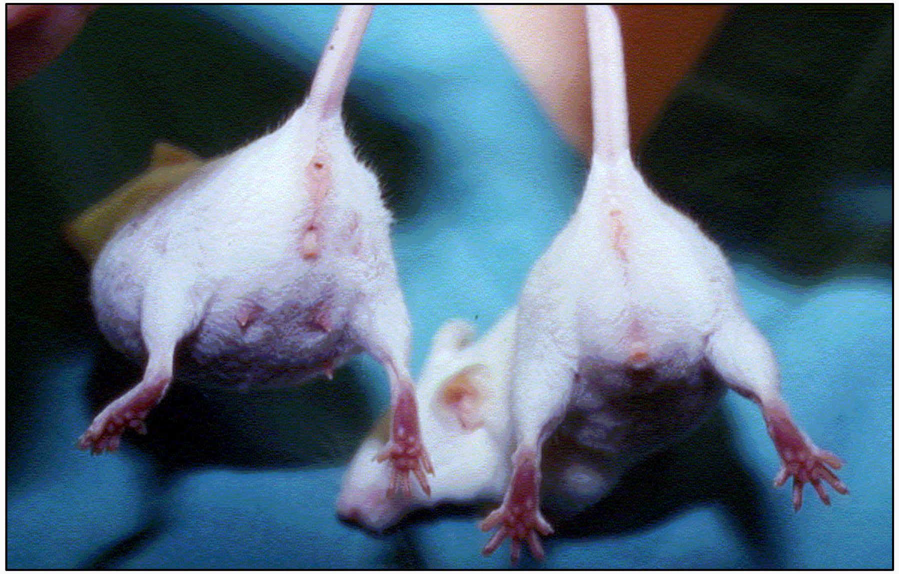
10 dias

21 dias

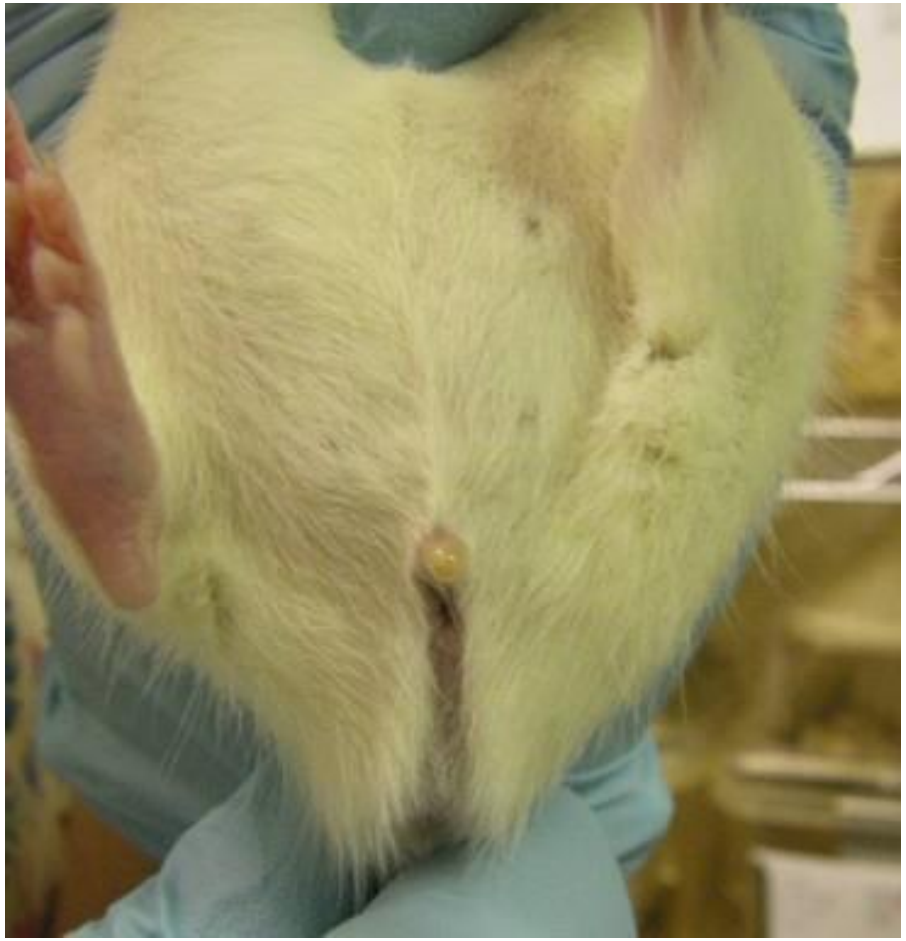
Sexagem: camundongo



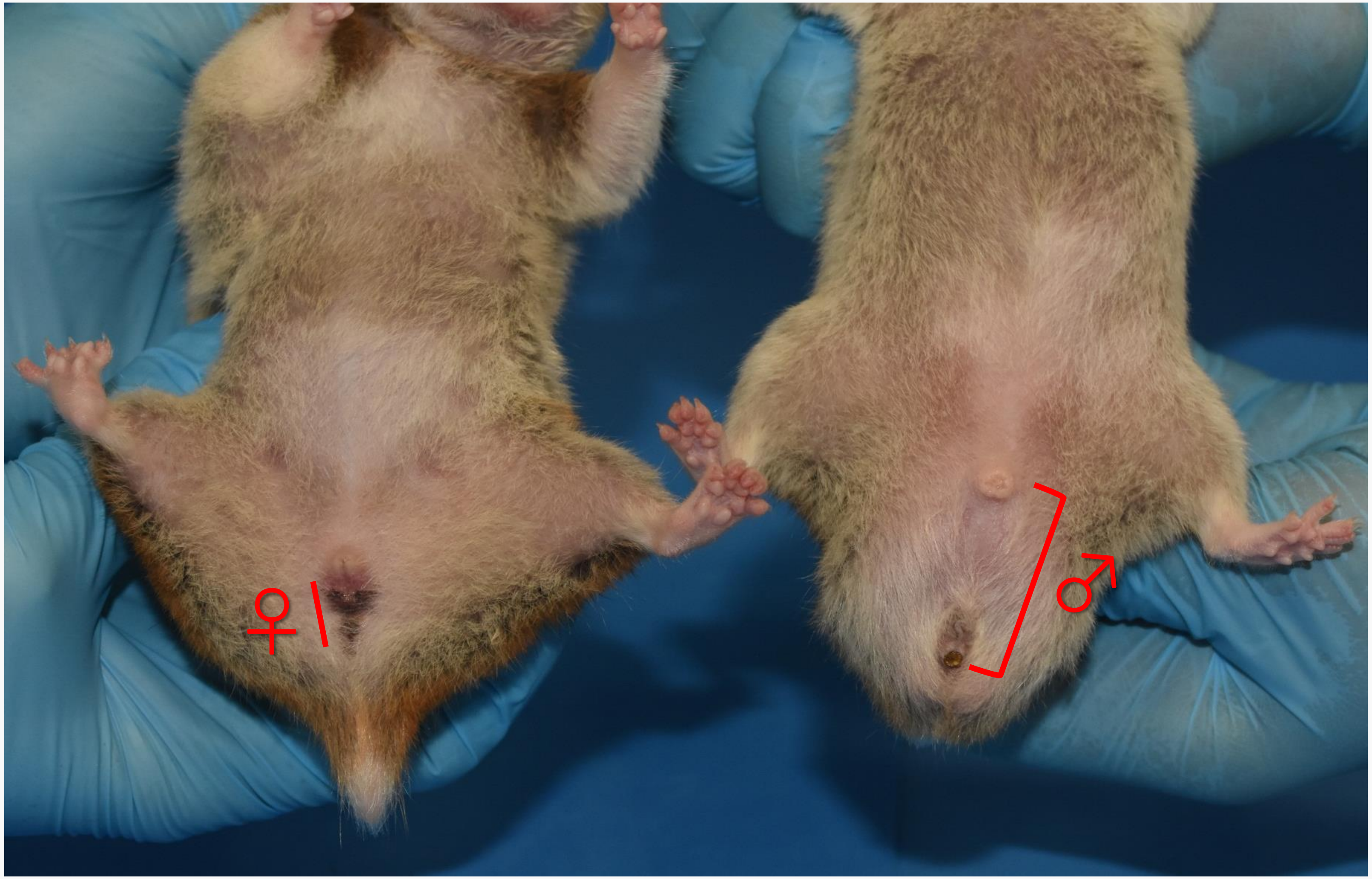




Sexagem: rato



Sexagem: hamster



Sexagem: cobaia

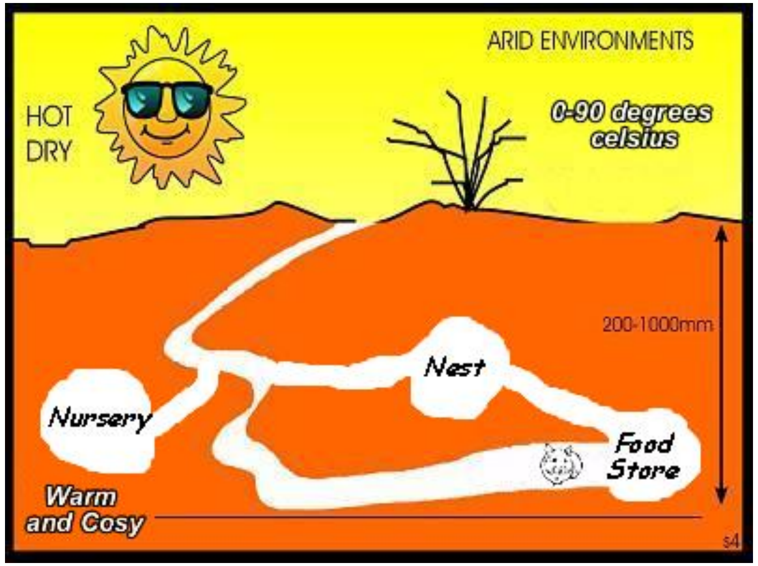
Sexagem: coelho

Origem

- **1930:** Aharoni - Aleppo no deserto da Síria

Principais Características

- Na natureza os hamsters são animais noturnos.
- Geralmente vivem solitários em tocas escavadas no chão, que garantem temperaturas mais baixas e humidade mais alta do que o ambiente no deserto.



Características Anatômicas e Fisiológicas

- Bolsas guturais – sítio de privilégio imunológico (desprovidas de glândulas e de drenagem linfática): utilizadas para estudos da microvasculatura, implante de tumores.
- Machos possuem glândulas laterais no flanco.



Reprodução

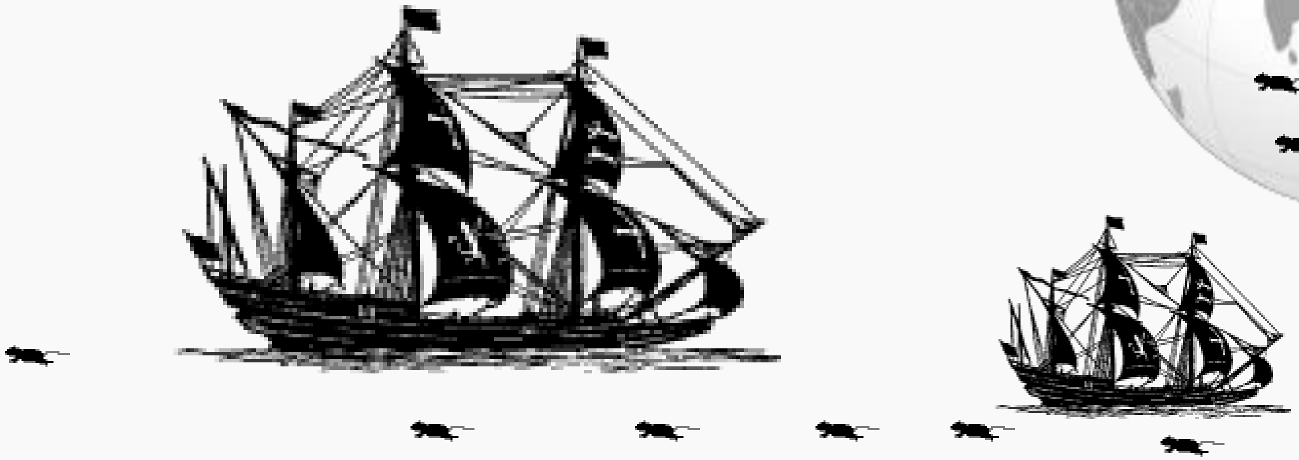
- Fêmeas que são submetidas ao estresse na 1ª semana pós parto tendem a canibalizar os filhotes.
- A fêmeas introduzem os filhotes nas bolsas que podem sufocar.



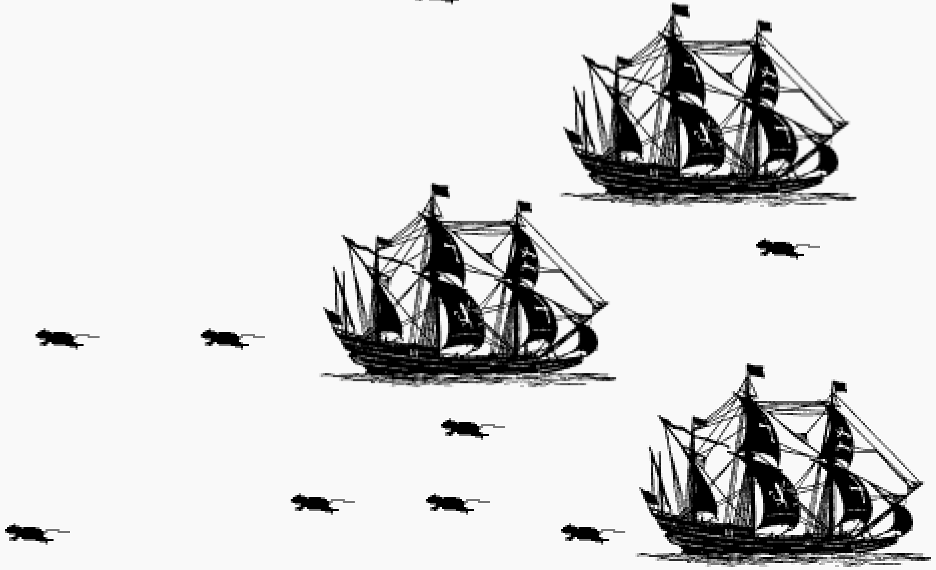

O rato de laboratório, origem...

https://lh5.googleusercontent.com/LK5-E_VcQESVizCr2upnutf9Qb-p8q9p6BXATHAB2aHSLfRxMg9Q_AdTS7CcM2ng8XwOAaYzdLfE8YiptTJgegWUjjUdvslEZ72UzctrIaKiU8jX8bUYYqT256Un9X2wX7n1Ovlv

Ásia Central → cosmopolita



Paris: 1728 e 1730
Estados Unidos: 1775
Groelândia: 1780
Suíça: 1809
Costa do Pacífico: 1851

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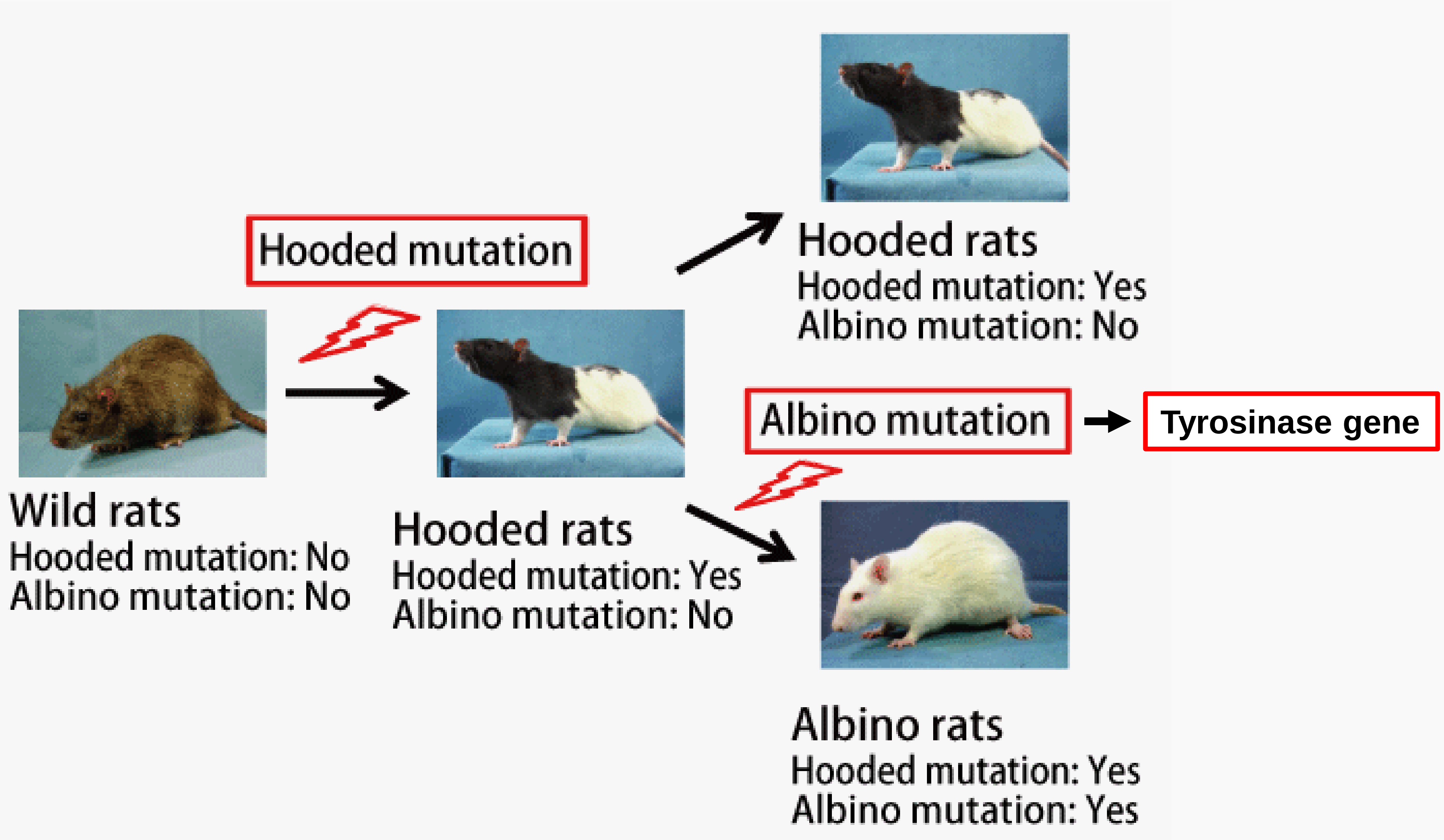
Europa século XVIII – rat-baiting

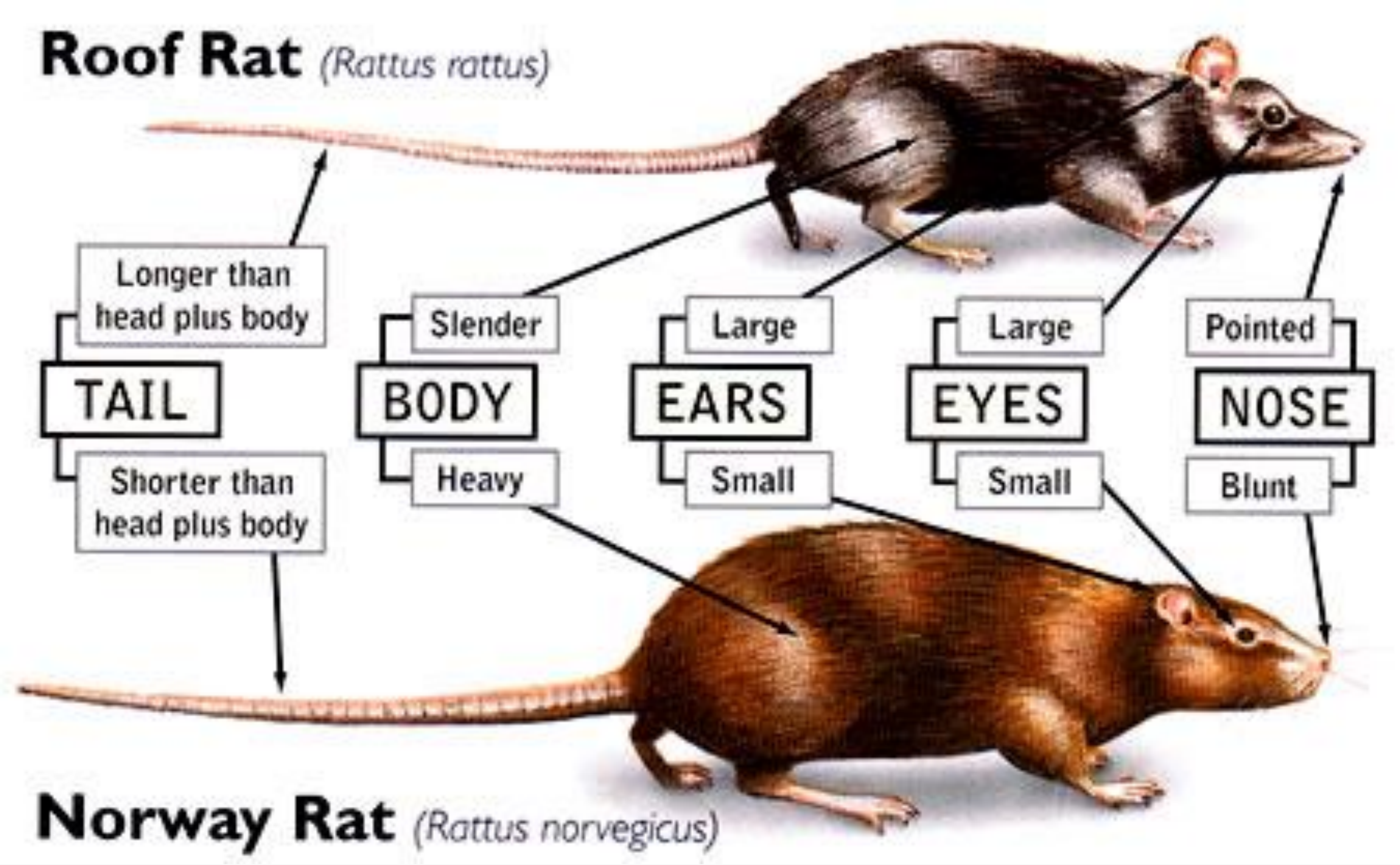
https://explorepahistory.com/kora/files/1/2/1-2-1B77-25-ExplorePAHistory-a0m5f5-a_349.jpg

Credit: Courtesy of The Wistar Institute, Wistar Archive Collection, Philadelphia, Pa.

Helen Dean King, a graduate of Bryn Mawr College, led the development and production of the first line of standardized laboratory rats, known as Wistar Rats, produced between 1906 and 1940. Today, more than half of all laboratory rats are descendants of the original WISTARAT line begun in 1906.

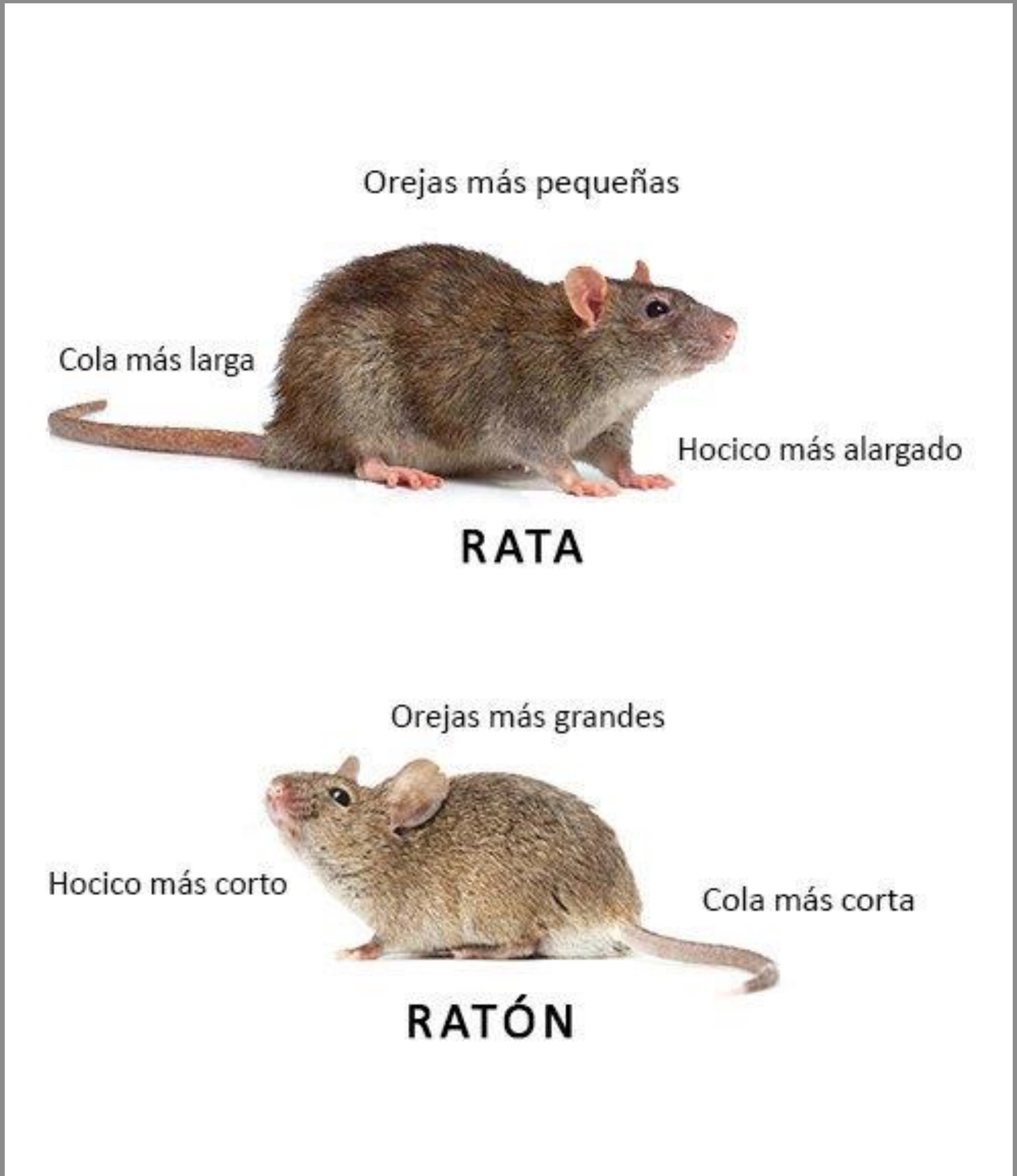
KURAMOTO, Takashi et al. Origins of albino and hooded rats: implications from molecular genetic analysis across modern laboratory rat strains. PloS one, v. 7, n. 8, p. e43059, 2012.



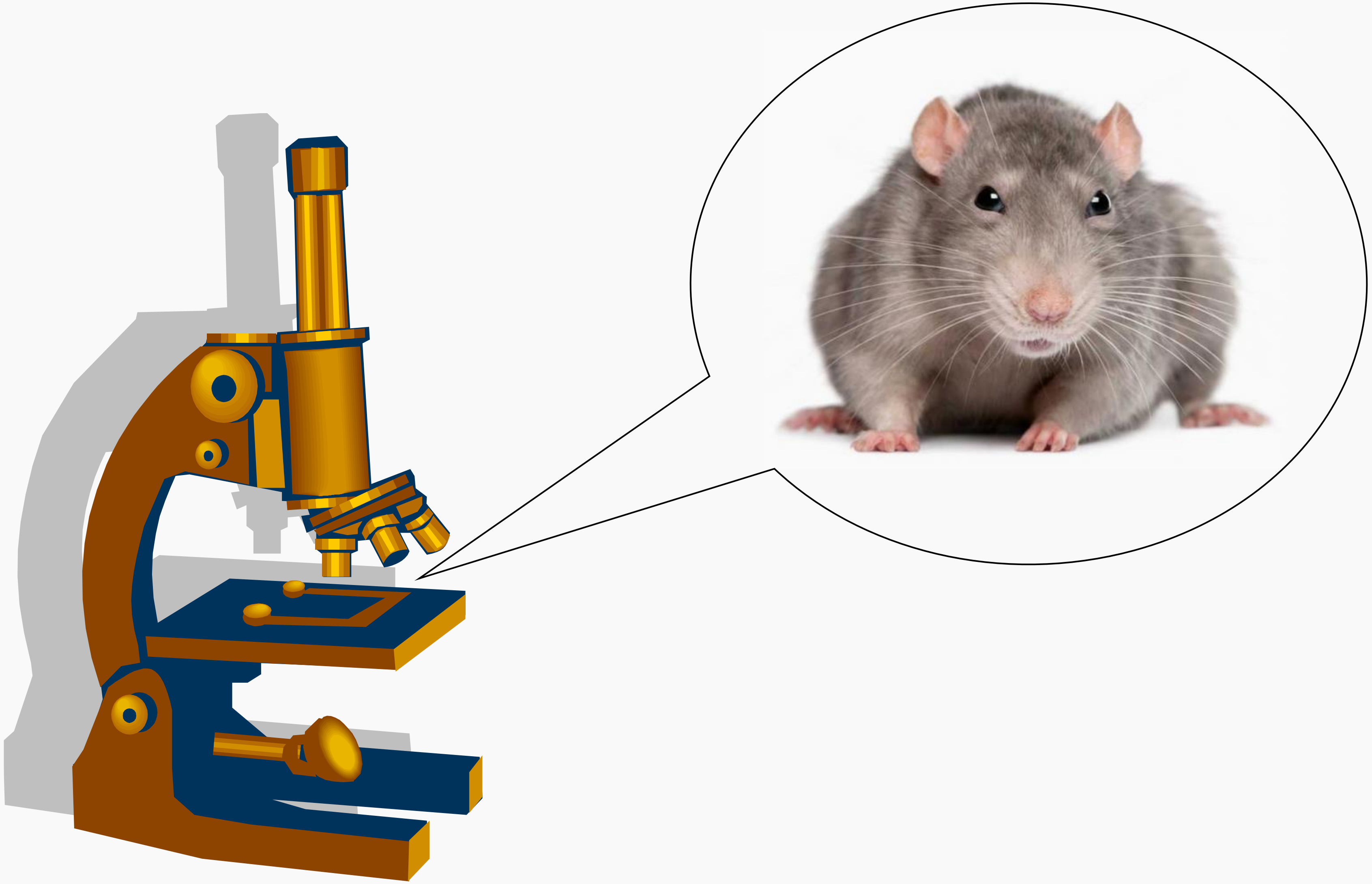

Roof Rat (Rattus rattus)
Longer than head plus body
TAIL
Shorter than head plus body
Slender
BODY
Heavy
Large
EARS
Small
Large
EYES
Small
Pointed
NOSE
Blunt
Norway Rat (Rattus norvegicus)


What's the
Difference?


E SOU UM RATO, NÃO UM CAMUNDONGO!


Orejas más pequeñas
Cola más larga
Hocico más alargado
RATA
Orejas más grandes
Hocico más corto
Cola más corta
RATÓN

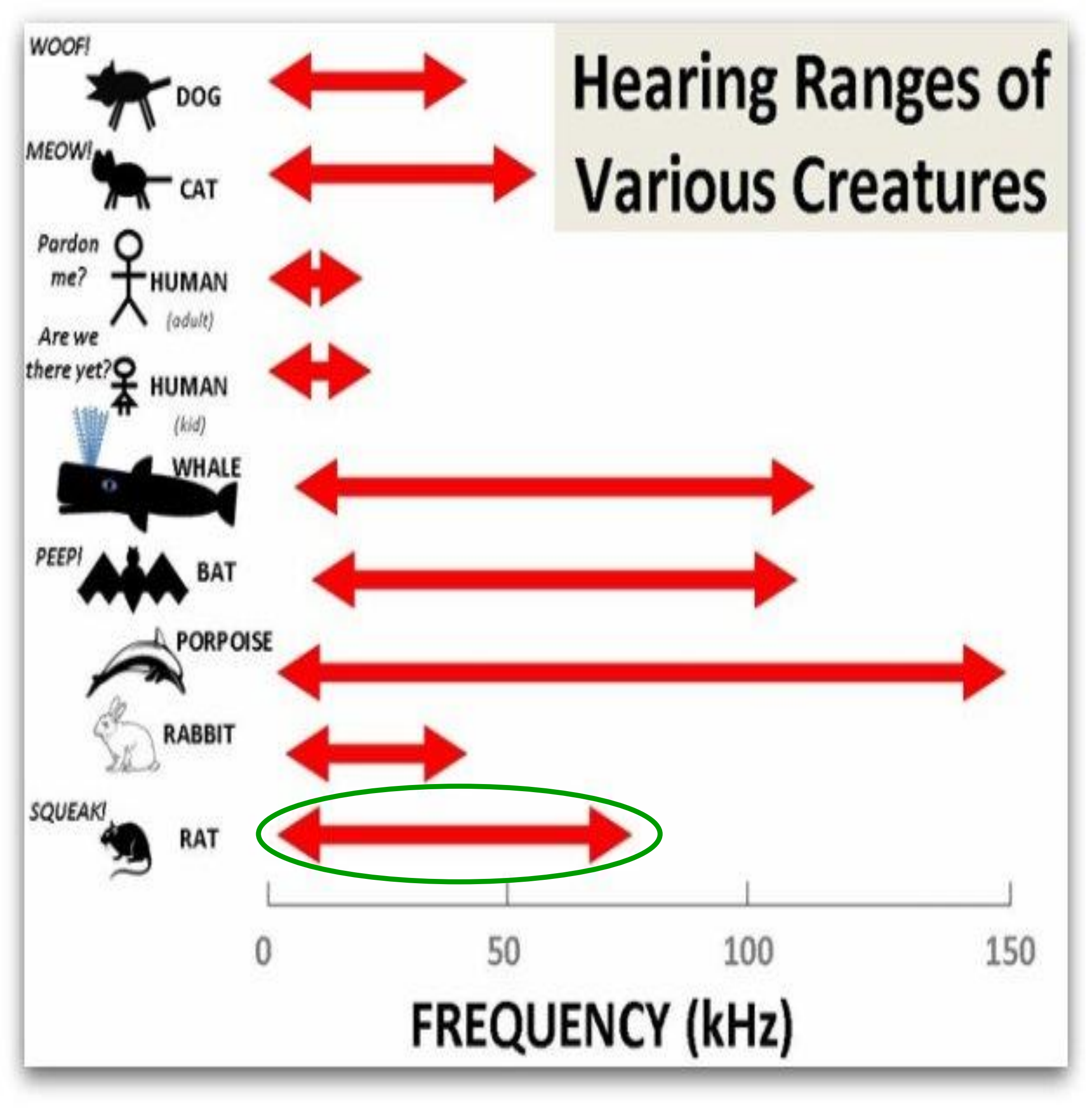
Conhecendo o Rato...



Principais características

- Hábitos noturnos
- Onívoros
- Facilmente adaptáveis
- Sociáveis
- Neofóbicos: comportamento curioso, mas cuidadosos com novos objetos

Audição



https://qph.fs.quoracdn.net/main-qimg-bee8ed0d3598aedb6a6510de8e05221e-c

Vocalização US:

22kHz - estímulo aversivo
40kHz - filhotes
50kHz – estímulo positivo

Original Article

Laboratory Animals
0(0) 1–12

DOI: 10.1177/0023677219850211
journals.sagepub.com/home/lan

Combination of ketamine and xylazine with opioids and acepromazine in rats: Physiological changes and their analgesic effect analysed by ultrasonic vocalization

Jilma Alemán-Laporte[1,2], Luciana A Bandini[1], Mariana SA Garcia-Gomes[1], Dennis A Zanatto[1], Denise T Fantoni[3], Marco A Amador Pereira[3], Pedro E Navas-Suárez[1], Thiago Berti Kirsten[4], Randall R. Jimenez[5], Gilbert Alvarado[1,6] and Claudia Cabrera Mori[1]

Abstract

In this study, the effect of four anaesthetic protocols that included the combination of xylazine (X) and ketamine (K) with acepromazine (A) and opioids (methadone (Me), morphine (Mo) or tramadol (T)) was evaluated in laboratory rats of both sexes. Ultrasonic vocalization (USV) was used as an indicator of pain during the recovery period. The objective was to evaluate the physiological parameters and the analgesic effect of each protocol to determine which protocol was the safest and fulfil the requirements of a balanced anaesthesia. The better protocols were the XKA protocol for both sexes and the XKMe protocol for females because the combinations achieve surgical plane of anaesthesia in rats. However, pain assessment during the formalin test revealed that rats anaesthetized with XKA produced more numbers of USV, suggesting that it is not a good protocol for the control of immediate postoperative pain. All protocols produced depression in body temperature and respiratory and heart rates, and had important effects, such as micturition and maintenance of open eyes. Only rats anaesthetized with XKA protocol did not present piloerection. These results demonstrated that good monitoring and care during anaesthesia must be included to prevent complications that compromise the life of the animal and to ensure a good recovery. The inclusion of analgesia in anaesthesia protocols must be used routinely, ensuring minimal presence of pain and thus more reliable results in the experimental procedures.

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 Current Neuropharmacology, 2015, *13*, 164-179

Rat Ultrasonic Vocalizations and Behavioral Neuropharmacology: From the Screening of Drugs to the Study of Disease

Nicola Simola*

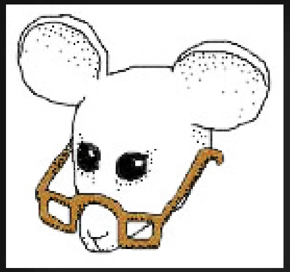
Department of Biomedical Sciences, Section of Neuropsychopharmacology, University of Cagliari, Via Ospedale, 72, 09124, Cagliari, Italy

N. Simola

Abstract: Several lines of evidence indicate that rats emit ultrasonic vocalizations (USVs) in response to a wide range of stimuli that are capable of producing either euphoric (positive) or dysphoric (negative) emotional states. On these bases, recordings of USVs are extensively used in preclinical studies of affect, motivation, and social behavior. Rat USVs are sensitive to the effects of certain classes of psychoactive drugs, suggesting that emission of rat USVs can have relevance not only to neurobiology, but also to neuropharmacology and psychopharmacology. This review summarizes three types of rat USVs, namely 40-kHz USVs emitted by pups, 22-kHz USVs and 50-kHz USVs emitted by young and adult animals, and relevance of these vocalizations to neuropharmacological studies. Attention will be focused on the issues of how rat USVs can be used to evaluate the pharmacological properties of different classes of drugs, and how rat USVs can be combined with other behavioral models used in neuropharmacology. The strengths and limitations of experimental paradigms based on the evaluation of rat USVs will also be discussed.

Keywords: Analgesic, antidepressant, anxiolytic, drug abuse, drug toxicity, psychostimulant.

Baixa acuidade visual



Humano, visão normal

Daltônico – não identifica o vermelho, cores fracas

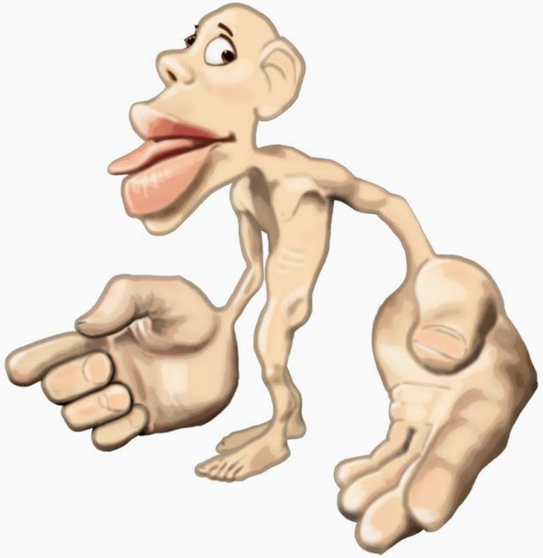
Ratos pigmentados têm visão embaçada, dicromática e com baixa saturação de cor

Ratos albinos enxergam muito embaçado, com luminosidade excessiva

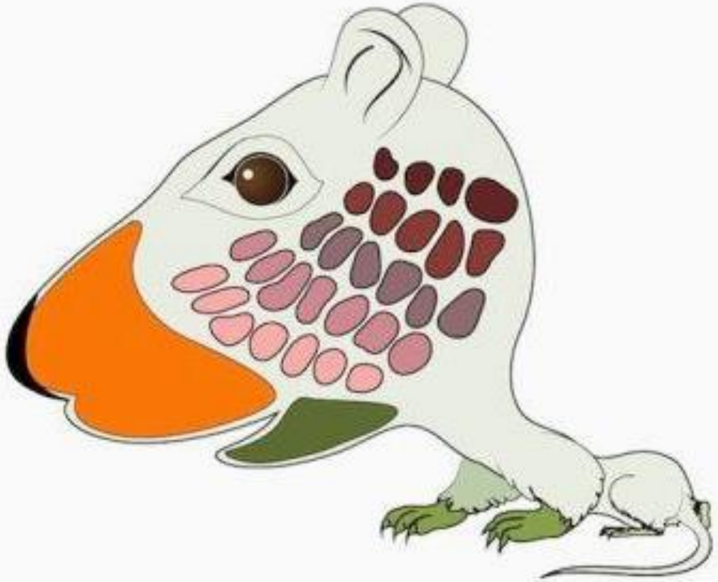
Na claridade, ratos albinos podem ficar completamente cegos

Olfato apurado, principal sentido dos roedores...

https://ohmy.disney.com/wp-content/uploads/2013/09/Ratatouille_Soup.jpg



Homunculus
https://canvas.brown.edu/courses/971296/files/48230407/preview?verifier=OYWTp3AJLXzsyEmemgG4ovf7FVqiMQuCg4smmvmJ



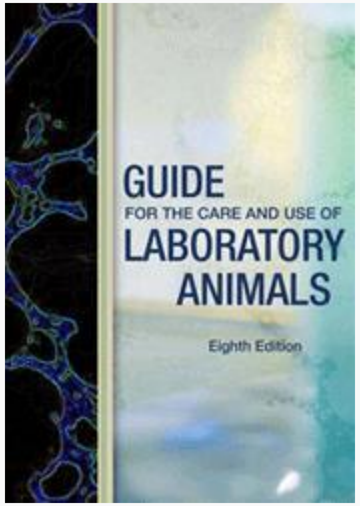
Mouseunculus
http://phenomena.nationalgeographic.com/files/2013/07/mouse-banner-long.001-660x296.jpg’

Manejo e Alojamento

- Condições ambientais
  - Renovação de ar no ambiente – ventilação e exaustão
  - Temperatura ⇨ 22 ± 2°C
  - Umidade relativa ⇨ 45 a 65%
  - Ciclo de Luz ⇨ 12 hora claro / 12 horas escuro

Normas e Recomendações

– Espaço mínimo para as diferentes espécies animais:

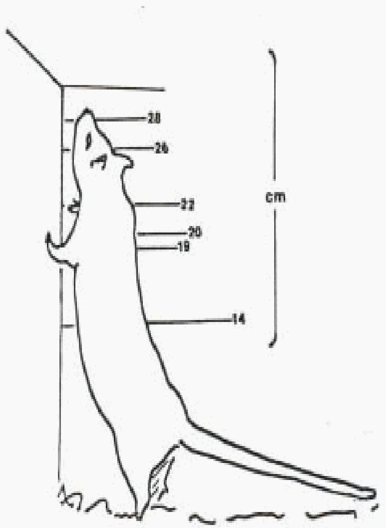


http://www.nap.edu/catalog/12910.html

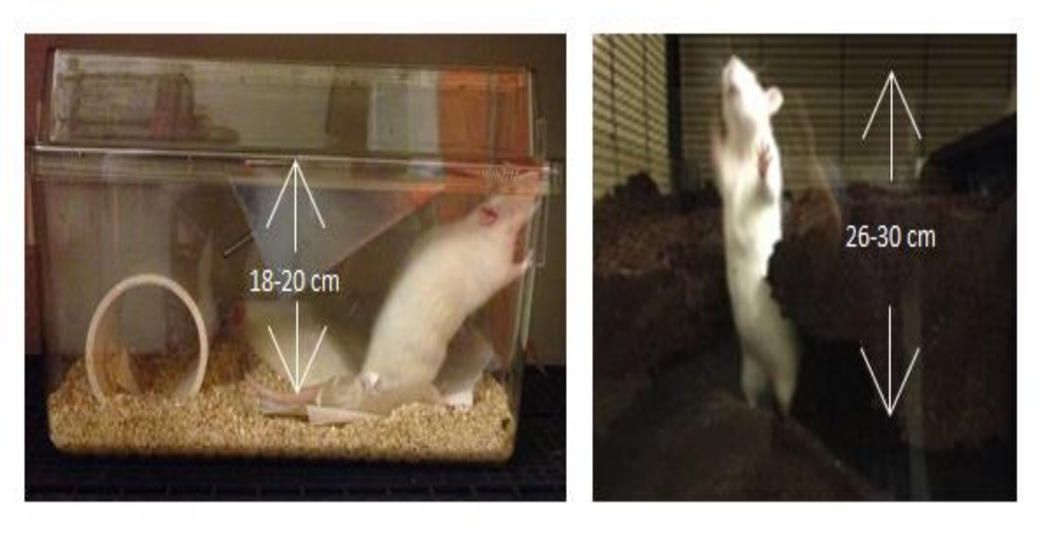
Animais	Peso (g)	Espaço/animal (cm^2)	Altura (cm)
Camundongos em grupos	<10	38,7	12,7
	10-15	51,6	12,7
	15-25	77,4	12,7
	>25	≥96,7	12,7
Fêmea + ninhada		330	12,7
Ratos em grupos	<100	109,6	17,8
	100-200	148,35	17,8
	200-300	187,05	17,8
	300-400	258,0	17,8
	400-500	387,0	17,8
	>500	≥451,5	17,8
Fêmea + ninhada		800	17,8

(Resolução Normativa 15 – CONCEA-MCT, 16 de dezembro de 2013)

Makowska IJ, Weary DM (2016). The importance of burrowing, climbing and standing upright for laboratory rats. *Royal Society Open Science* 3: 160136 doi: 10.1098/rsos.160136



http://ebooks.lib.ntu.edu.tw/1_file/AWI/96122405/06.files/rat-2.gif

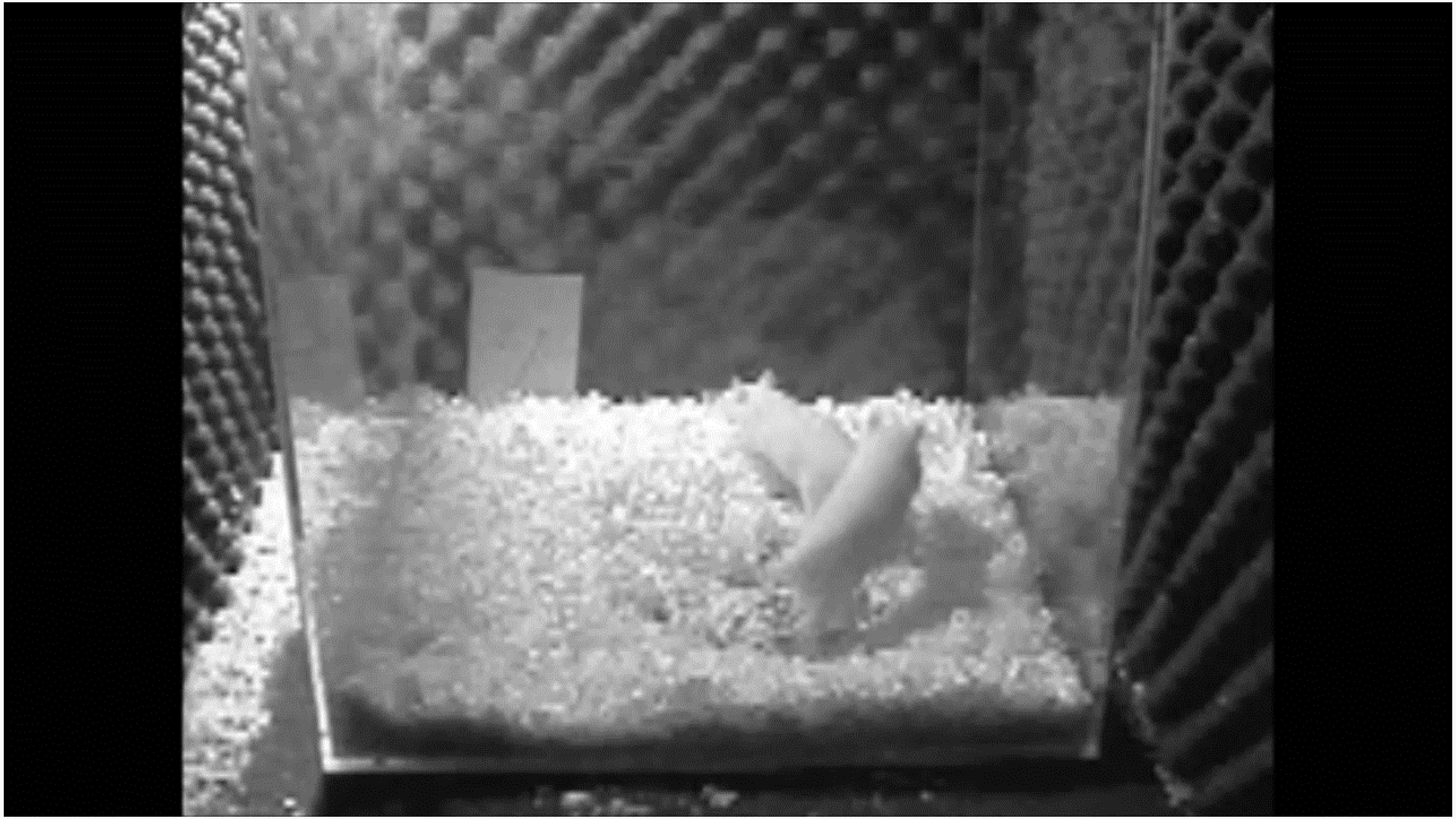


https://nc3rs.org.uk/sites/default/files/Images/News/Cage_size_0.png

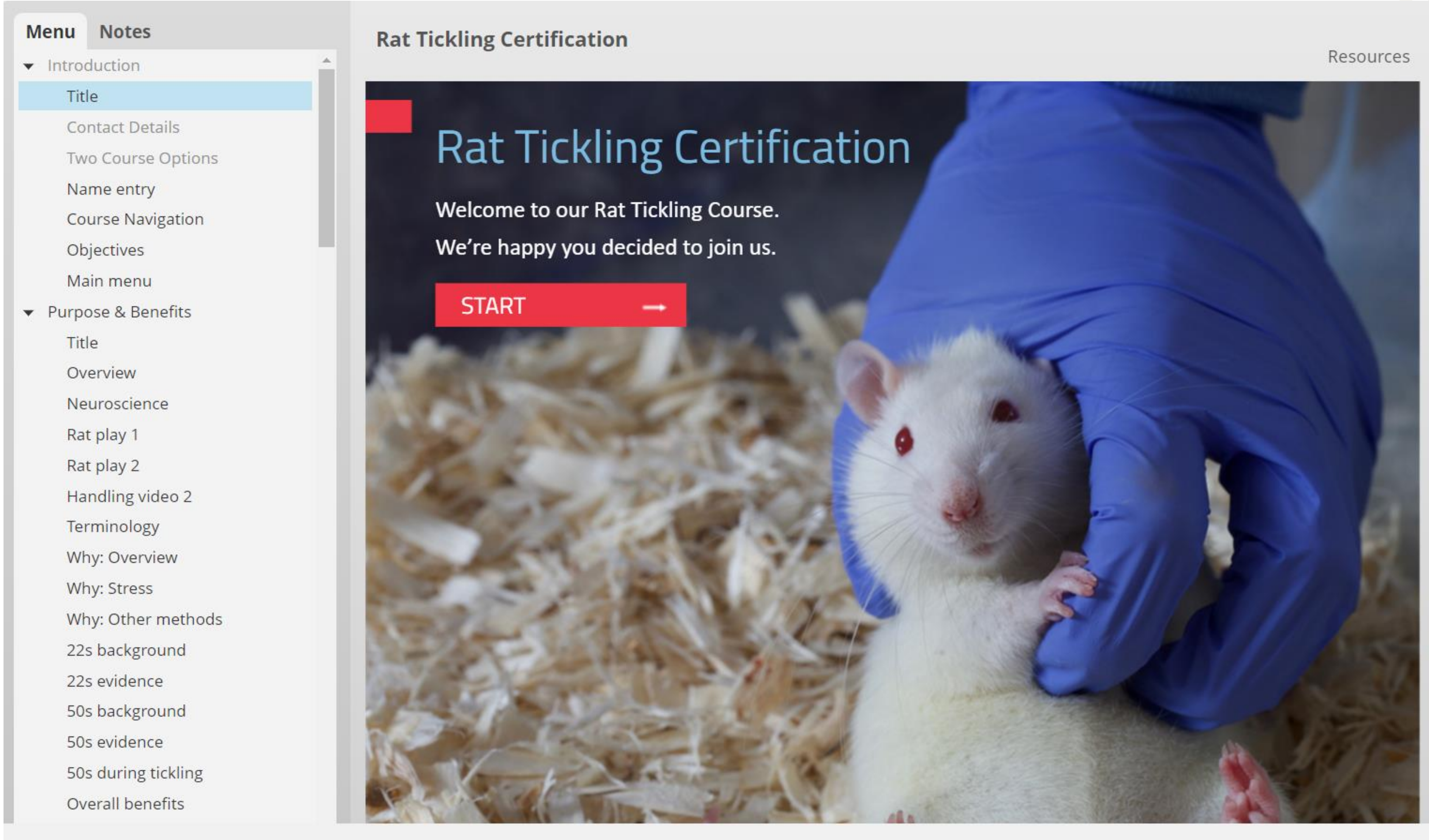
Comportamento reprodutivo

Comportamento social

TREZZA, Viviana; BAARENDSE, Petra JJ; VANDERSCHUREN, Louk JMJ. The pleasures of play: pharmacological insights into social reward mechanisms. **Trends in pharmacological sciences**, v. 31, n. 10, p. 463-469, 2010.



https://youtu.be/4zBkLzAenrw



http://storage.googleapis.com/ecourses/Rat%20Tickling%20Certification/story_html5.html

https://youtu.be/d-84UJpYFRM

NATURE | NEWS

Rat models on the rise in autism research

Neuroscientists switch to rats as genetically modified strains become increasingly available.

Ewen Callaway

23 November 2011

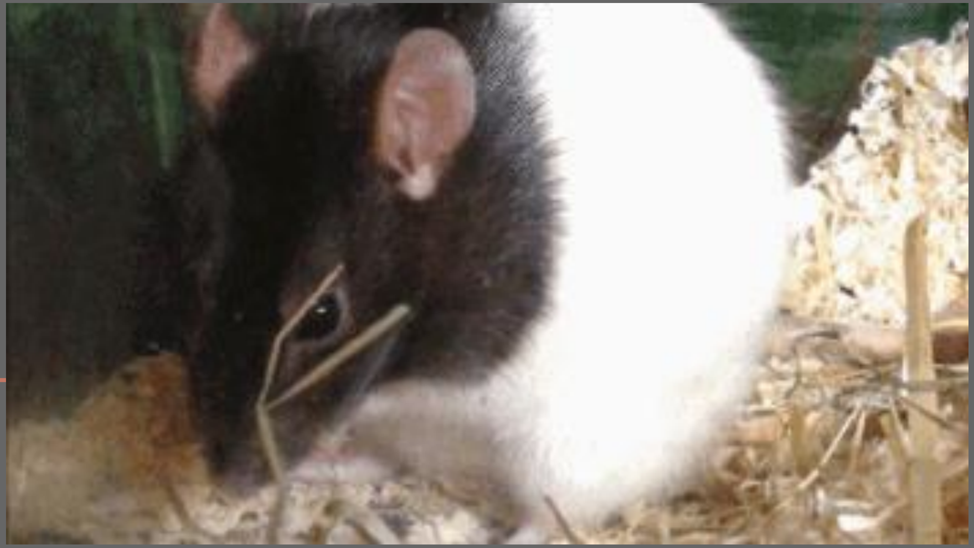
Put two young mice in a cage and they will politely sniff one another. Two rat pups, by contrast, quickly become a blur of fur as they begin some “really rough-and-tumble play”, says Richard Paylor, a neuroscientist at Baylor College of Medicine in Houston, Texas. Such behaviour makes rats an ideal animal model for studying autism spectrum disorder, given that children who have the disorder are often less interested in play than children without it.

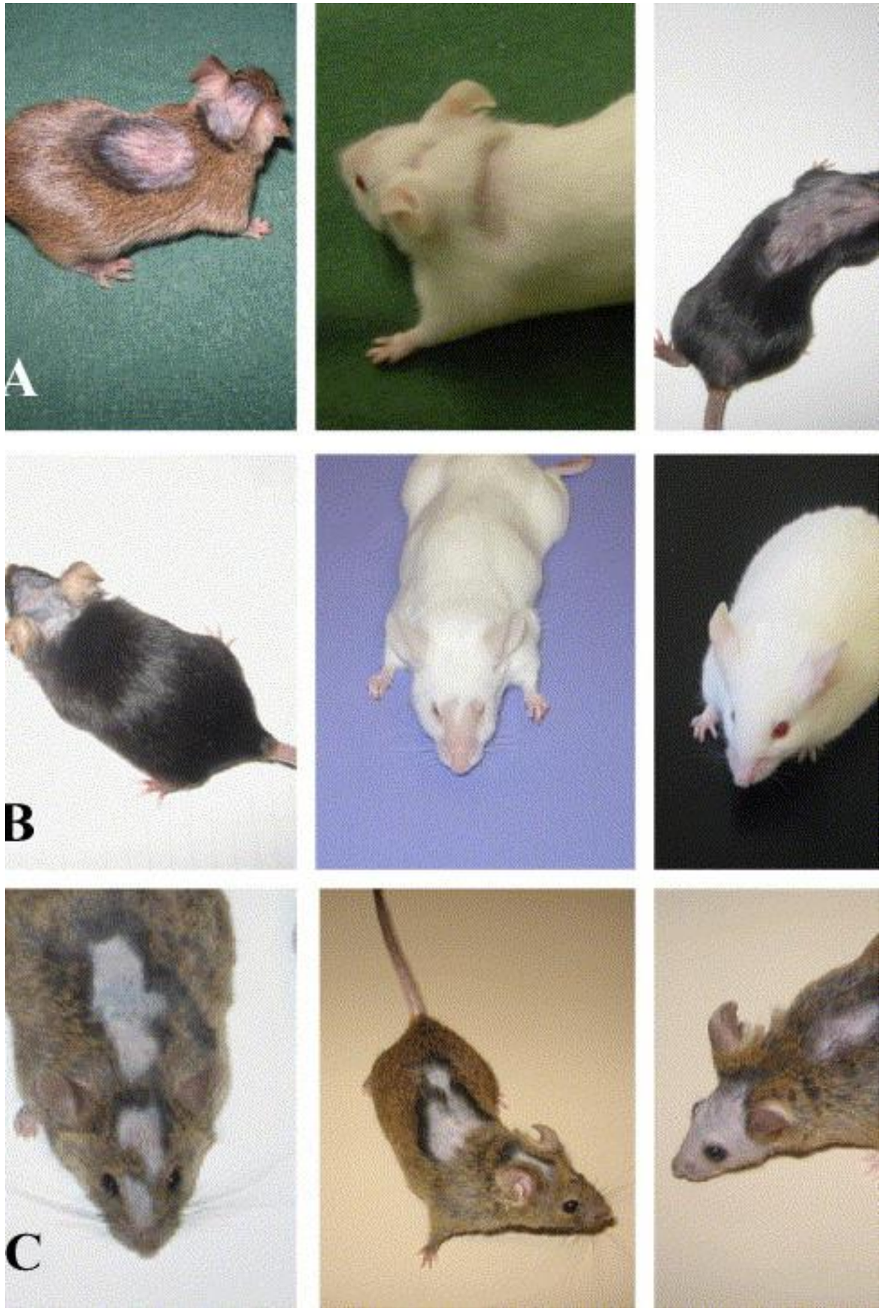
Paylor is one of the first scientists to use transgenic rats to study neurodevelopmental diseases such as autism, and presented his team’s work at the Society for Neuroscience meeting in Washington DC last week. Transgenic rats, Paylor and others say, are a better proxy than mice for the behavioural and cognitive problems experienced by people with autism. And because rats are a preferred model for the pharmaceutical industry, their use in basic research may speed new treatments.

PHOTOSPIN

Rats are making a comeback as the lab animal of choice for neuroscientists.

Grooming





Barbering em camundongos

Neurobiology of rodent self-grooming and its value for translational neuroscience

Allan V. Kalueff[1,2,3,4], *Adam Michael Stewart*[2], *Cai Song*[1,5,6], *Kent C. Berridge*[7], *Ann M. Graybiel*[8] *and* †*John C. Fentress*[5]

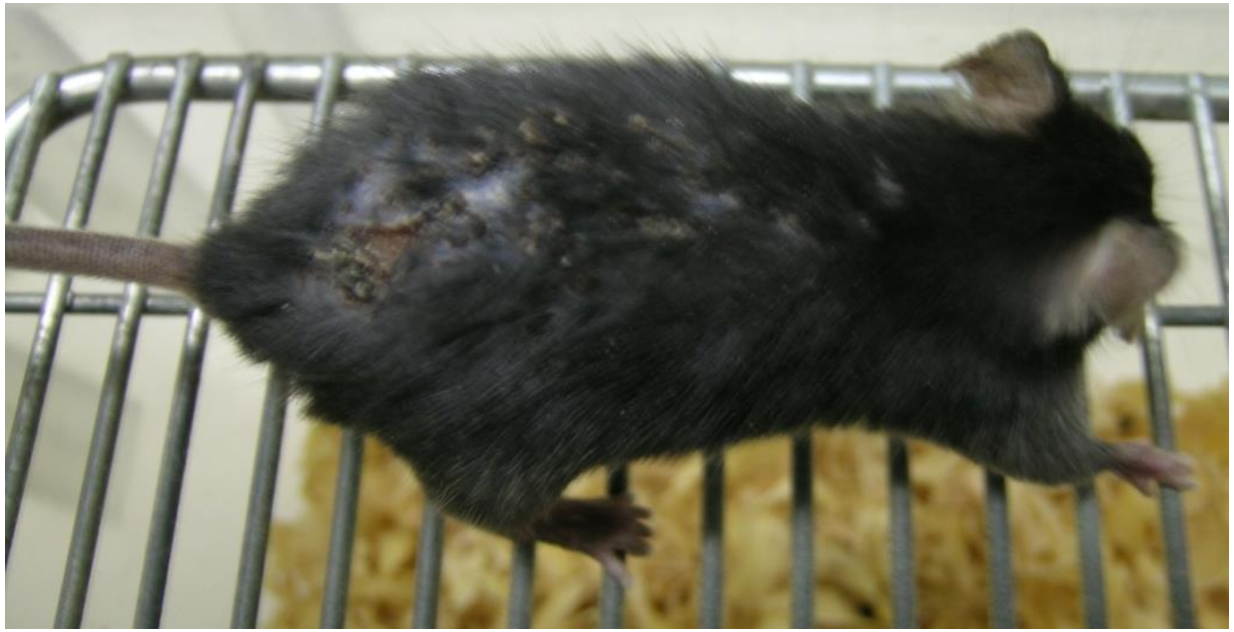
Abstract | Self-grooming is a compl
sequencing pattern and is one of th
rodents. In this Review, we discuss t
studies of rodent models of neurop
spectrum disorder and obsessive co
phenotypes. We suggest that roder
behaviour in such models, and ther
of rodent self-grooming may also b
involved in complex sequential pat

Table 2 | Disease symptoms that may be modelled in rodents by the assessment of self-grooming behaviour

Human disease	Symptom	Relevant rodent self- grooming phenotype	Refs
OCD	Compulsive hand washing	Increased self-grooming	37,143–145
Trichotillomania	Compulsive hair pulling	Increased self-grooming	128,199
Body dysmorphic disorder	Obsessive cosmetic grooming	Increased self-grooming	92
Excoriation	Compulsive skin-picking	Increased self-grooming	92
ASD	Behavioural perseveration	Increased self-grooming	16,19–22,33
Tourette syndrome	Tics	Increased self-grooming	29
Anxiety disorders and panic disorder	Stress-induced displacement behaviour	Increased self-grooming	7,27,31,158
Schizophrenia	Hyperarousal	Increased self-grooming	92
Trichotillomania	Compulsive hair-pulling	Increased self-barbering*	27,45
ASD	Behavioural perseveration	Grooming patterning rigidity	89–91
Depression	Behavioural perseveration	Grooming patterning rigidity	92
Anxiety disorders and panic disorder	Hyperarousal	Disrupted grooming patterning	27,28,159
Basal ganglia disorders	Impaired action sequencing	Disrupted grooming patterning	64
Depression	Anhedonia and poor hygiene	Reduced grooming activity	92
Neurodegenerative disorders	General decline in motor function	Reduced grooming activity	160

ASD, autism spectrum disorder; OCD, obsessive compulsive disorder. *Self-inflicted hair and whisker loss frequently seen in laboratory rodents in different contexts[128]. This grooming-related behaviour is an important rodent phenotype sensitive to various environmental and genetic manipulations (see Supplementary information S4 (table)).

Comportamento agressivo



Comai, Stefano et al. "The psychopharmacology of aggressive behavior: a translational approach: part 1: neurobiology." *Journal of clinical psychopharmacology* vol. 32,1 (2012): 83-94. doi:10.1097/JCP.0b013e31823f8770

Comai, Stefano et al. "The psychopharmacology of aggressive behavior: a translational approach: part 2: clinical studies using atypical antipsychotics, anticonvulsants, and lithium." *Journal of clinical psychopharmacology* vol. 32,2 (2012): 237-60. doi:10.1097/JCP.0b013e31824929d6

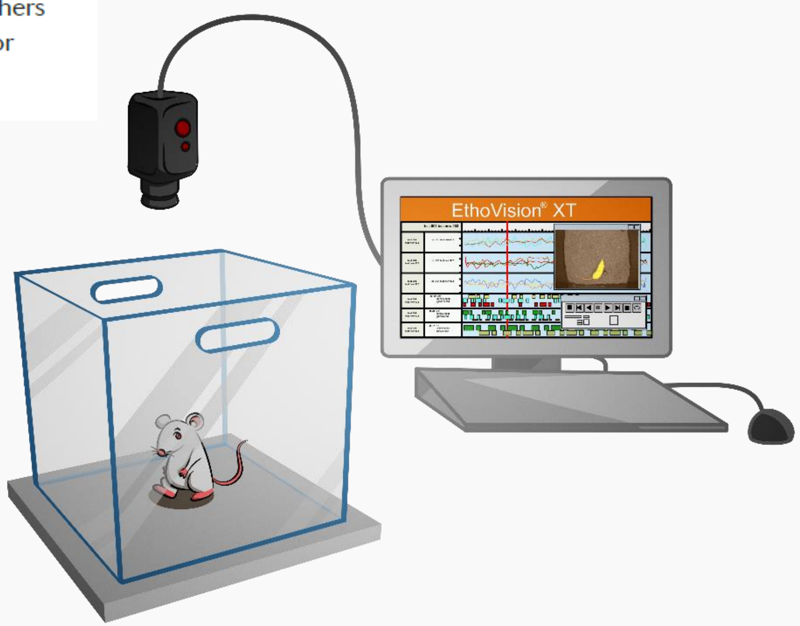
Avaliação comportamental

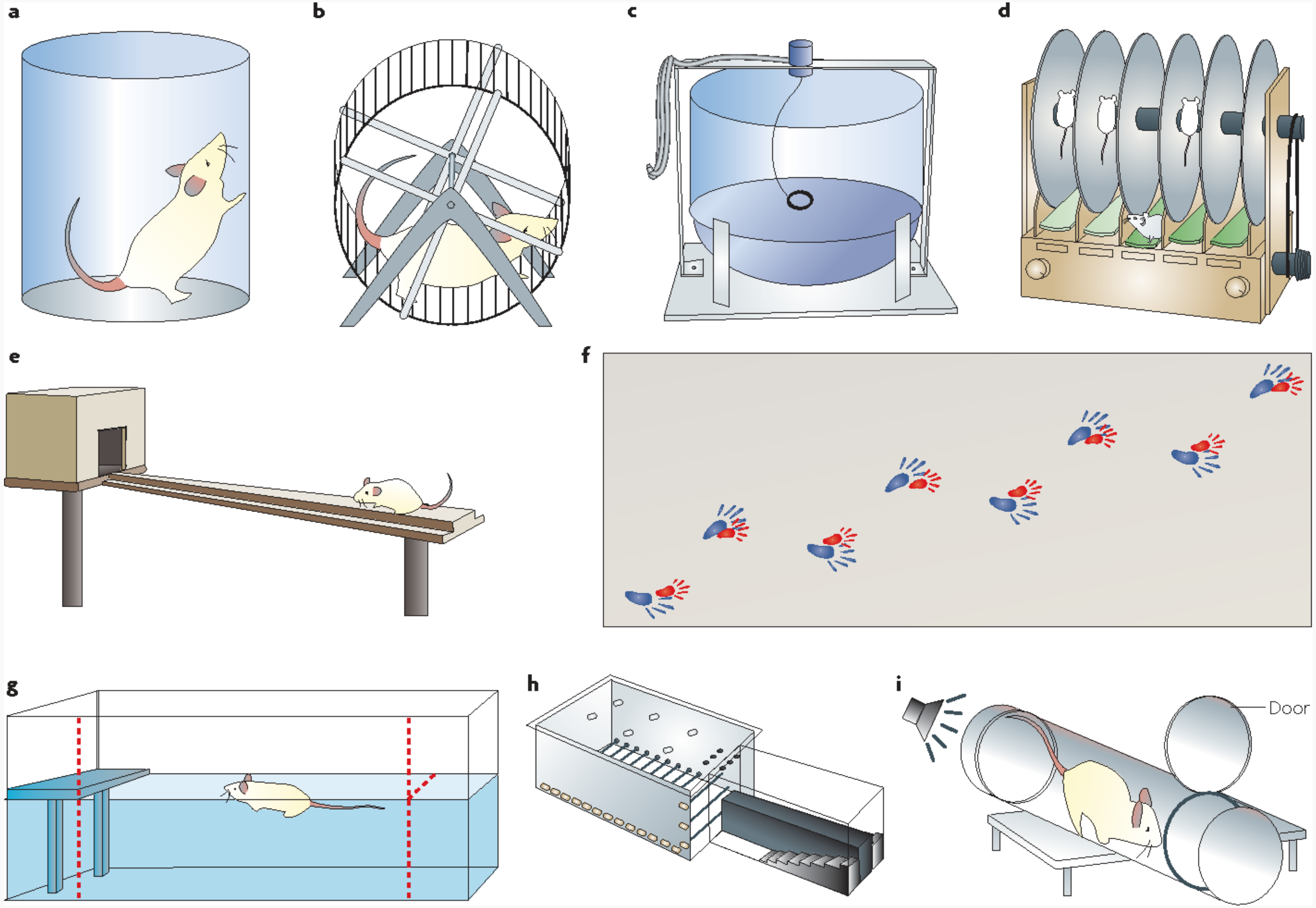
Tests to assess motor phenotype in mice: a user's guide

Simon P. Brooks and Stephen B. Dunnett

Abstract | The characterization of mouse models of human disease is essential for understanding the underlying pathophysiology and developing new therapeutics. Many diseases are often associated with more than one model, and so there is a need to determine which model most closely represents the disease state or is most suited to the therapeutic approach under investigation. In the case of neurological disease, motor tests provide a good read-out of neurological function. This overview of available motor tasks aims to aid researchers in making the correct choice of test when attempting to tease out a transgenic phenotype or when assessing the recovery of motor function following therapeutic intervention.

Brooks, Simon Philip and Stephen B. Dunnett. "Tests to assess motor phenotype in mice: a user's guide." *Nature Reviews Neuroscience* 10 (2009): 519-529.

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http://www.ratlife.org/Home/0Main-frameset/Mainframeset.htm