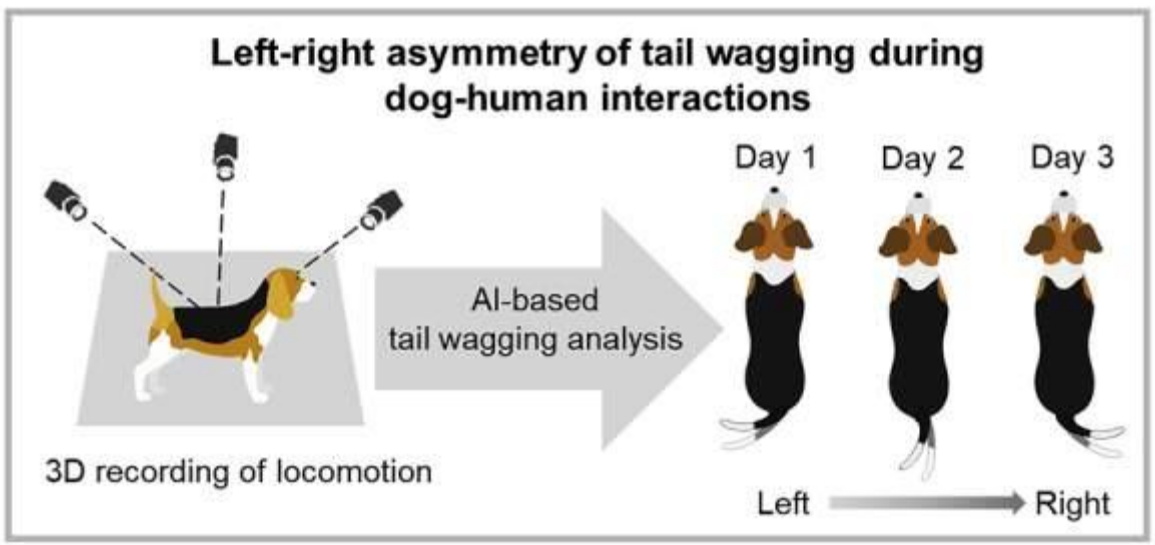
From Companion to Model:
The Canine Models in Modern Biological and Biomedical Research

邢丽敏 王姣 王红蕾

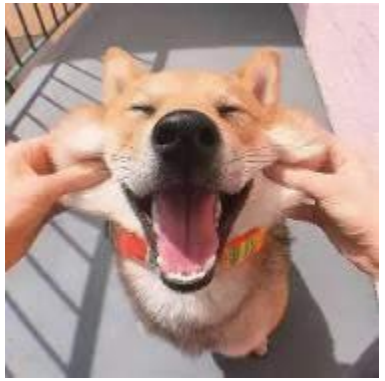
2025-11-25

“三江大讲堂”系列学术报告——湖北大学张永清教授：孤独症的新型动物模型—家犬模型

发布者：吴心龙 发布时间：2024-10-11 浏览次数：389



Dog is a highly promising research model



I: How do dogs express or perceive emotions? How do dogs establish emotional or behavioral interactions with human?

II: What researches are conducted using canine models? What are the main research directions of dogs in the field of biomedicine?

1. Overview of research progress on canine models. ——XLM

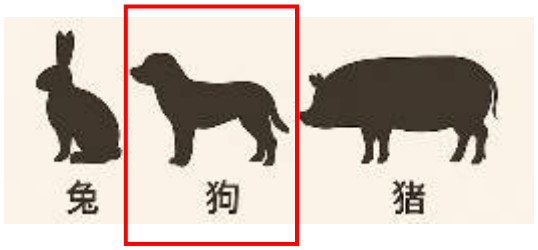
2. Behavioral and emotional research in canine models. ——WJ

3. Canine model in typical disease research. ——WHL

PART 1:

Overview of Research Progress on Canine Models

XLM




灵长类动物

小鼠 (*Mus musculus*)	基因编辑模型、免疫学、肿瘤、代谢疾病
大鼠 (*Rattus norvegicus*)	神经电生理、药理毒理、行为学

家兔 (*Oryctolagus cuniculus*)	动脉粥样硬化、免疫、抗体制备
狗 (*Canis familiaris*)	心血管、药理安全性、神经行为、老化
猪 (*Sus scrofa domesticus*)	代谢病、器官移植、外科训练、心血管

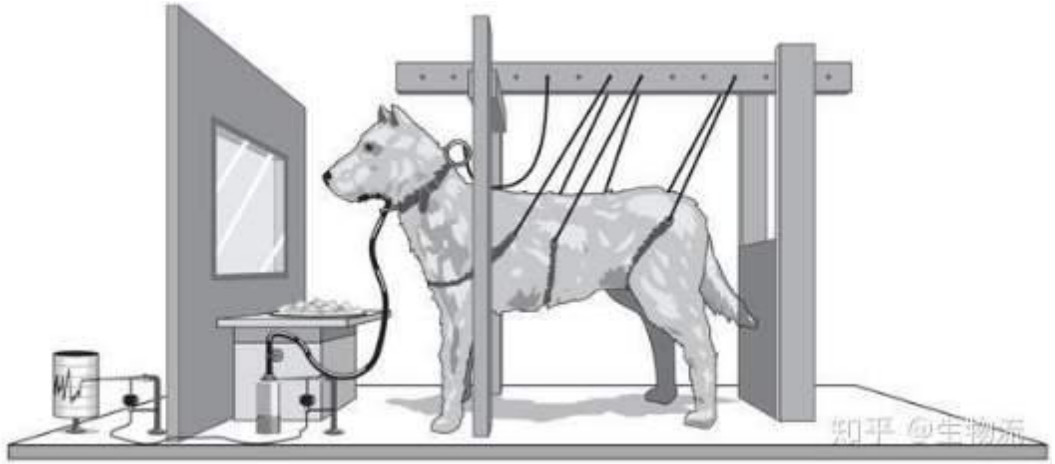
恒河猴 (*Macaca mulatta*)	视觉、认知、运动控制、脑机接口
狨猴 (*Callithrix jacchus*)	神经发育、社会行为、基因编辑

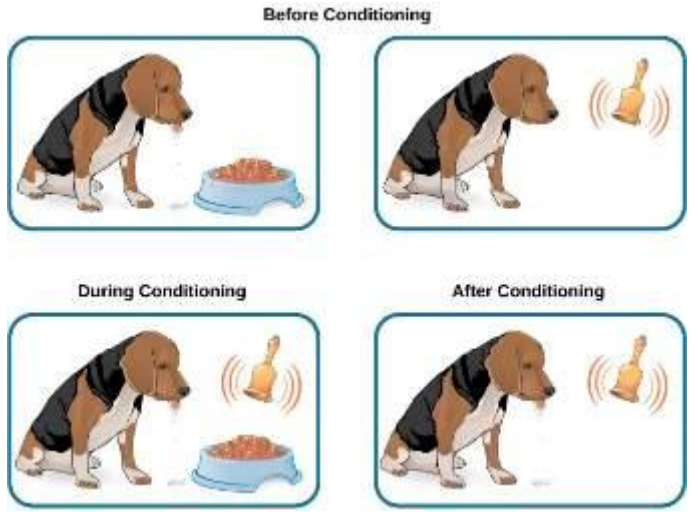
“是否能在不触碰灵长类伦理边界的情况下，
获得更贴近人类生理与行为的哺乳动物模型？”

犬作为动物模型的独特优势

1. 是唯一一种与人类共同进化的社会性哺乳动物。
2. 它们与人类共享许多重大疾病，包括癌症、糖尿病、心血管疾病和神经退行性疾病。
3. 许多疾病在犬身上会自然发生，提供了无需人工诱导的自发性疾病模型。

When it comes to experimental dogs, what do you think of?





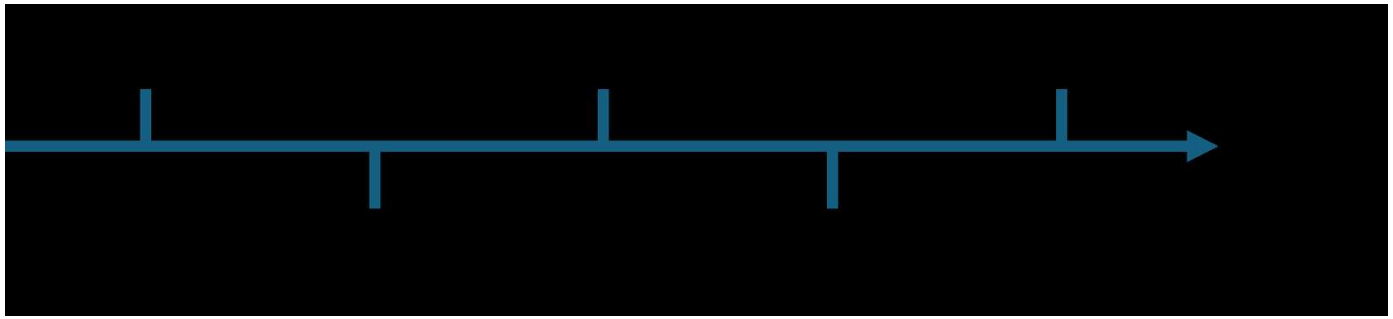
“经典条件反射研究”
沿用至今

Nobel Prize in Physiology or Medicine 1904

Photo from the Nobel Foundation archive.

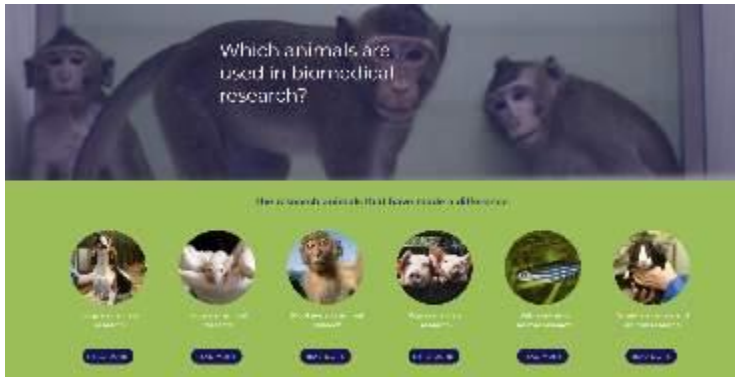
Ivan Petrovich Pavlov

Prize share: 1/1



Why are canine models now used less in research?

- 周期与成本高
- 遗传操作门槛高
- 标准化不足
- 伦理与社会观感



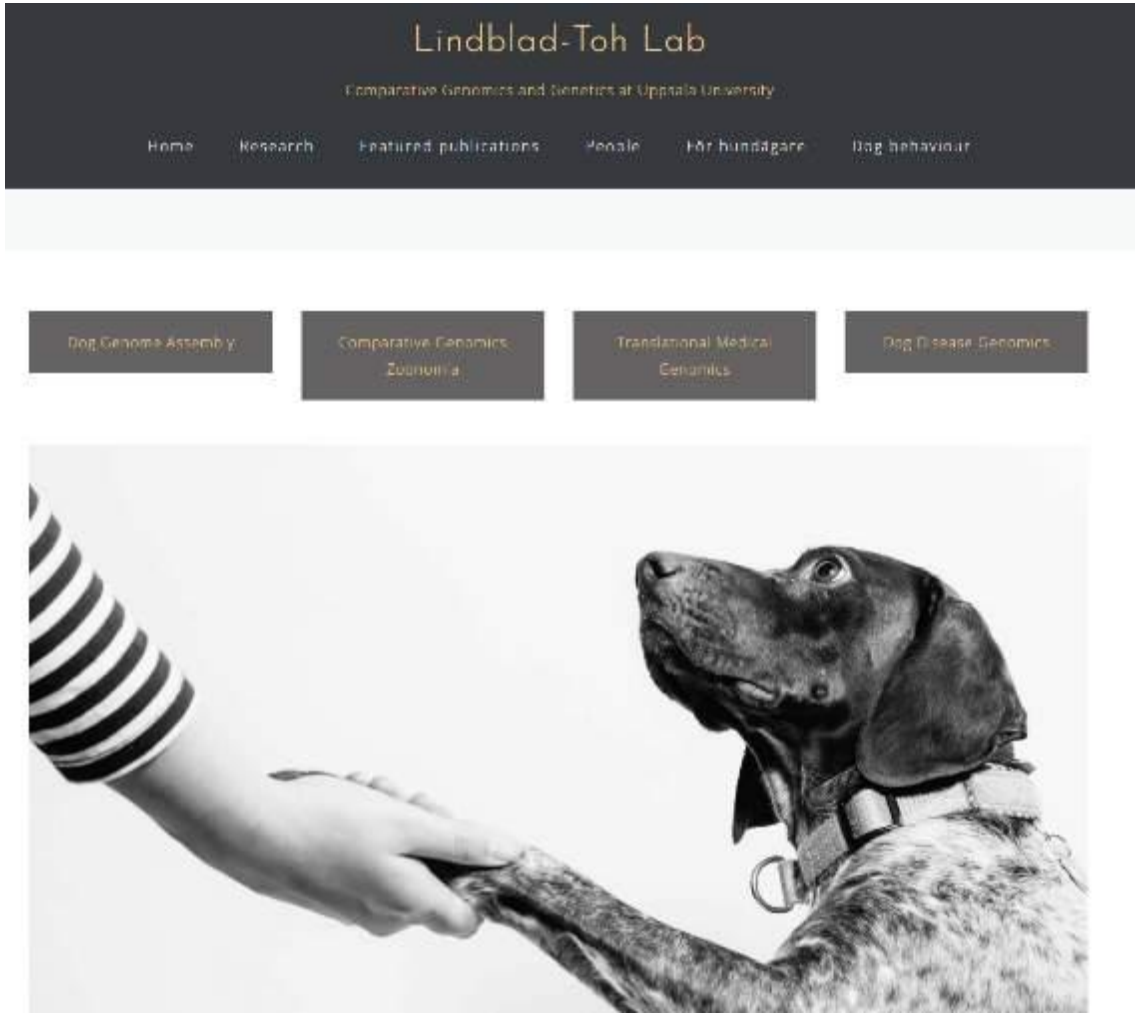
Why are dogs used in biomedical research?
When is it essential to use dogs in biomedical research?
What is being done to replace and reduce the use of dogs?

- 比较医学/自然发生疾病
- 单基因或强效变异的遗传病
- 行为与感知
- 外科医学

Reducing severity in dog research
Medical treatments to help dogs
How are dogs cared for in research?

3R 原则:
Replacement 替代
Reduction 减量
Refinement 优化

Which laboratories work on canine models,
and what are their main research directions?



Kerstin Lindblad-Toh

UPPSALA UNIVERSITY 瑞典

External website (Uppsala University)
External website (Broad Institute)

1. 破译人类基因组的功能
2. 了解基因组进化的机制及其与表型适应的联系
3. 识别狗和人类的疾病基因

Tengvall K, Sundström E, Wang C, Bergvall K, Wallerman O, Pederson E, Karlsson Å, Harvey ND, Blott SC, Olby N, Olivry T, Brander G, Meadows JRS, Roosje P, Leeb T, Hedhammar Å, Andersson G, Lindblad-Toh K. **Bayesian model and selection signature analyses reveal risk factors for canine atopic dermatitis.** Commun Biol. 2022 Dec 8;5(1):1348. doi: 10.1038/s42003-022-04279-8. PMID: 36482174.

皮炎

Dahlqvist J, Ekman D, Sennblad B, Kozyrev SV, Nordin J, Karlsson Å, Meadows JRS, Hellbacher E, Rantapää-Dahlqvist S, Berglin E, Stegmayr B, Baslund B, Palm Ø, Haukeland H, Gunnarsson I, Bruchfeld A, Segelmark M, Ohlsson S, Mohammad AJ, Svärd A, Pullerits R, Herlitz H, Söderbergh A, Rosengren Pielberg G, Hultin Rosenberg L, Bianchi M, Murén E, Omdal R, Jonsson R, Eloranta ML, Rönnblom L, Söderkvist P, Knight A, Eriksson P, Lindblad-Toh K. 2021. **Identification and functional characterization of a novel susceptibility locus for small vessel vasculitis with MPO-ANCA.** Rheumatology. 2022 Aug 3;61(8):3461-3470. doi: 10.1093/rheumatology/keab912.

血管炎

Lundtoft C, Sjöwall C, Rantapää-Dahlqvist S, Bengtsson AA, Jönsen A, Pucholt P, Wu YL, Lundström E, Eloranta ML, Gunnarsson I, Baecklund E, Jonsson R, Hammenfors D, Forsblad-d'Elia H, Eriksson P, Mandl T, Bucher S, Norheim KB, Johnsen SJA, Omdal R, Kvarnström M, Wahren-Herlenius M, Truedsson L, Nilsson B, Kozyrev SV, Bianchi M, Lindblad-Toh K; DISSECT consortium; ImmunoArray consortium, Yu CY, Nordmark G, Sandling JK, Svenungsson E, Leonard D, Rönnblom L. 2022. **Combined genetic deficiencies of the classical complement pathway are strongly associated with both systemic lupus erythematosus and primary Sjögren's syndrome.** Arthritis Rheumatol. 2022 Jun 21. doi: 10.1002/art.42270. Online ahead of print.

系统性红斑狼疮

Lundtoft C, Pucholt P, Martin M, Bianchi M, Lundström E, Eloranta ML, Sandling JK, Sjöwall C, Jönsen A, Gunnarsson I, Rantapää-Dahlqvist S, Bengtsson AA, Leonard D, Baecklund E, Jonsson R, Hammenfors D, Forsblad-d'Elia H, Eriksson P, Mandl T, Magnusson Bucher S, Norheim KB, Auglaend Johnsen SJ, Omdal R, Kvarnström M, Wahren-Herlenius M, Notarnicola A, Andersson H, Molberg Ø, Diederichsen LP, Almlöf J, Syvänen AC, Kozyrev SV, Lindblad-Toh K; DISSECT Consortium; ImmunoArray Development Consortium, Nilsson B, Blom AM, Lundberg IE, Nordmark G, Diaz-Gallo LM, Svenungsson E, Rönnblom L. 2022. **Complement C4 Copy Number Variation is Linked to SSA/Ro and SSB/La Autoantibodies in Systemic Inflammatory Autoimmune Diseases.** Arthritis Rheumatol. 2022 Aug;74(8):1440-1450. doi: 10.1002/art.42122. Epub 2022 Jun 27.

自身免疫疾病

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NEWS CV RESEARCH TEACHING

ENIKŐ KUBINYI > CV

Prof. Enikő Kubinyi is head of the Department of Ethology at Eötvös Loránd University, Budapest. She joined the Family Dog Project in 1994 and later earned an MSc in biology, teaching, and video communication, a PhD in ethology, and a DSc in neurobiology. Supported by an ERC Starting Grant, she founded the Senior Family Dog Project and the Canine Brain and Tissue Bank. She currently leads the MTA-ELTE "Momentum" Companion Animal Research Group and co-leads the NAP Olfaction Research Group.

Her research focuses on dog social behaviour and cognition, wolf–dog comparisons, ethorobotics, collective motion, and human–animal interactions, using behavioural testing, EEG, fMRI, movement-tracking, microbiome, and genetic analyses. She has published over 130 peer-reviewed articles and teaches behavioural genetics, domestication, animal personality, and human ethology.

Prof. Kubinyi has received the L'Oréal-UNESCO for Women in Science, Junior Prima, and APA Frank A. Beach Awards. She is an alumna of the Young Academies of Europe and Hungary, and her work has been featured widely in international media (e.g., **BBC Horizon/NOVA**, **Knowable**, **Animal Allies book**, **Forbes**, **Le Monde**, **The Times**, **Wired**, **ScienceAlert**, **The Telegraph**, **Impakter**, **Daily Mail**, **NBC**, **Newsweek**, **ScienceShot**, **Phys.org**, **The Guardian**, **Qubit** and **other** popular **science journals**). She is married and has three children.

Keywords: animal behaviour, ethology, ethorobotics, comparative cognition, cognitive ageing, behaviour genetics, animal personality, tissue bank, welfare, dog, wolf

PERSONAL INFORMATION

- Family name, First name: Kubinyi, Eniko
- Affiliation: **Department of Ethology**, ELTE Eötvös Loránd University, Pázmány P. sétány 1/c, 1117, Budapest, Hungary

匈牙利

- 犬认知功能（attention, memory, learning）
- 人-犬情绪交互
- 犬老龄化（含 Dog Aging 相关）
- 脑影像（fMRI）、基因组学、行为追踪
- 比较认知：犬 vs 狼 vs 人类
- 进化与驯化科学（Domestication）

Enikő Kubinyi 是欧洲研究犬行为、比较认知、老龄化与人-犬关系的**最主要科学家之一。**

她所在的 **ELTE – Family Dog Project** 是世界上最早、规模最大的"家犬科学研究团队"，在行为学、进化心理学、犬认知神经科学方面是**公认的世界顶尖实验室之一。**

美国密苏里大学

Current Research Projects:

Chronic Superficial Keratitis (Pannus)

Gastric (Stomach) Cancer

Gingival Enlargement or Hyperplasia

Hemangiosarcoma, Lymphoma, Histiocytic sarcoma

Juvenile Renal Disease in Boxers

Genomic analyses identify 15 risk loci and reveal *HDAC2*, *SOX2-OT*, and *IGF2BP2* in a naturally occurring canine model of gastric cancer.
Cook SR, Hugen S, Hayward JJ, Famula TR, Belanger-Sandoval JM, Feiten H, Oberbauer AM, Leegwater PAJ, Ostrander EA, Mandigers PJJ, Evans JM. (2025) *Proc Natl Acad Sci USA*, 122 (22) e2416723122. [PubMed Abstract]

A *VWF* missense variant in Havanese dogs with Type 3 von Willebrand disease.
Armas-Jimenez AC, Randolph A, Clark LA, Evans JM*, Brooks MB*, Goggs R* (2025) *Animal Genetics* 56(3):e70021. [PubMed Abstract] *co-corresponding authors

Who we are:

The Research Center for Human-Animal Interaction (ReCHAI), founded in 2005, in College of Veterinary Medicine has a mission of education and conducting programs and studies about the benefits of human-animal interaction. ReCHAI is on the leading edge of programs and studies that explore how the human-animal bond has an impact on the health of people and animals.

ReCHAI is designed to:

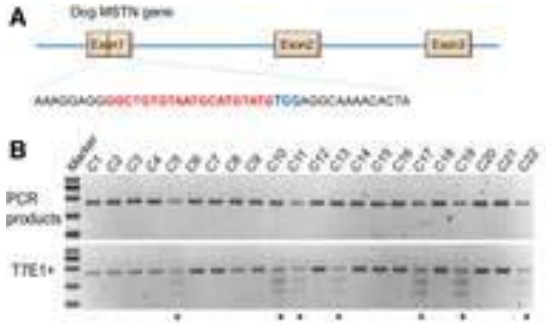
- Develop a program for research and education to study the health benefits of human-animal interaction (HAI).
- Promote the science of HAI.
- Document evidence demonstrating Animal Assisted Interventions (AAI) as a beneficial form of complementary therapy.
- Foster educational and research opportunities for MU students, as well as students from around the country and globe.
- Collaborate with other centers nationally and internationally to promote HAI.
- Foster public understanding of benefits of HAI.

南京大学 NANJING UNIVERSITY | MARC 模式动物研究所 Model Animal Research Center

首页 概述 新闻中心

图一：世界首例基因敲除犬类模型，左为“大力神”，右为“天狗”

“肌肉生长抑制素”（myostatin）



Types of transplantation	Embryo flushed	Embryo injected	Embryo transferred	Host mother	Pregnancy	Birth	Mutation	Biallelic mutation
Allo-transplantation	30	25	25	6	0	0	0	0
Auto-transplantation	48	35	35	10	8	27	2	2

Qingjian Zou, *et al.* , *Journal of Molecular Cell Biology.*, 2015

湖北大学 HUBEI UNIVERSITY 生命科学学院 SCHOOL OF LIFE SCIENCES

Article | Published: 17 October 2023

Modeling *SHANK3*-associated autism spectrum disorder in Beagle dogs via CRISPR/Cas9 gene editing

Rui Tian, Yuan Li, Hui Zhao, Wen Lyu, Jianping Zhao, Xiaomin Wang, Heng Lu, Huijuan Xu, Wei Ren, Qing-quan Tan, Qi Shi, Guo-dong Wang, Ya-ping Zhang, Liangxue Lai, Jidong Mi, Yong-hui Jiang ✉ & Yong Q. Zhang ✉

Molecular Psychiatry **28**, 3739–3750 (2023) Cite this article

2307 Accesses **24** Citations **113** Altmetric Metrics

SCIENCE ADVANCES | RESEARCH ARTICLE

NEUROSCIENCE

Autism-like atypical face processing in *Shank3* mutant dogs

Siqi Yuan[1,2], Chenyu Pang[3], Liang Wu[1,2], Li Yi[3], Kun Guo[4], Yong-hui Jiang[5], Yong Q. Zhang[1,2,6]*, Shihui Han[3]*

Atypical face processing is a neurocognitive basis of social deficits in autism spectrum disorder (ASD) and a candidate cognitive marker for the disease. Although hundreds of risk genes have been identified in ASD, it remains unclear whether mutations in a specific gene may cause ASD-like atypical face processing. Dogs have acquired exquisite face processing abilities during domestication and may serve as an effective animal model for studying genetic associations of ASD-like atypical face processing. Here, we showed that dogs with *Shank3* mutations exhibited behavioral and attentional avoidance of faces, contrasting with wild-type controls. Moreover, neural responses specific to faces (versus objects) recorded from the electrodes over the temporal cortex were significantly decreased and delayed in *Shank3* mutants compared to wild-type controls. Cortical responses in the frontal/parietal region underlying categorization of faces by species/breeds were reduced in *Shank3* mutants. Our findings of atypical face processing in dogs with *Shank3* mutations provide a useful animal model for studying ASD mechanisms and treatments.

一、基本信息

张永清，博士，教授，博士生导师

研究领域: 发育神经生物学和重大神经疾病的动物模型

研究方向：以果蝇、非人灵长类猕猴和家犬为实验体系，通过多学科的研究手段包括基因编辑，脑影像和电生理分析以及行为学和认知功能分析等致力于研究神经突触的发育和功能调控，发现了多个调控突触发育的新通路和新机制，以及相关重大神经疾病特别是自闭症的分子细胞和神经环路机制。

1. 以非人灵长类、家犬和果蝇为模式动物研究人类重要神经疾病包括自闭症的分子遗传和神经环路机制，从而为这类疾病的预防和治疗提供理论依据。传统的模式动物果蝇便于分子遗传和信号通路的解析，而基因编辑大动物模型研究结果更便于临床转化应用。

2. 以果蝇为材料，用分子、细胞、遗传、发育和神经生物学为主要实验检测手段研究神经系统特别是神经突触的结构和功能调控机制。

科学研究

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The laboratory of Genetics and Evolution of Behavior

学科组简介 人员 新闻 成果

王国栋

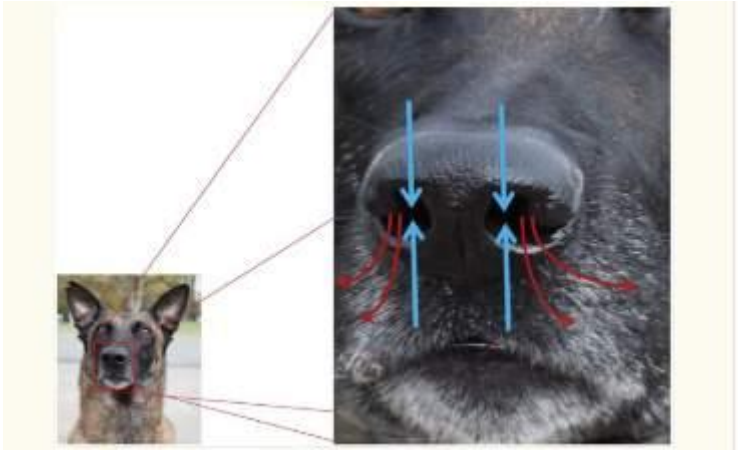
中国科学院昆明动物研究所
研究员（博士生导师）
动物学博士
E-mail: wanggd@mail.kiz.ac.cn

主要研究方向：

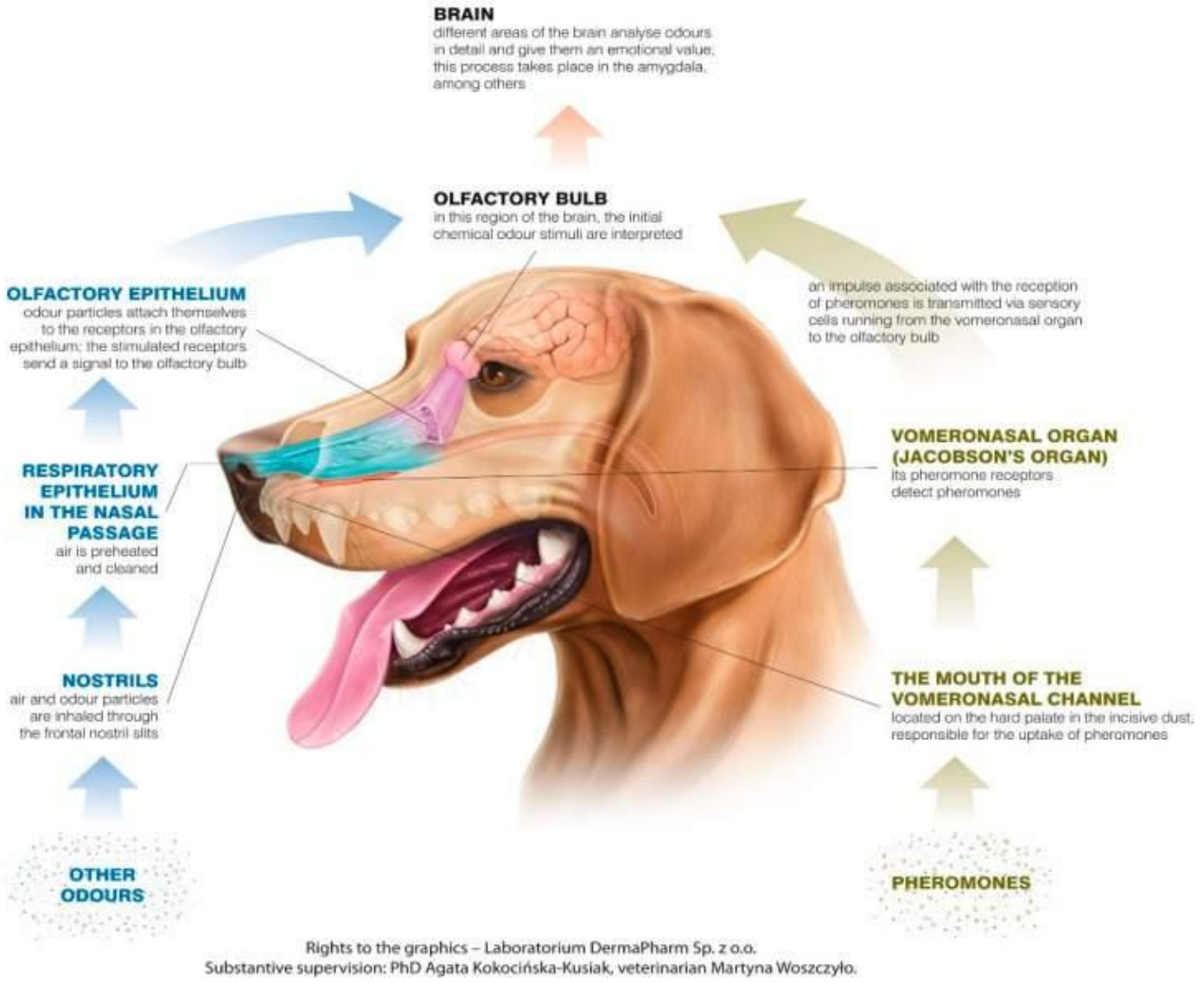
1）家犬的起源、驯化、和人工选择的遗传机制。利用古DNA技术和基因组学探究家犬的起源和驯化历史。利用群体遗传学探究家犬的突变速率、遗传图谱、等位基因频谱，和人工选择的遗传机制，探讨人工选择与自然选择在底层遗传驱动力上的异同。

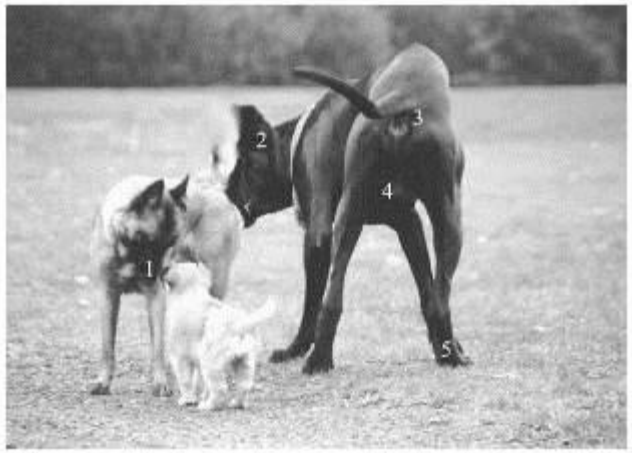
2）家犬复杂行为的多基因相互作用机制。本方向以家犬为研究对象，利用高精度计算神经行为学定量行为性状，利用组学、神经生物学等技术解析复杂行为的遗传和细胞生物学机制，利用基因编辑技术在大动物中重现复杂行为性状并创建家犬的精神疾病模型。

Dogs have a sensitive sense of smell



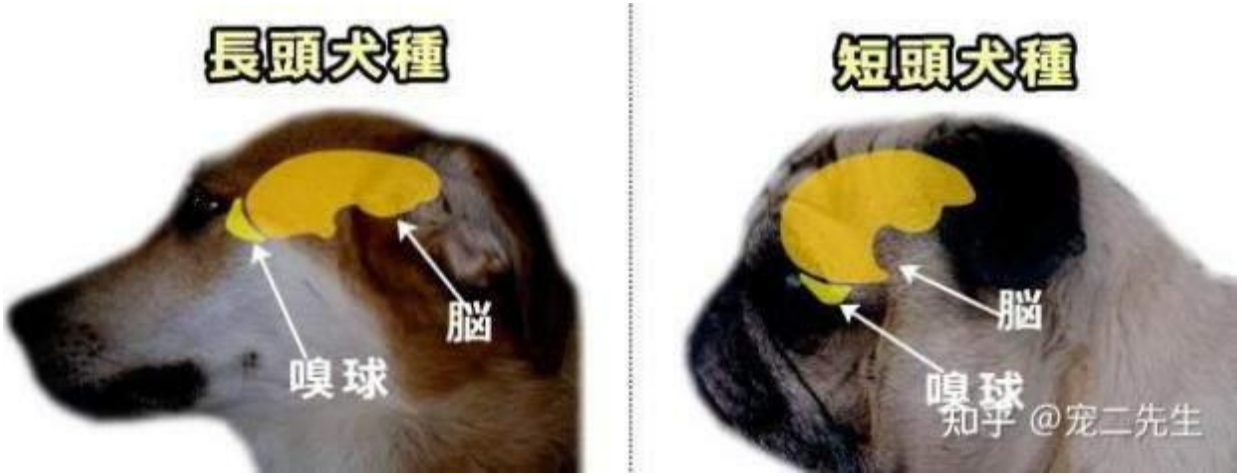
The canine olfactory system consists of the main olfactory epithelium (MOE) and the vomeronasal organ (VNO)

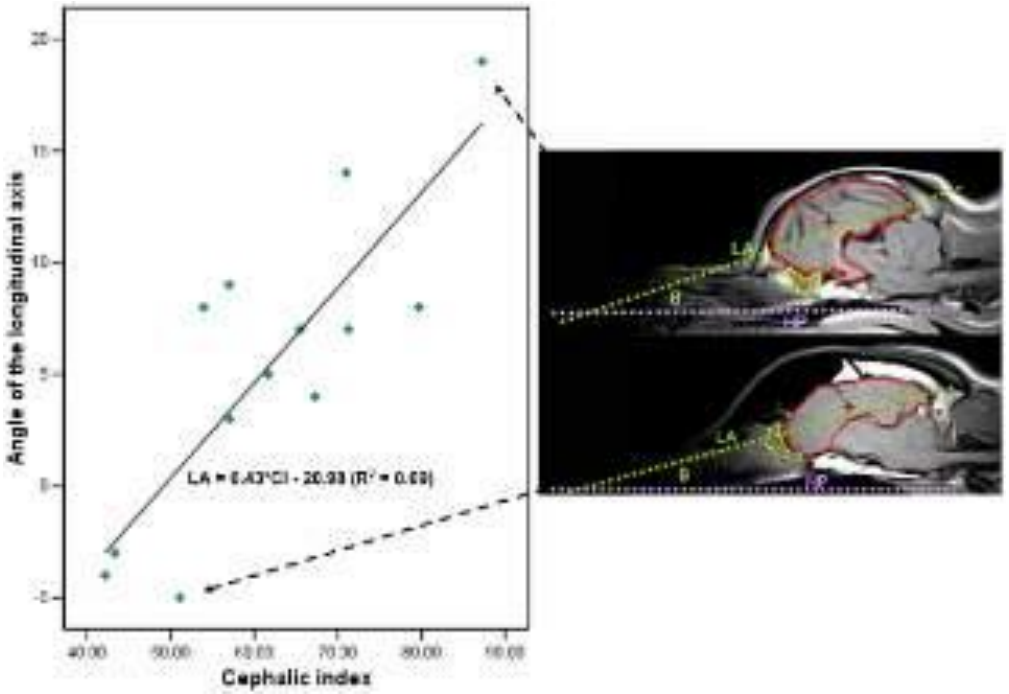




主嗅上皮（MOE）和犁鼻器（VNO）

Human Induced Rotation and Reorganization of the Brain of Domestic Dogs

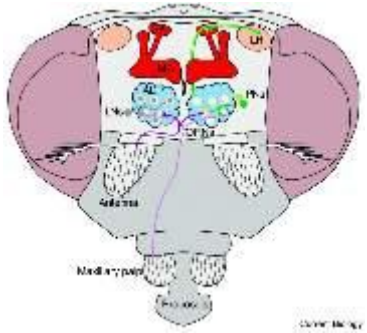


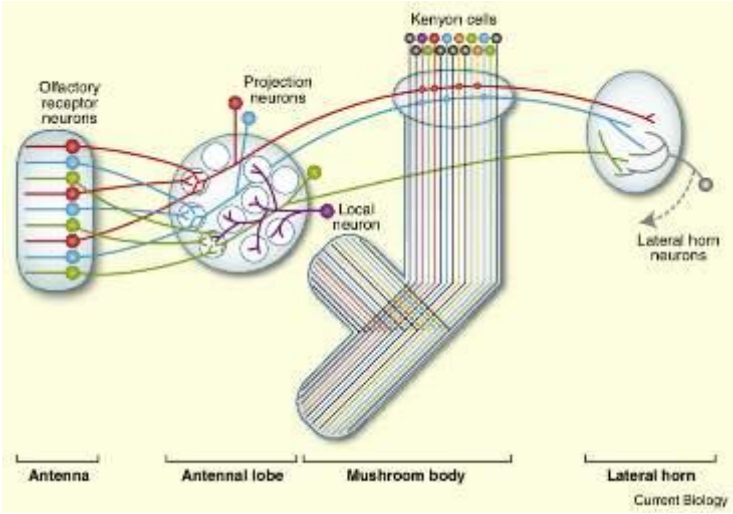


Roberts T, *et al. PLoS ONE.* 2010

Comparison of olfactory receptor genes among different species

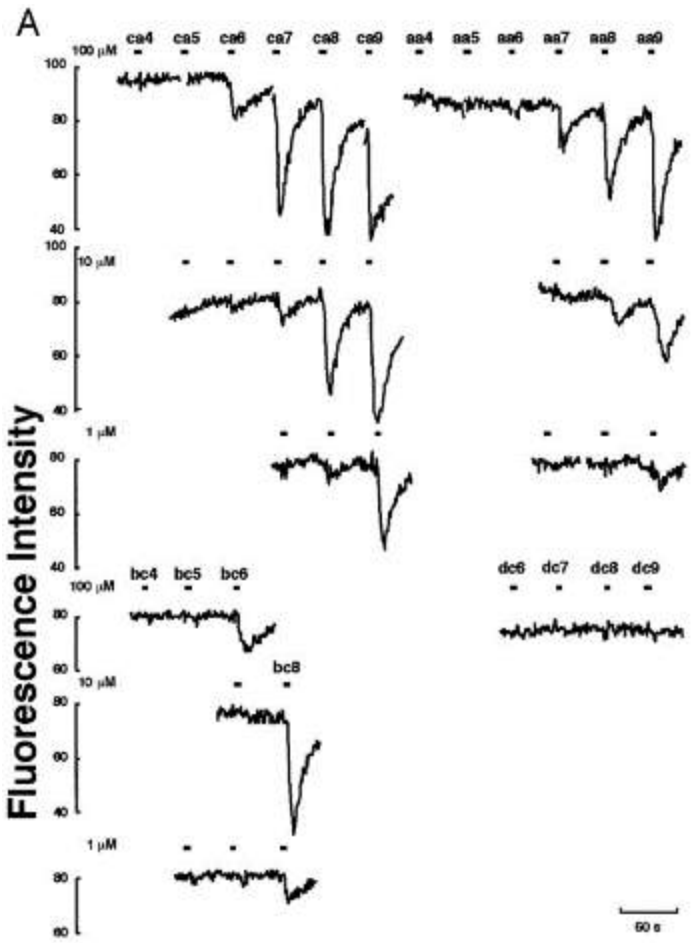
物种	主要嗅觉受体家族	功能性 OR 基因数（约）
果蝇 (*D. melanogaster*)	OR（+ Orco） + IR	~60 个 OR 基因；~66 个 IR 基因
小鼠	OR	1037 个功能性 OR
狗	OR	≈800–900 个功能性 OR（总共 ~970–1094 个 OR 基因）
人	OR	388 个功能性 OR



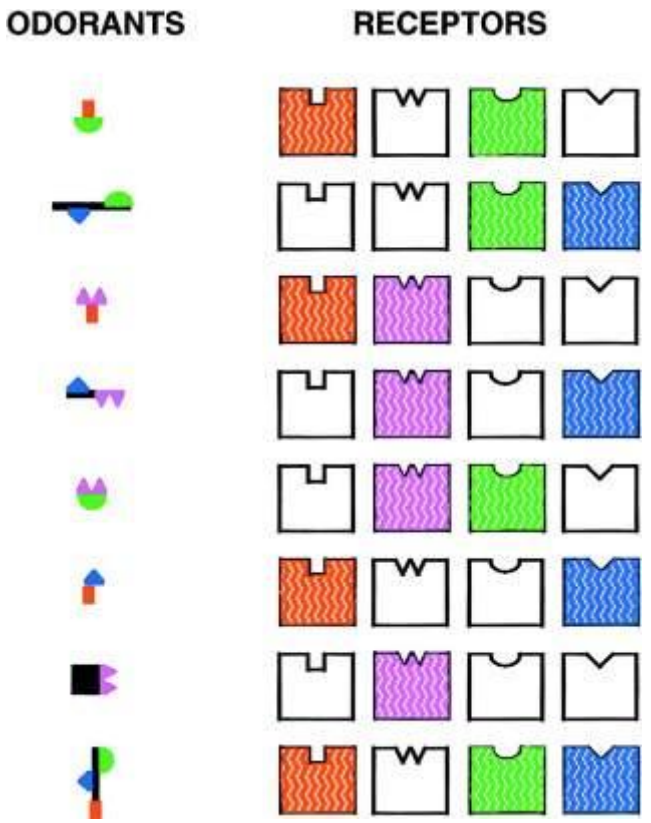


Masse NY, *et al. Curr Biol.* 2009

Combinatorial coding in the mammalian olfactory system

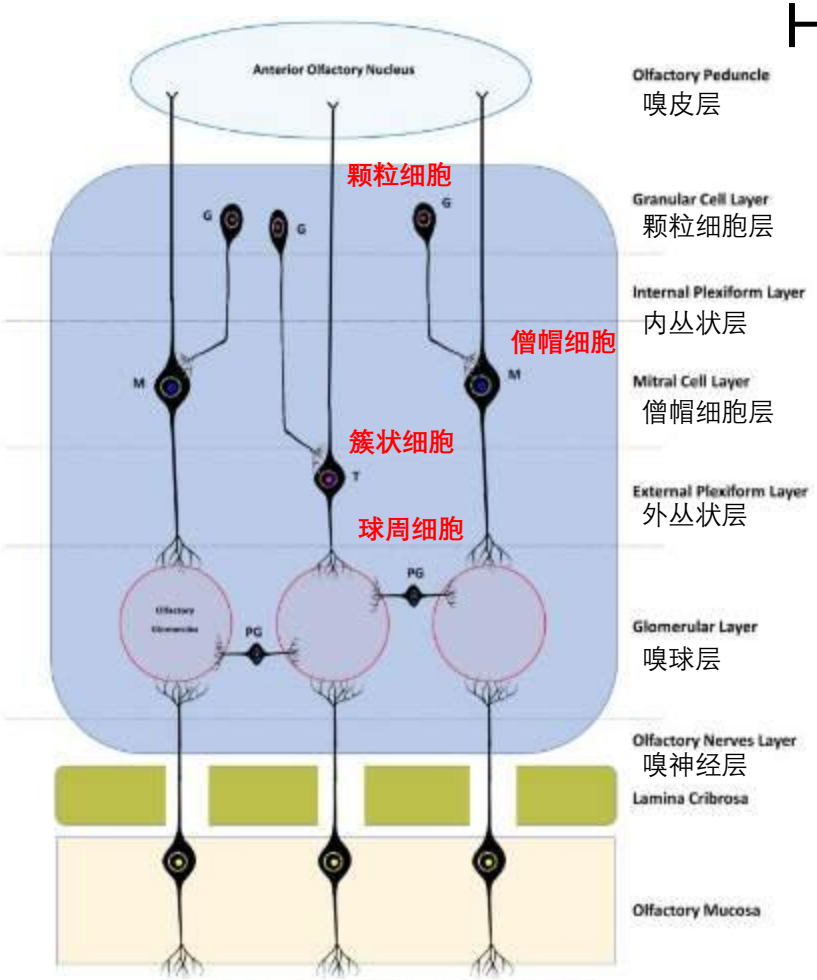


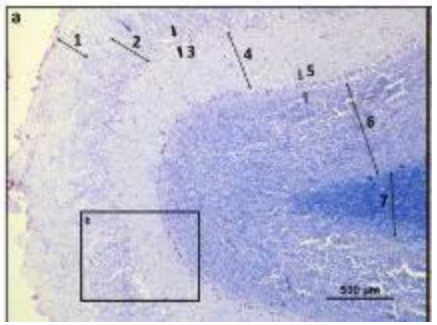
odorants \ ORs	S 1	S 3	S 6	S 18	S 19	S 25	S 41	S 46	S 50	S 51	S 79	S 83	S 85	S 86
butanoic acid														
pentanoic acid														
hexanoic acid					●									
heptanoic acid	●			●	10		●			●	●			
octanoic acid	●			●	10		●	●		10	●	10		
nonanoic acid	10			10	1		●	10		10		1		10
pentanol	a	●	a					b						
hexanol	b	●	a			●		b						
heptanol	b	●			●	●		b						
octanol	b			●	10		●	b		●				
nonanol	b			●	1		●	b		10		1		
bromobutanoic acid													●	
bromopentanoic acid													●	
bromohexanoic acid					●		●						1	
bromooctanoic acid	10			●	1		●	●		10		10	1	
hexanedioic acid													●	
heptanedioic acid													●	
octanedioic acid			●								●		●	
nonanedioic acid			10						10		1		●	



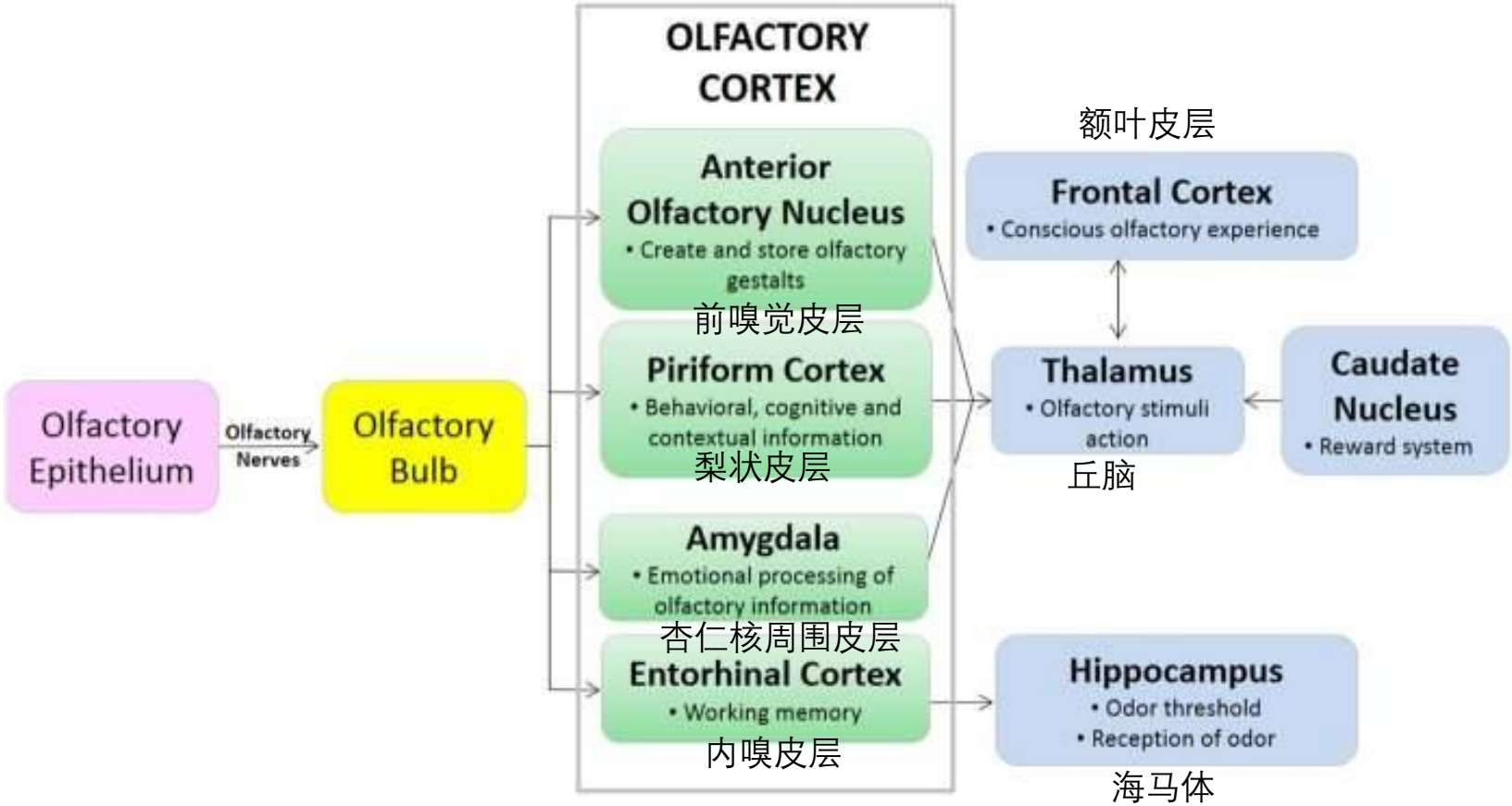
Malnic, Bettina *et al. Cell*, 1999.

Histology of the Olfactory Bulb





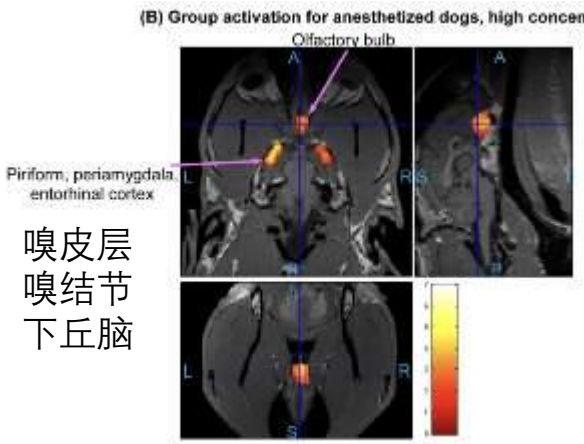
颗粒细胞通过强力的抑制网络精细调整这些输出、提高分辨率并参与嗅觉学习。



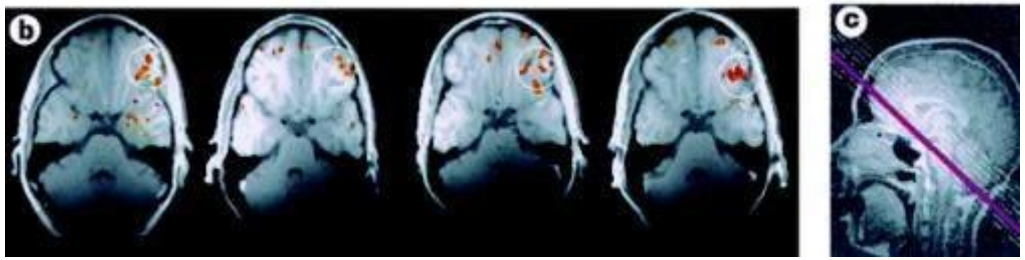
Alvites R, *et al., Brain Sci.* 2023.
Jenkins EK, *et al., Front Vet Sci.* 2018

A broadly similar olfactory core pathway for sniffing and smell

smelling

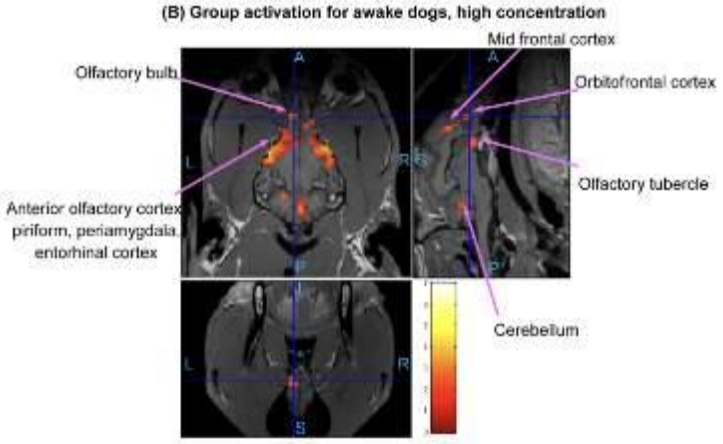


嗅皮层
嗅结节
下丘脑

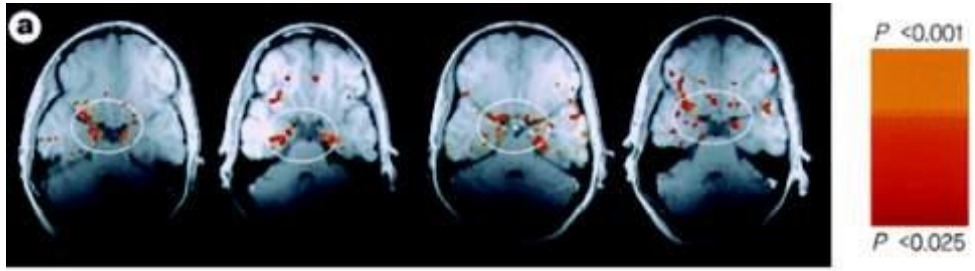


气味存在时引发的激活主要发生在眶额前部的外侧和前部区域

sniffing



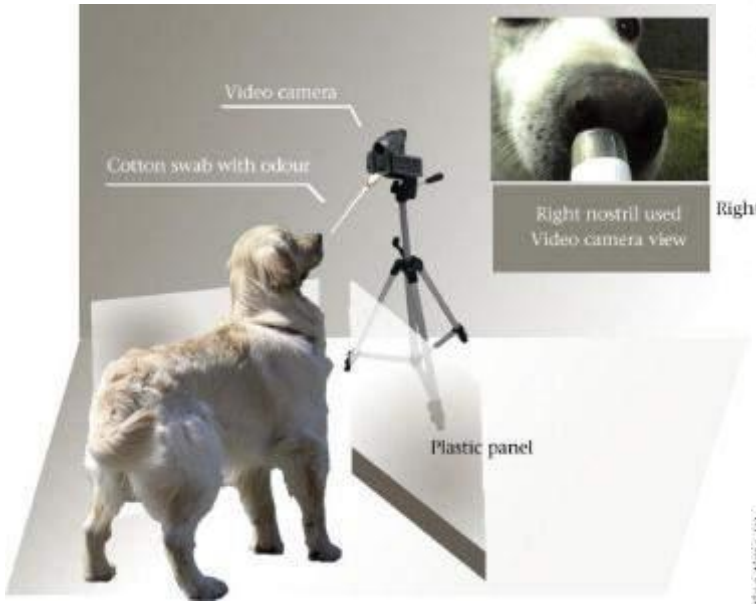
额外招募前额叶 / 眶额皮层
小脑以及顶叶 / 枕叶

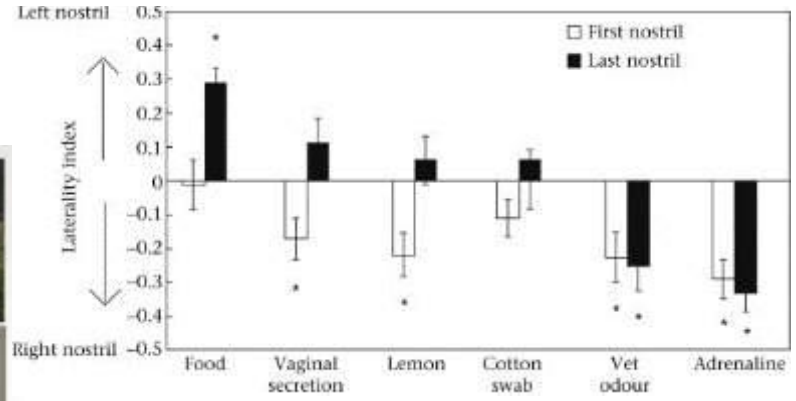


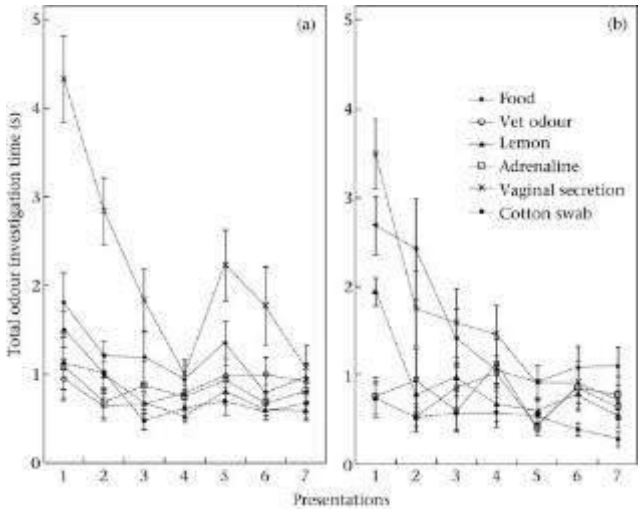
嗅闻动作引发的激活主要发生在颞叶的梨状皮层区域以及额叶的内侧和后部眶额回区域

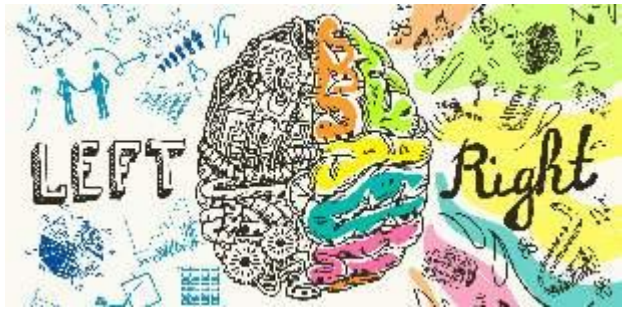
Jia H. *et al., PLoS One.* 2014
Sobel, N.*et al. Nature.* 1998

Lateralization of response to odor stimuli in dogs

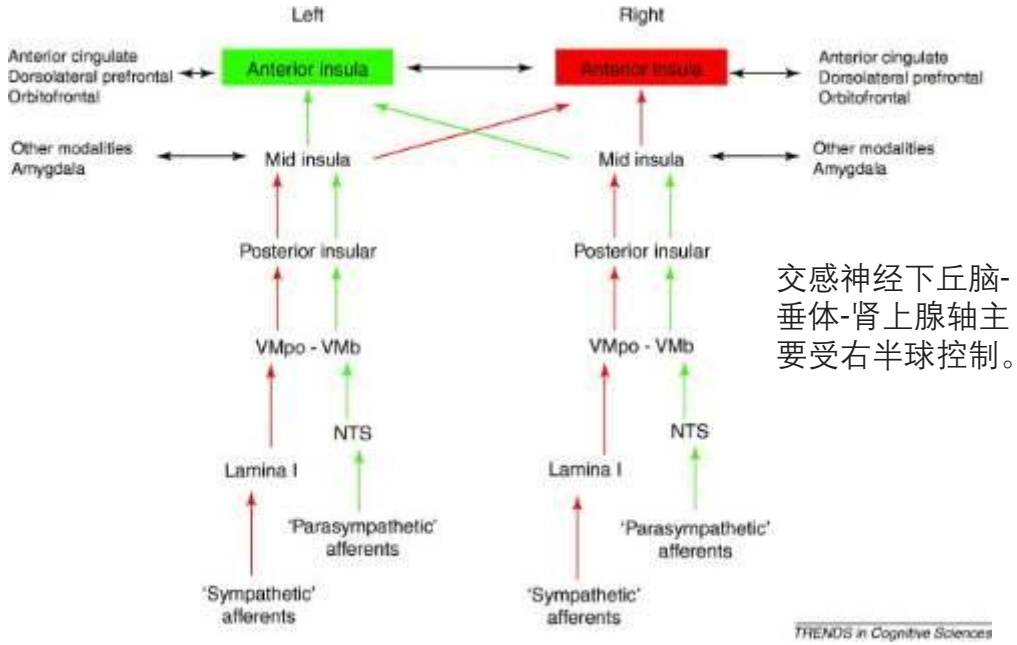








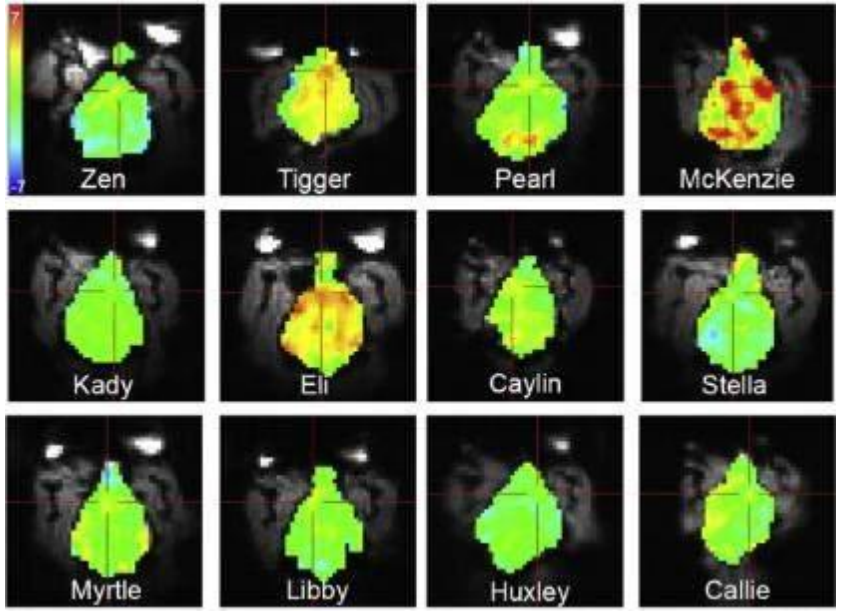
对常规行为的控制　　处理新奇刺激物

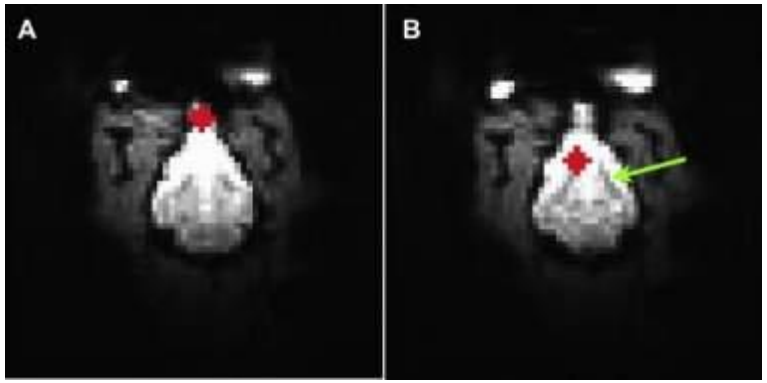


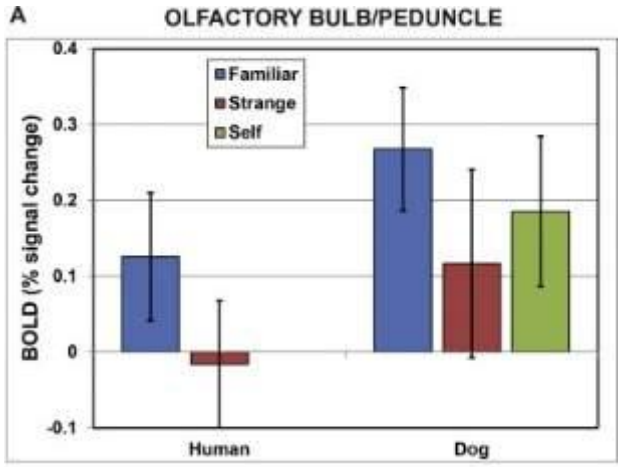
交感神经下丘脑-垂体-肾上腺轴主要受右半球控制。

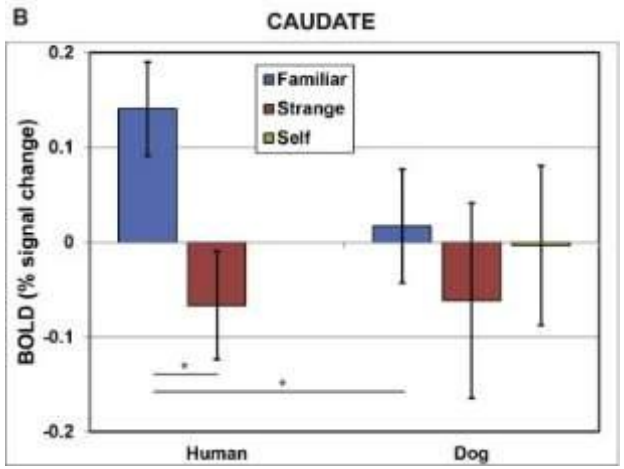
Marcello Siniscalchi. *et al. Animal Behavi*our. 2011
Craig, A.D. *Trends in Cognitive Sciences*. 2005

The maximal activation in the caudate region was triggered by the familiar odor of human



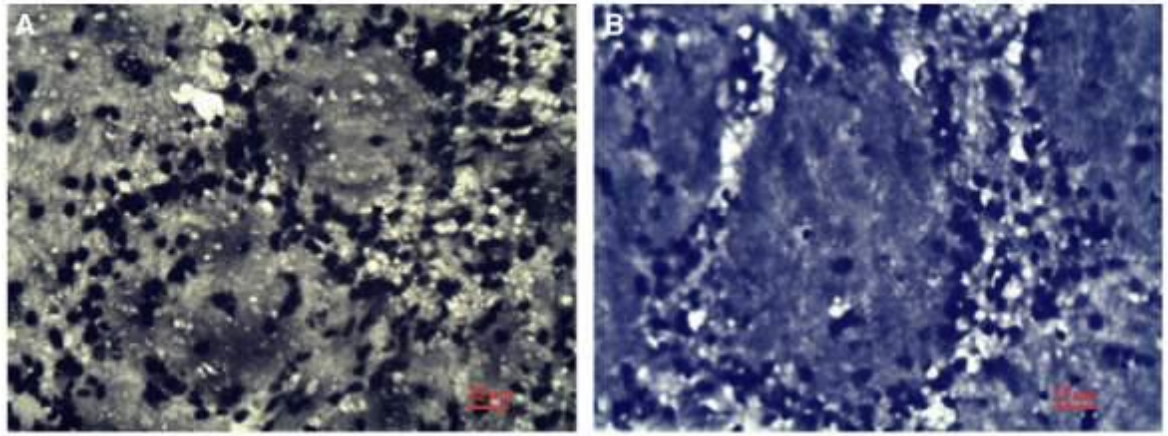






Berns GS., *et al., Behav Processes.* 2015

Cells in the olfactory bulbs of female dogs are more active than those in males



c-fos 是经典的即刻早期基因，编码具有转录因子活性的 c-Fos 蛋白，其表达对神经元活动高度敏感，常被用作“活动依赖性神经元”的标记。

Age and sex Variables	Adult male Number of *c-fos*-positive cells (*N*)	Adult female Number of *c-fos*-positive cells (*N*)	Parameter *P*
GL	3.06 ± 0.15	3.19 ± 0.18	0.766
ML 僧帽细胞	42.89 ± 0.92	57.07 ± 0.49	0.012
GRL	5.32 ± 0.28	5.97 ± 0.30	0.504

N: number of *c-fos*-positive cells per 1000 μm^2 in the GL and GRL and number of *c-fos*-positive cells per visual field in the ML.

Wei, Qinguo., *et al. Acta Zoologica.* 2016

The Use of Canine Olfactory Skills

TECHNICAL NOTES | MAY 01 2003

Cadaver Dog and Handler Team Capabilities in the Recovery of Buried Human Remains in the Southeastern United States

AE Lasseter, BA, KP Jacobi, PhD, R Farley, L Hensel

+ Author & Article Information

J. Forensic Sci. (May 2003) 48 (3): 1–5.
https://doi.org/10.1520/JFS2002296 Article history

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Explosives detection by military working dogs: Olfactory generalization from components to mixtures

Lucia Lazarowski *, David C. Dorman

Department of Molecular and Biomedical Sciences, North Carolina State University, College of Veterinary Medicine, Raleigh, NC, USA

SCIENTIFIC REPORTS
nature research

OPEN

Detection of Impending Aggressive Outbursts in Patients with Psychiatric Disorders: Violence Clues from Dogs

Uriel Bekeman[1,2], Hodaya Eilam[2,3], Clara Moray Schild[4], Dan Grinstein[5], Yuval Eshed[6], Morris Laster[7], Ester Fride[5] & Sharon Anavi-Goffer[1,2*]

Forensic Science International: Synergy

Preliminary accuracy of COVID-19 odor detection by canines and HS-SPME-GC-MS using exhaled breath samples

Julian Mendel[1,2,3], Kelvin Franck[1,3], Lourdes Edlin[4], Kelley Hall[4], Denise Webb[4], John Mills[4], Howard K. Holness[1,3], Kenneth G. Furton[1,3,*], DeEtta Mills[1,3,*]

Why do dogs' eyes glow in the dark?

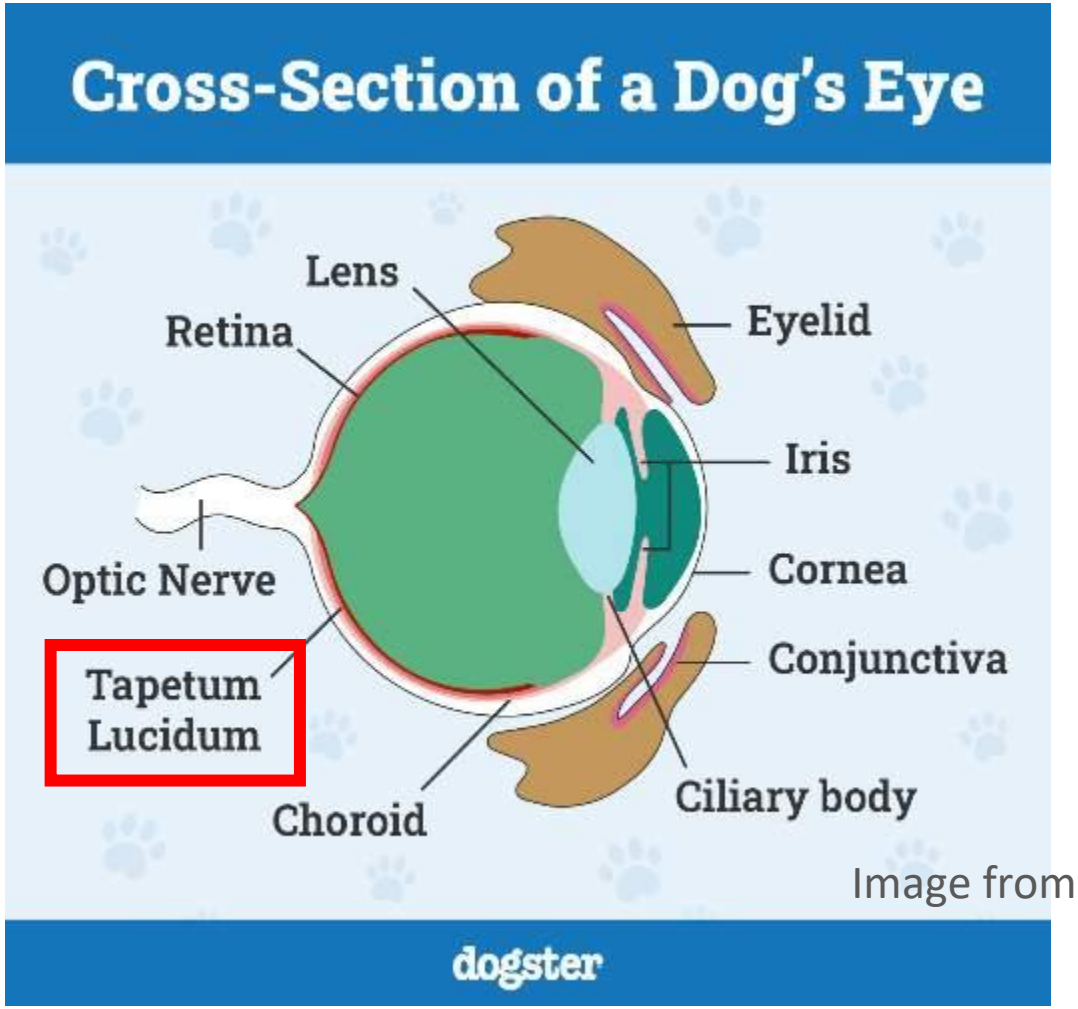
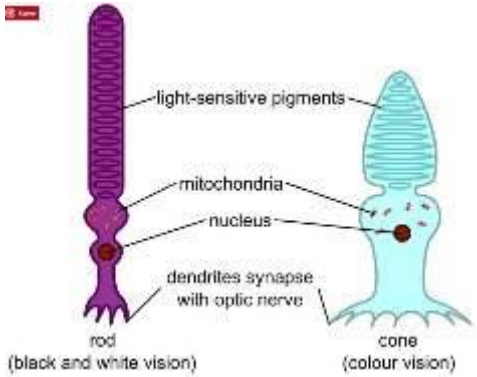
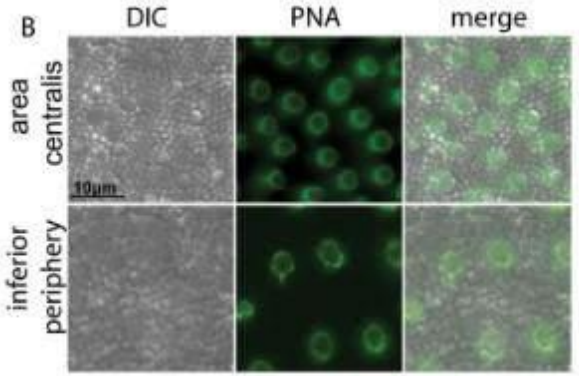


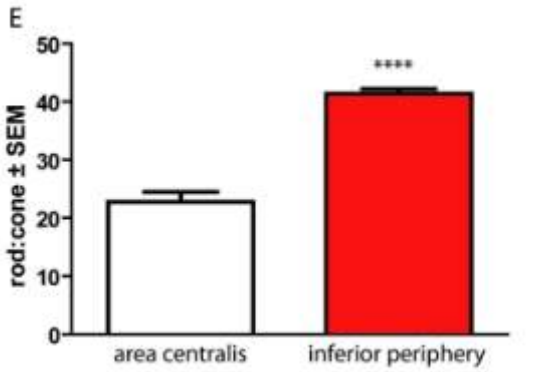
Image from Dogster

The tapetum lucidum enhances the vision of dogs in the dark

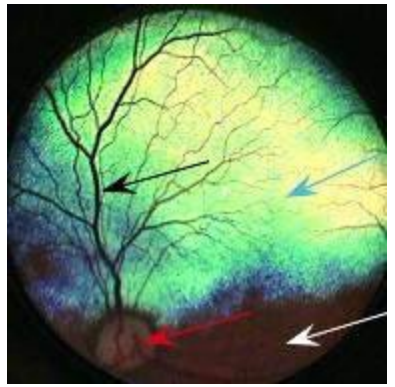
The high proportion of rod cells in the retina enables dogs to have better vision in the dark







视杆远多于视锥（典型"夜行捕食者"型）

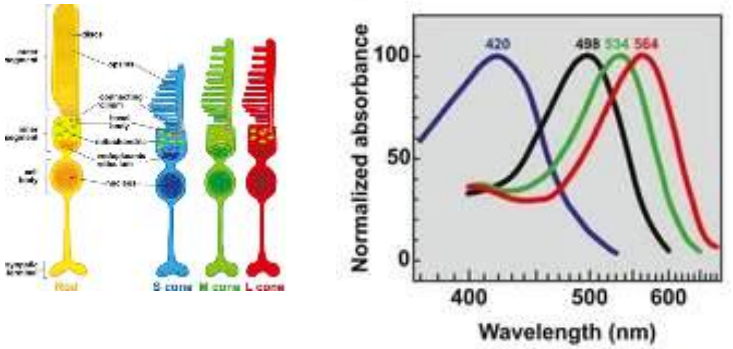


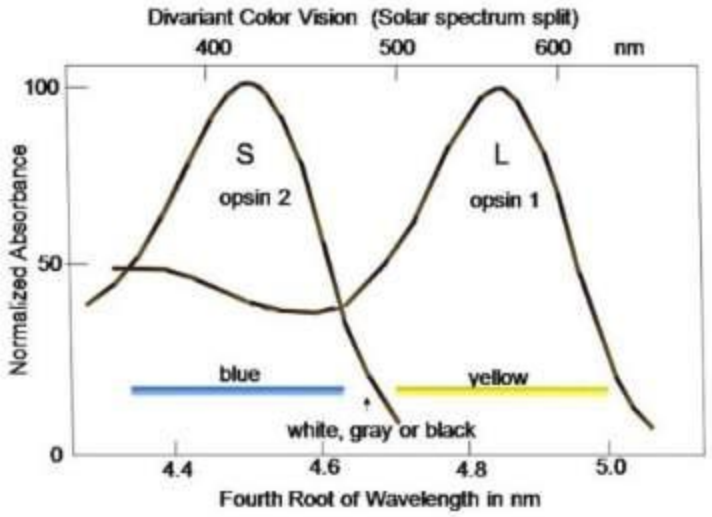
Mowat FM. *et al. Mol Vis.* 2008

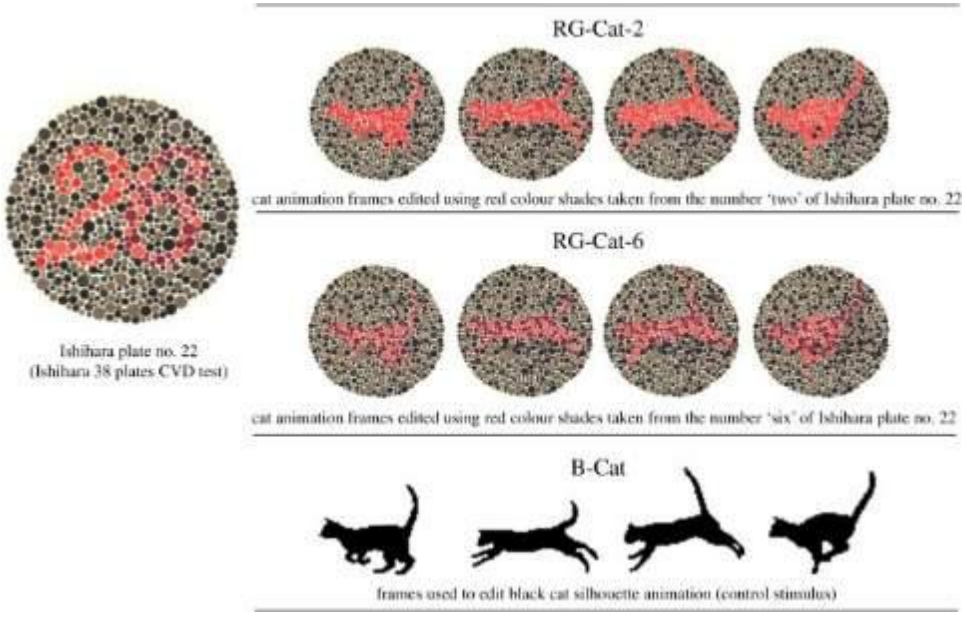

SPWY2

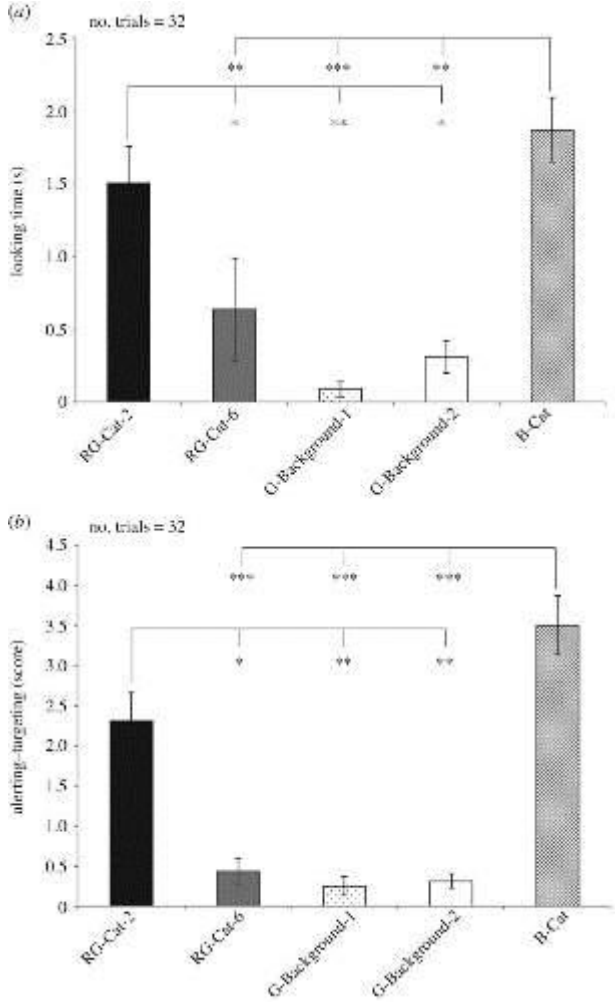

Are dogs color blind?
A dog's view
A human's view
petMD
by chewy

Dogs have dichromatic color vision









•短波锥（**S-cone**）：峰值大约 429–435 nm（蓝紫）
•中长波锥（**L/M-cone**）占多数：峰值大约 555 nm（黄绿）

Hussey KA, , *et al. Front Cell Dev Biol. 2022*
Erica Rydhed. 2014
Siniscalchi M, *et al. R Soc Open Sci. 2017*

Conclusions

- Canine model research mainly focuses on canine evolution, human-canine interaction, and human-related diseases.
- Dogs possess a wide range of olfactory receptors and complex olfactory neural circuits, enabling highly sensitive odor detection.
- Dogs have dichromatic vision, and tapetum lucidum together with well-developed rod cells enhances their ability to see under low-light conditions.

SOCIAL EVOLUTION

Oxytocin-gaze positive loop and the coevolution of human-dog bonds

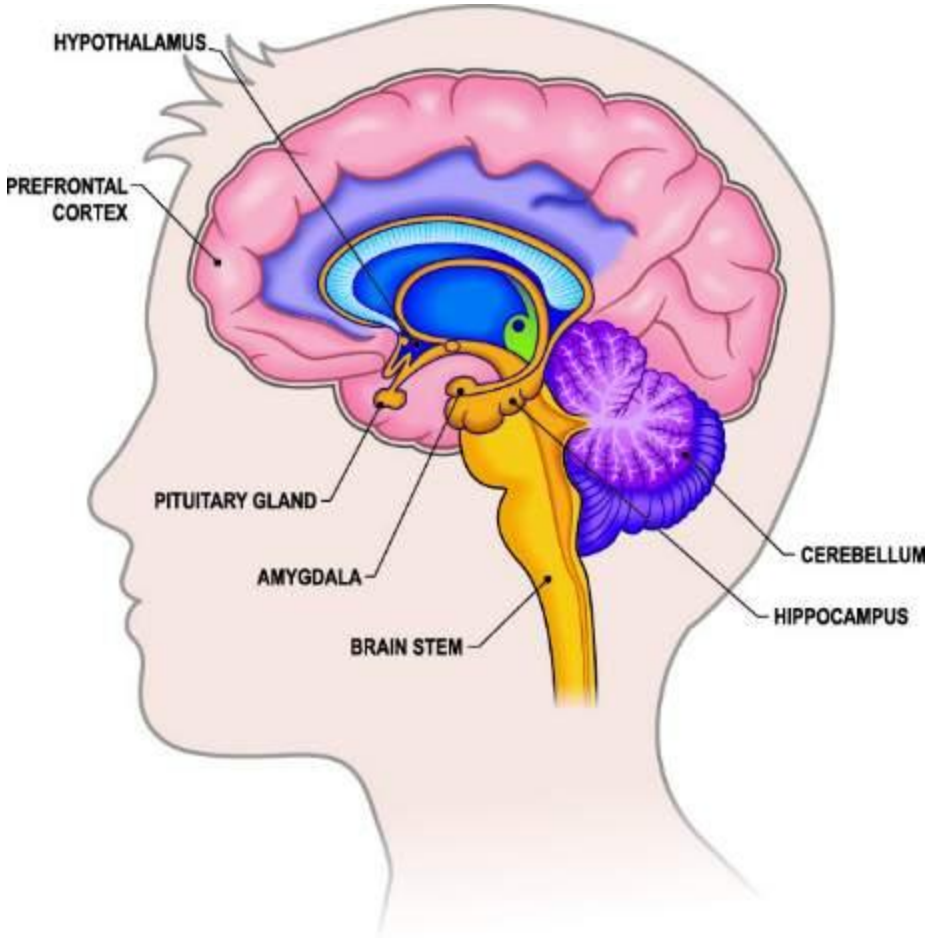
Miho Nagasawa,[1,2] Shouhei Mitsui,[1] Shiori En,[1] Nobuyo Ohtani,[1] Mitsuaki Ohta,[1] Yasuo Sakuma,[3] Tatsushi Onaka,[2] Kazutaka Mogi,[1] Takefumi Kikusui[1]*

PART 2:

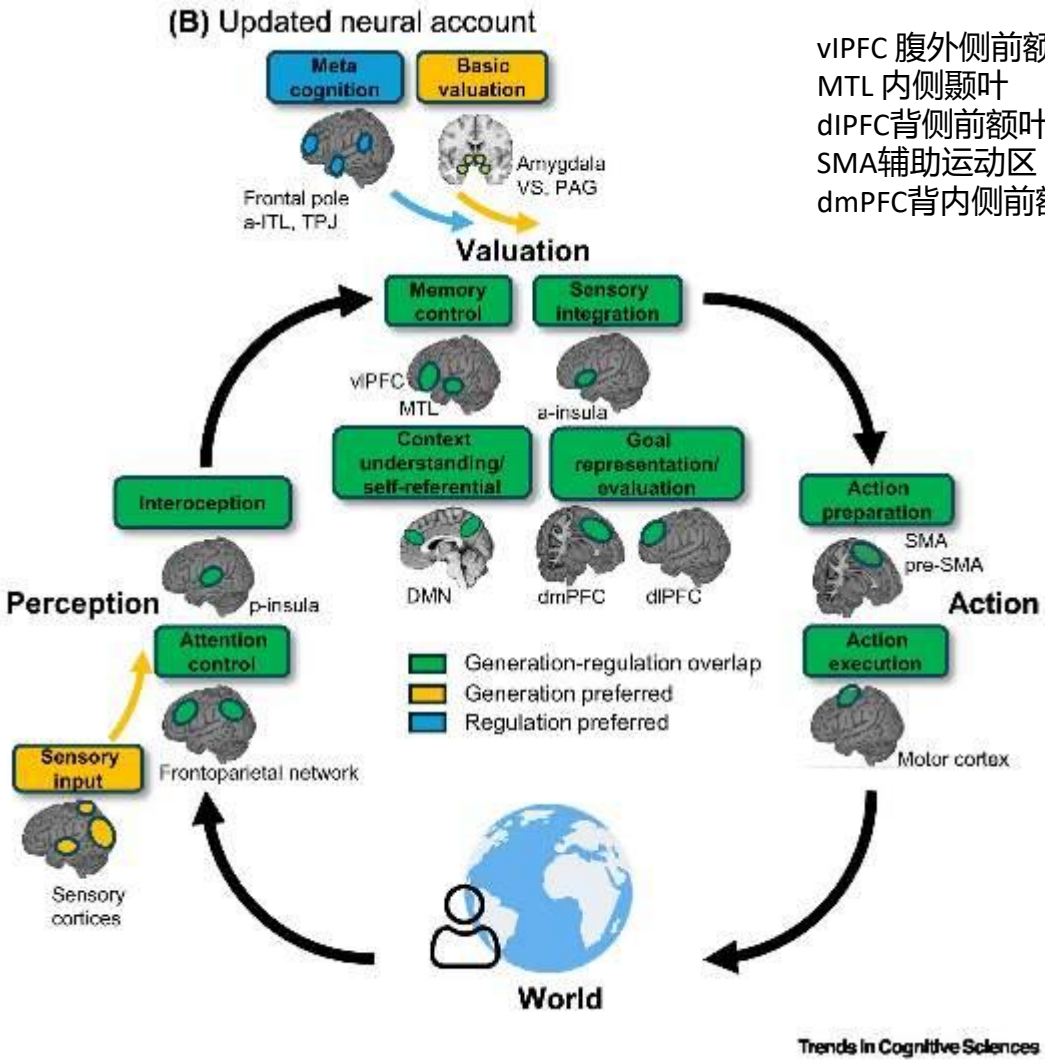
Behavioral and Emotional Research in Canine Models

WJ

How do emotions process?



The limbic system



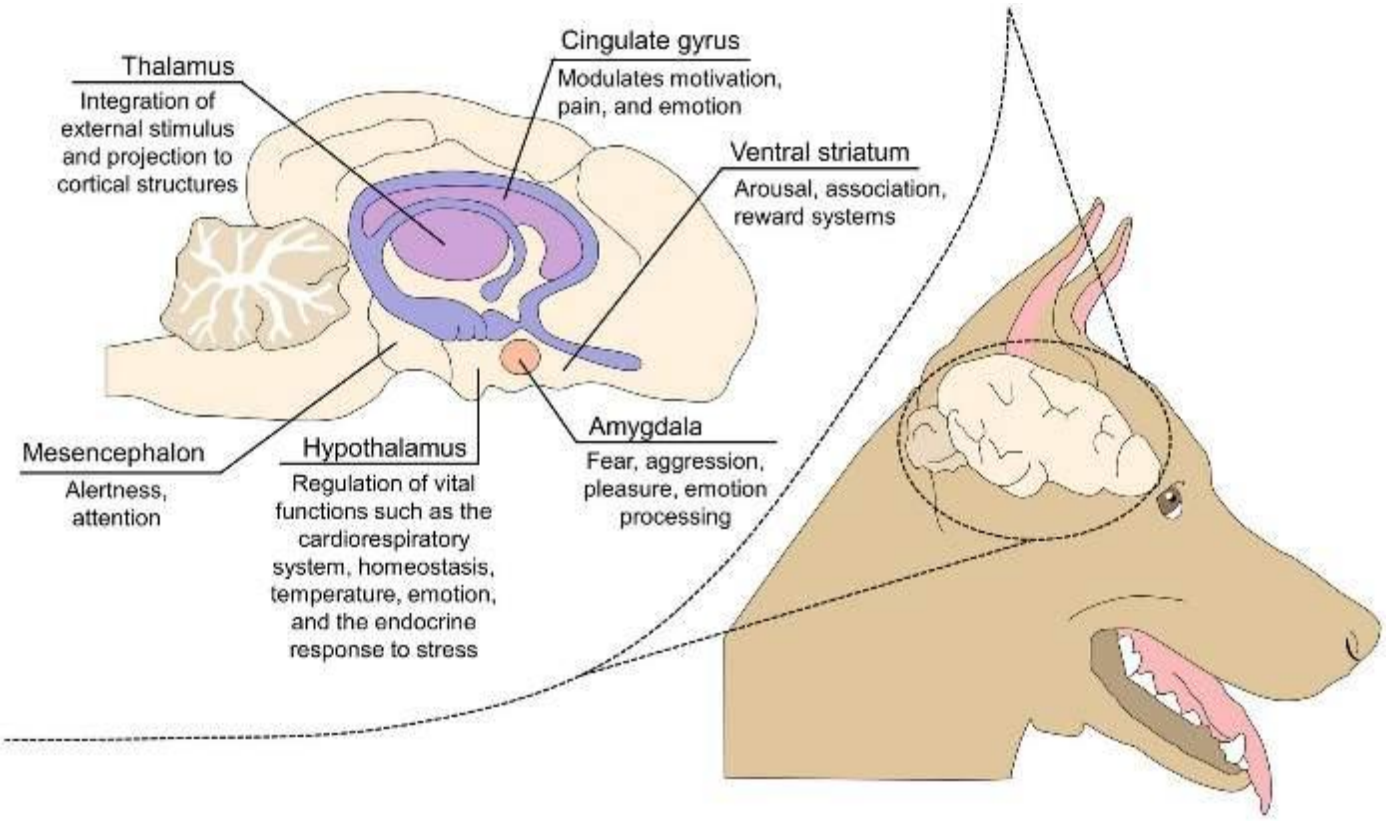
vIPFC 腹外侧前额叶皮层
MTL 内侧颞叶
dIPFC背侧前额叶皮层
SMA辅助运动区
dmPFC背内侧前额叶皮层

人类大脑情绪处理网络

Zhang JX, et al. Trends Cogn Sci. 2025 .

Do Dogs Have Feelings?

Do Dogs Have Feelings?



犬类中参与行为表现和情绪处理发展的边缘系统主要结构

angry

fear

happy

“guilty”（fear）

Mota-Rojas D,et al. Front Vet Sci. 2025.

Canine fear and aggression

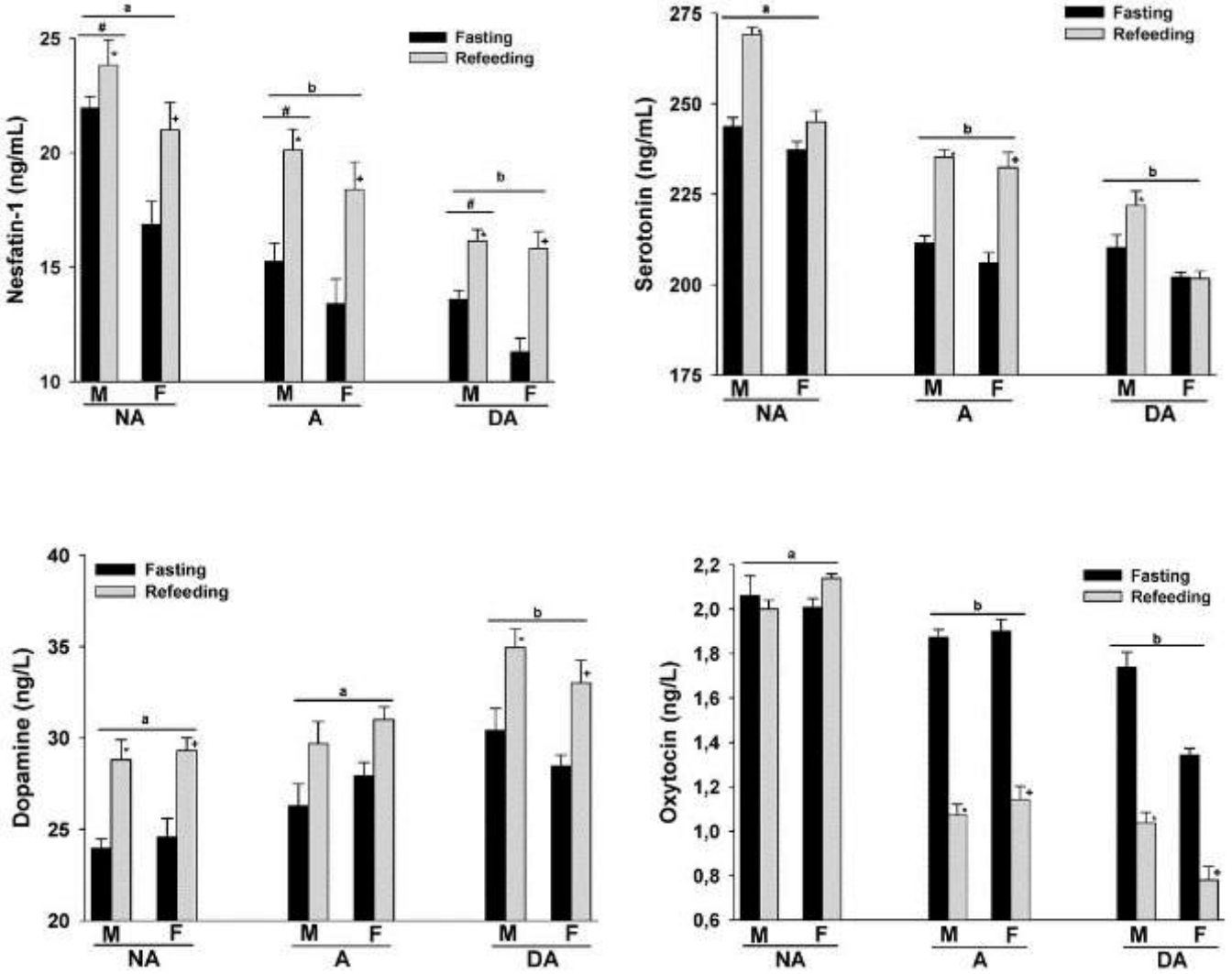
遗传

狩猎本能

恐惧

Aggression

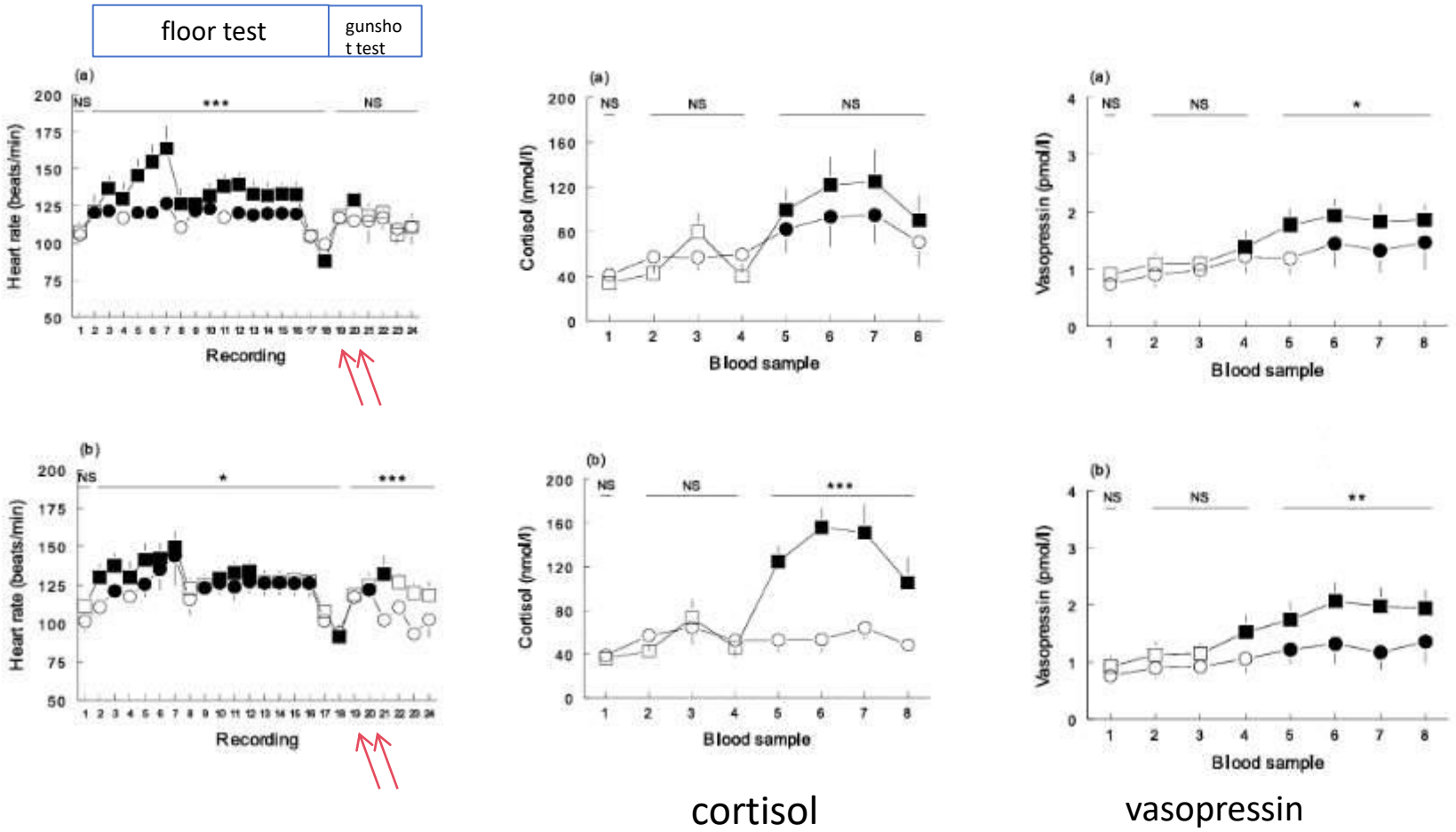
缺乏早期社会化



攻击行为与中枢神经系统内神经肽的复杂相互作用有关

Guvenc-Bayram G, et al. Animals (Basel). 2024 .

Canine fear and aggression



cortisol

vasopressin

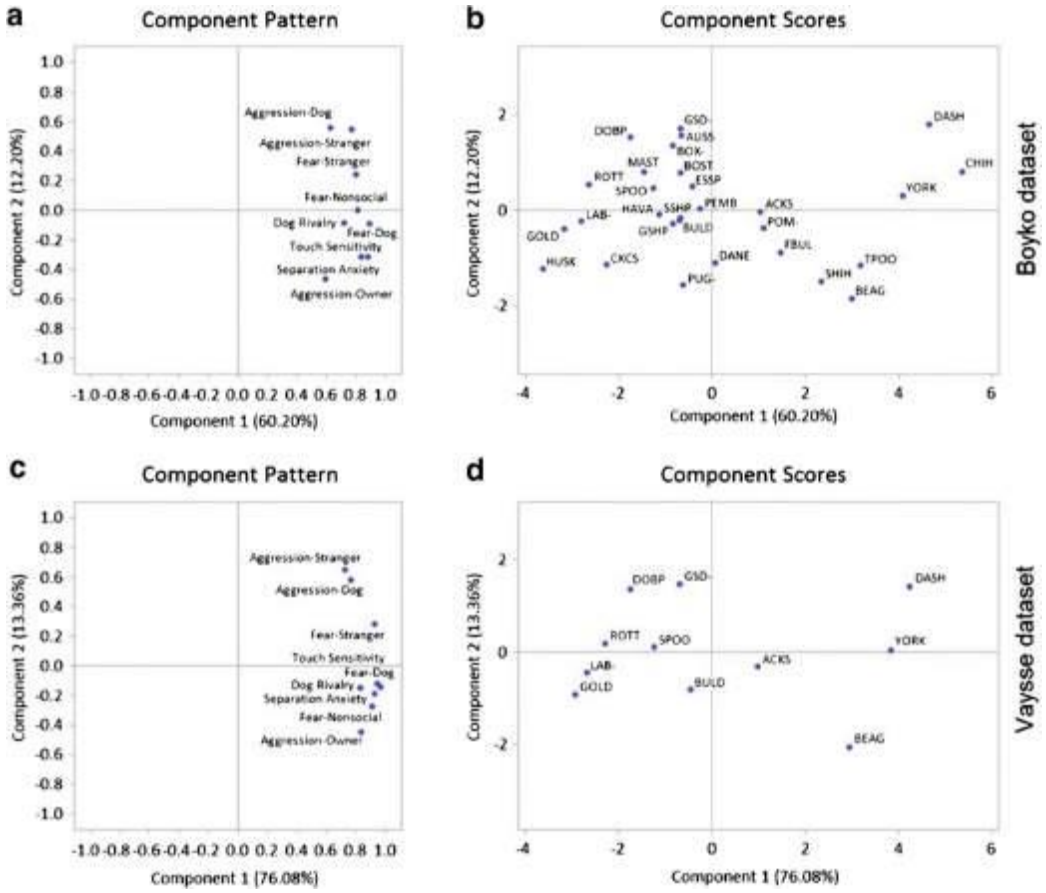
fearful or fearless of floors

fearful or fearless of gunshot

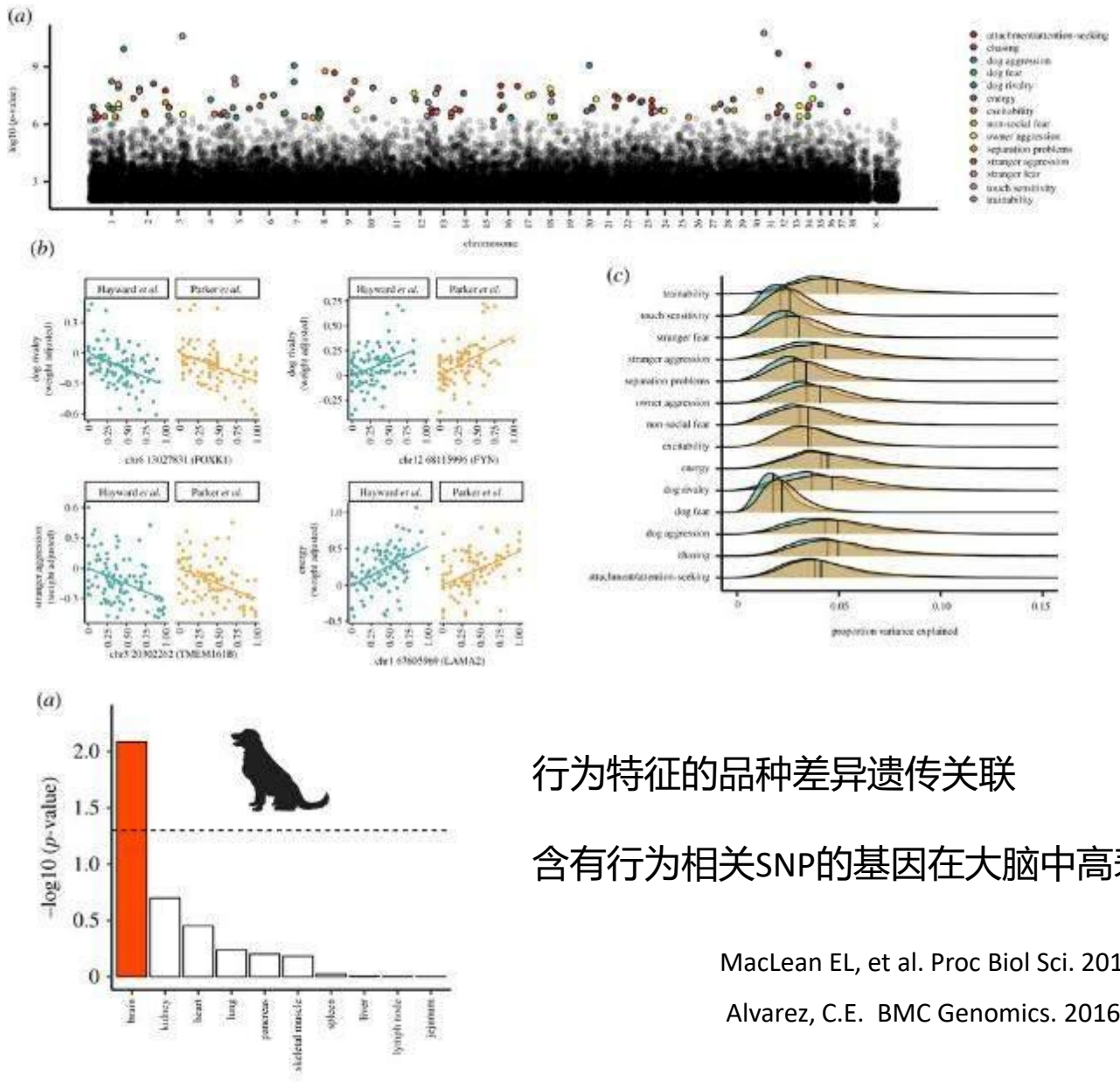
恐惧是由于个体面临的严重压力，可通过生理变量进行监测。
不同的恐惧源，生理应激影响不同

Hydbring-Sandberg E, et al. J Endocrinol. 2004.

Canine fear and aggression



恐惧和攻击性具有遗传关联



行为特征的品种差异遗传关联

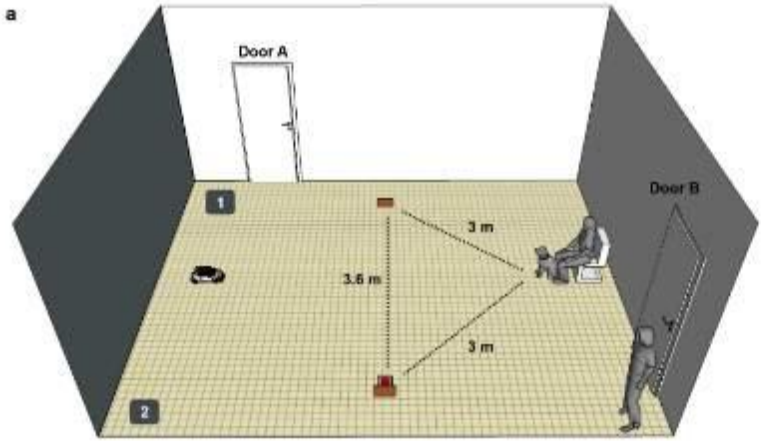
含有行为相关SNP的基因在大脑中高表达

MacLean EL, et al. Proc Biol Sci. 2019 .

Alvarez, C.E. BMC Genomics. 2016.

Jealousy in Dogs

a



b

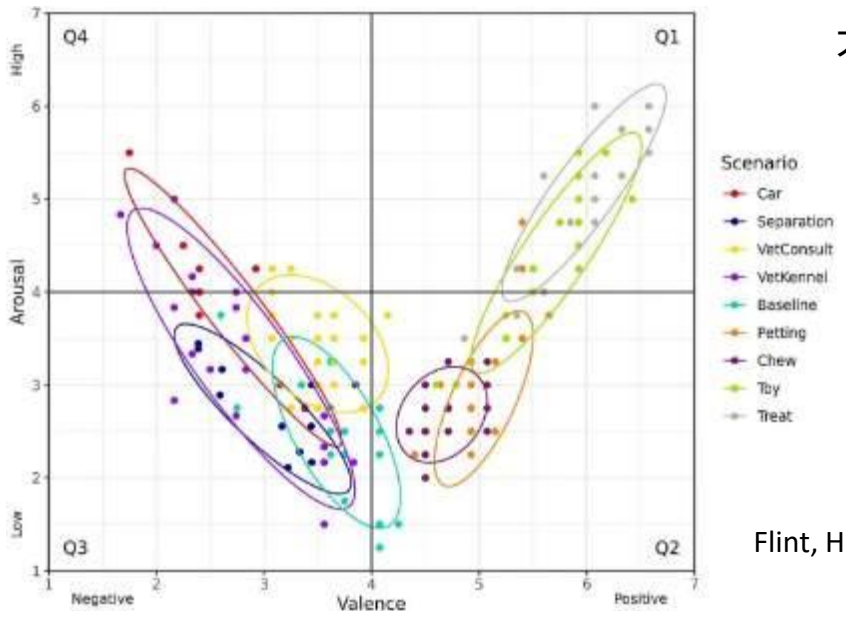
(1) draw the partner's attention toward themselves
(2) disrupt the interaction between the rival and the partner
(3) aim to remove the rival

社交性越强的竞争对手（同屋犬只 > UMO > 杂志），越能触发犬的嫉妒行为

	Dog vs. reading	Dog vs. UMO	UMO vs. reading
Owner-related behaviours (no difference between groups)	Dog > reading	ns	ns
Test partner-related behaviours (no difference between groups)	Dog > Reading	Dog < UMO	UMO > Reading
Interaction-related behaviours (no difference between groups)	ns	ns	ns
Frequency of interruption—Interactive UMO	Dog > Reading	ns	ns
Frequency of interruption—Non-interactive and Mechanistic UMO	Dog > Reading	Dog > UMO	ns
Frequency of snapping at the test partner (no difference between groups)	Dog > Reading	Dog > UMO	UMO > Reading
Frequency of vocalization (no difference between groups)	Dog > Reading	ns	ns

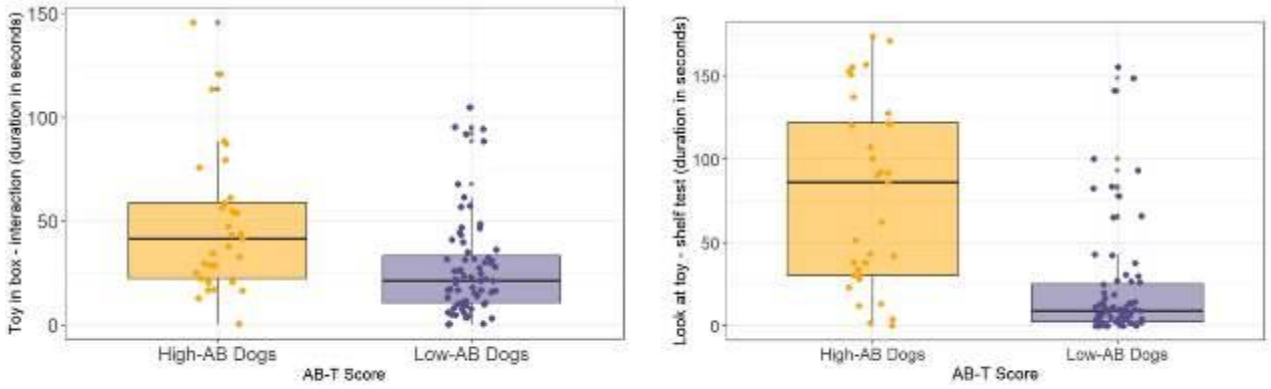
Abdai, J. et al. Sci Rep ,2025.

Positive emotion and play behavior in Dogs



犬对不同情境的反应

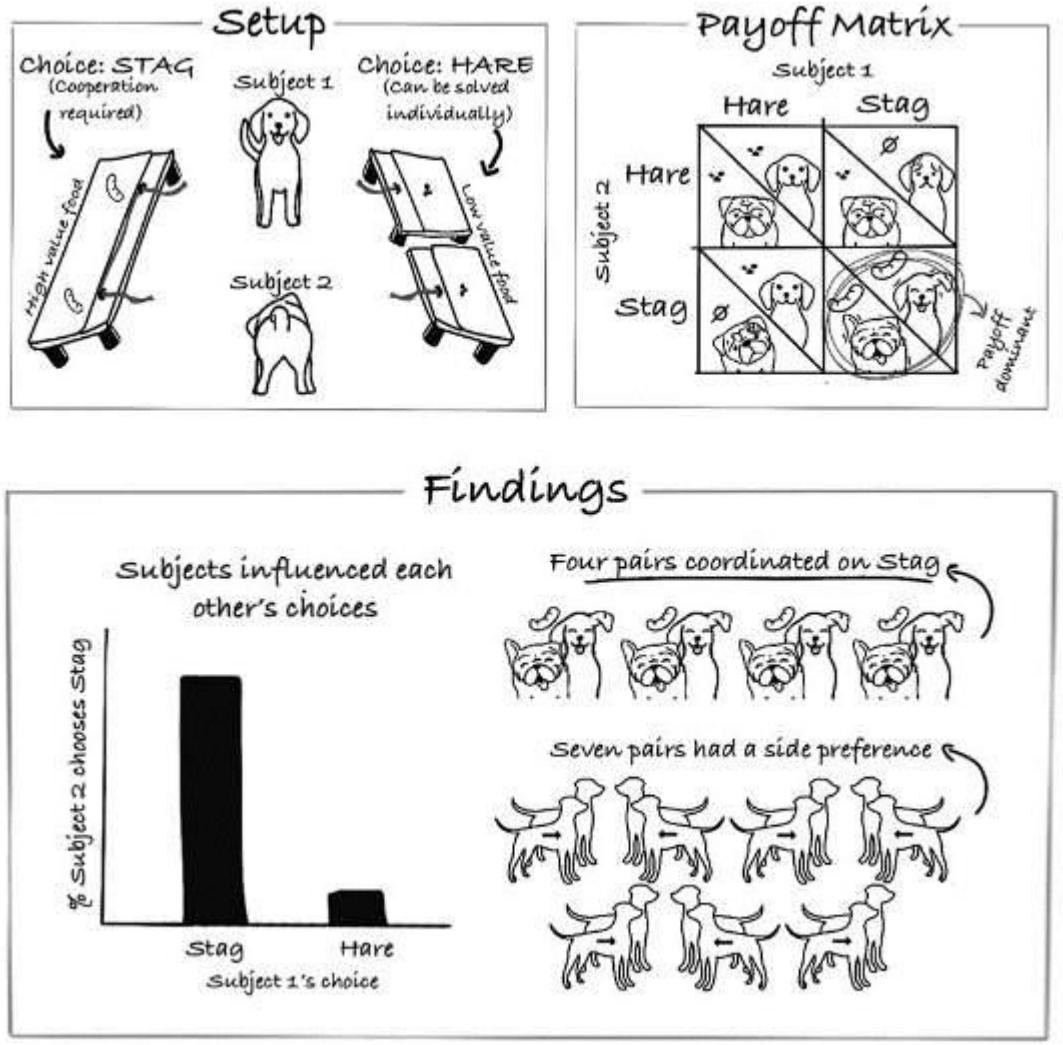
Flint, H.E. et al.Sci Rep. 2024.



(e) (f)

爱玩的狗会表现出一定的类成瘾行为（Addictive-like behaviour）

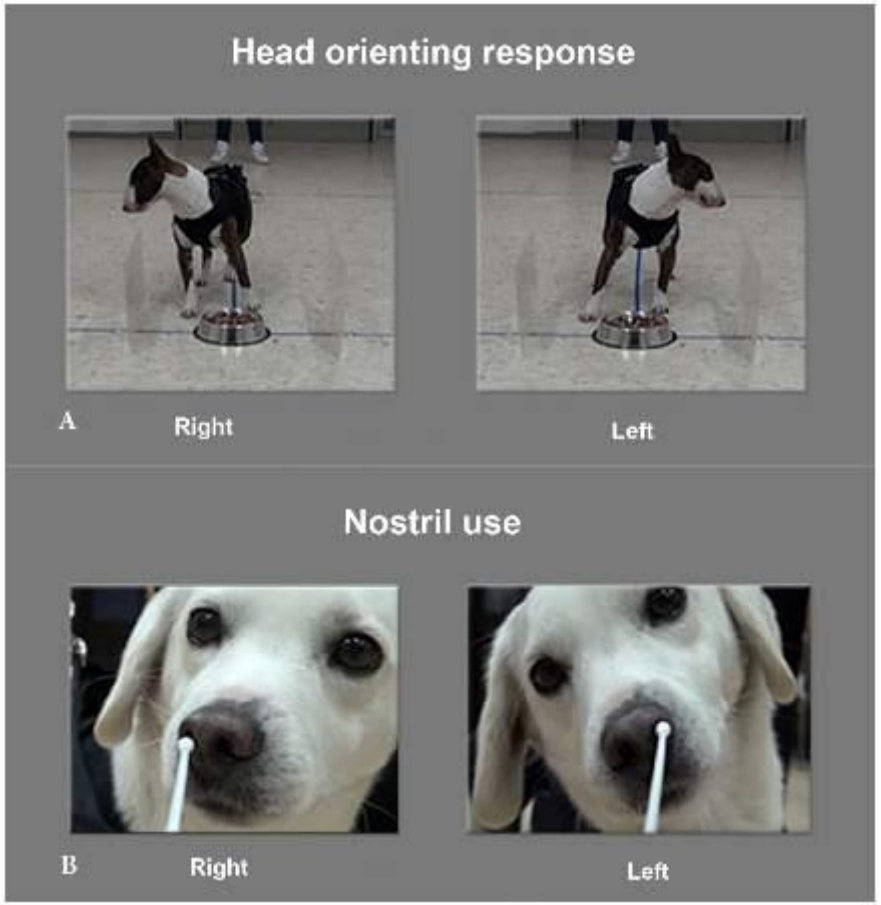
Mazzini, A. et al. Sci Rep .2025.



某些犬类能在保证博弈中识别收益占优的结果

Martínez M. et al. iScience. 2023.

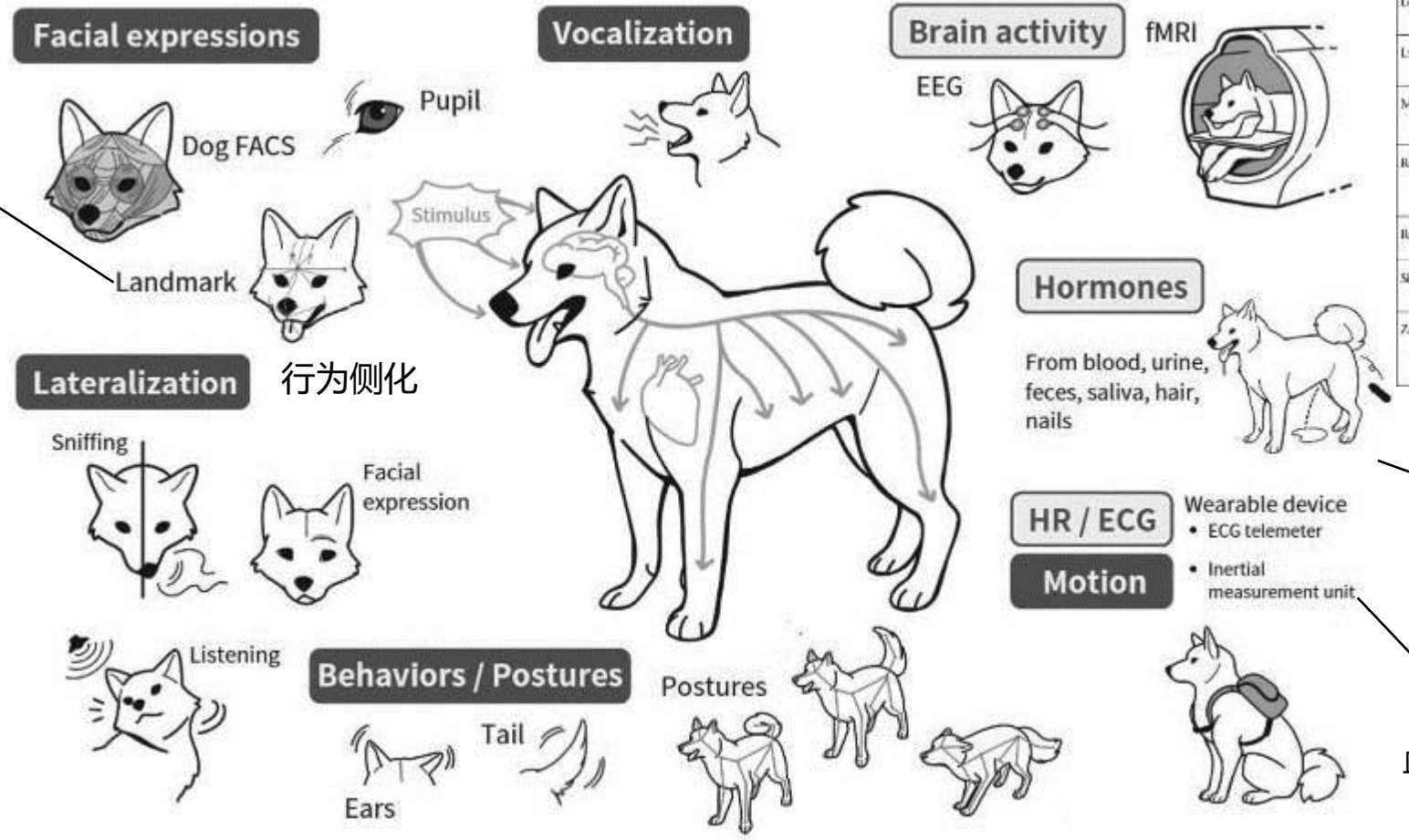
How do Dogs feel Humans emotions and response?

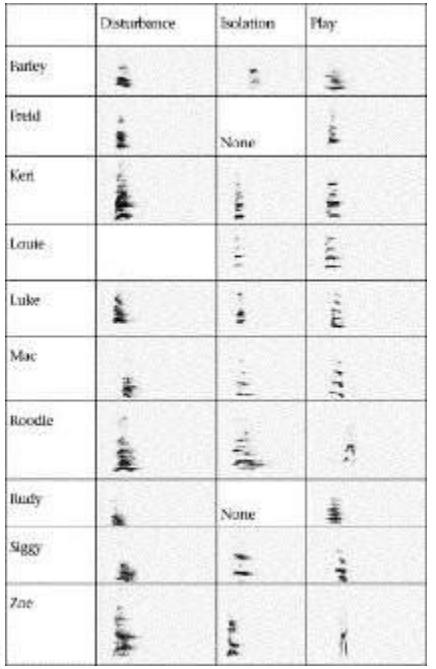


- Visual perception of emotion cues in dogs
- Auditory senses in dogs’ recognition of human emotions
- Olfaction in the perception of emotion in dogs

How to measure emotion of dogs

行为指标





	Disturbance	Isolation	Play
Farley			
Freid		None	
Keri			
Louie			
Luke			
Mac			
Roodle			
Rudy		None	
Siggy			
Zoe			

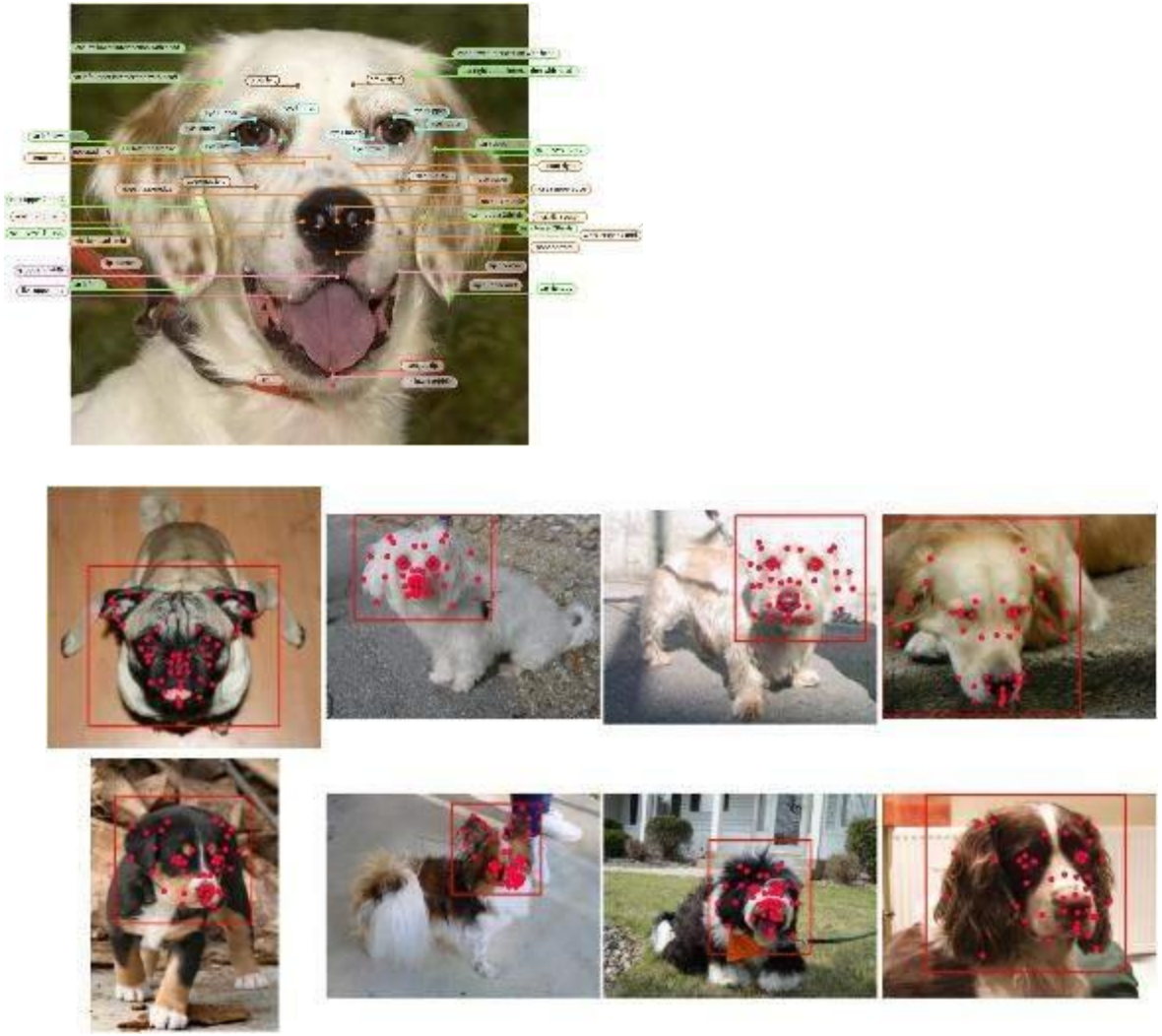
- 皮质醇
- 催产素

血压、心率和体温等

生理指标

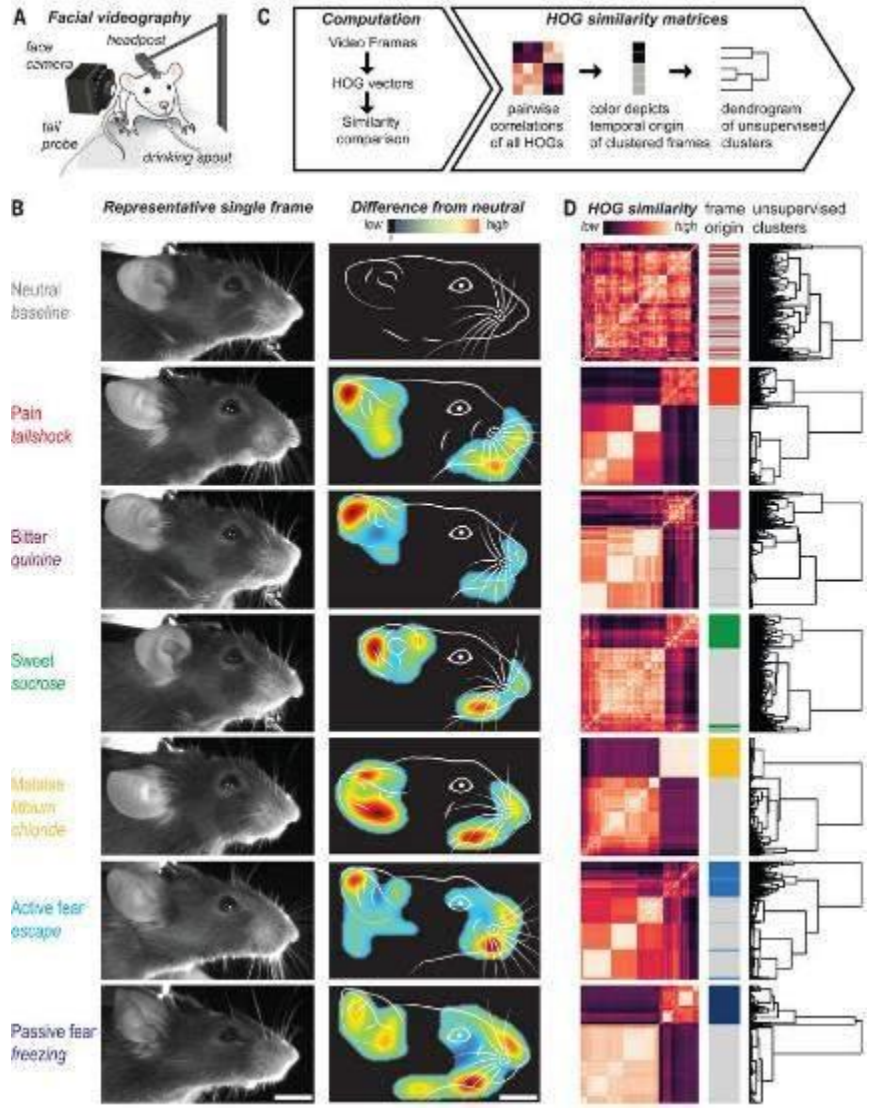
Koyasu, H. et al. Advanced Robotics. 2024.

Sophia Yin. Animal Behaviour. 2004.



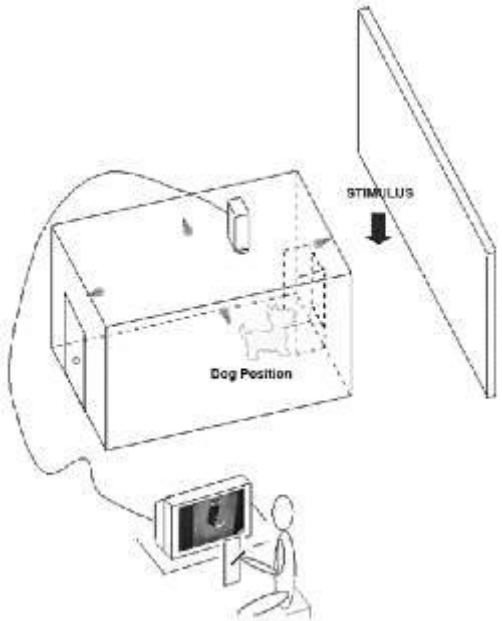
facial expressions in dogs

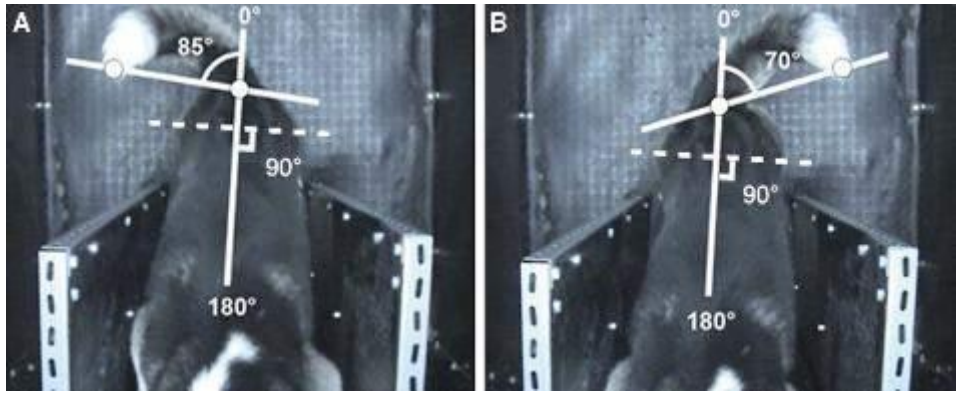
Martvel, G. et al. Sci Rep. 2025.

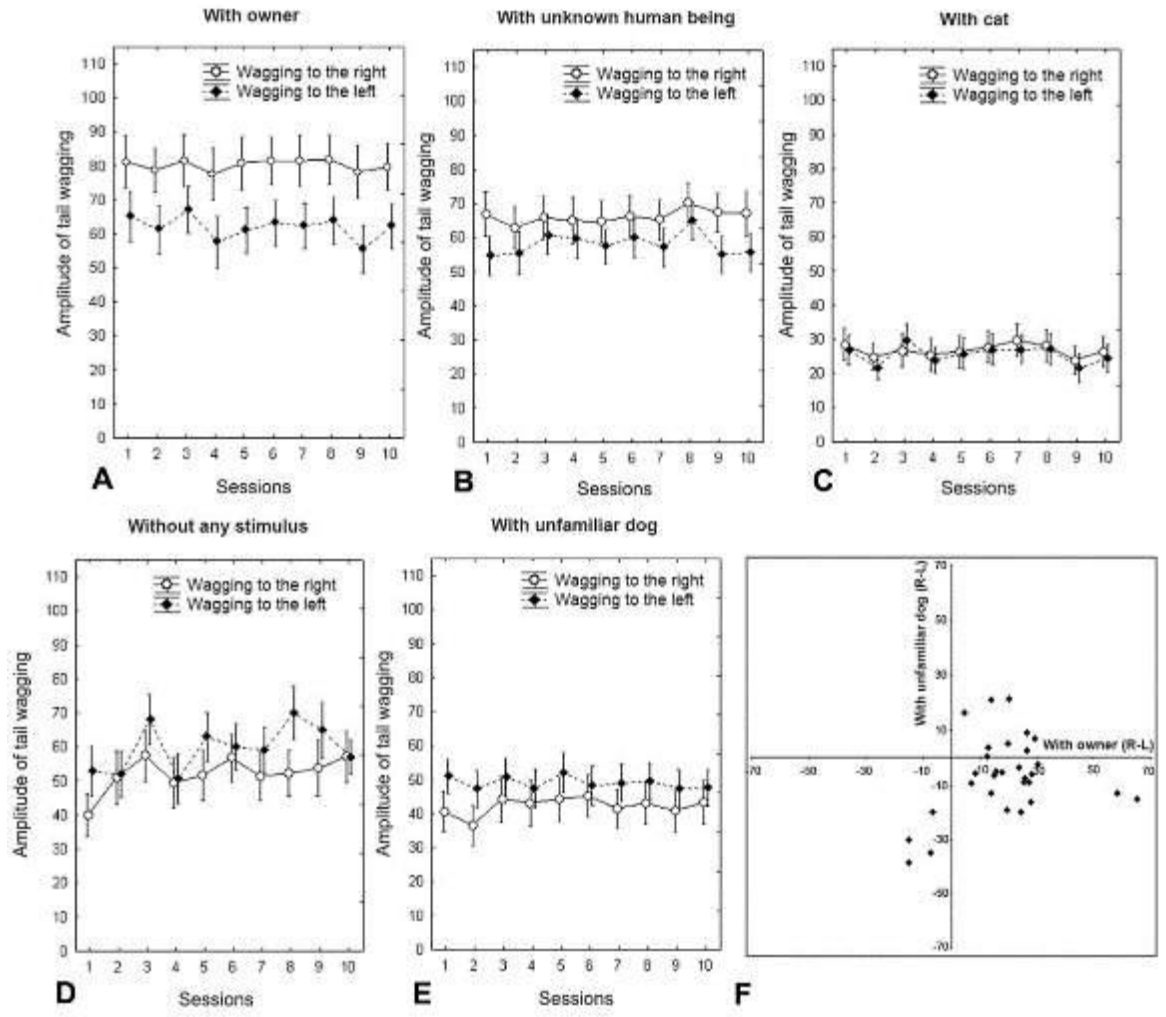


facial expressions in mice

Nate Dolensek et al. Science. 2020.





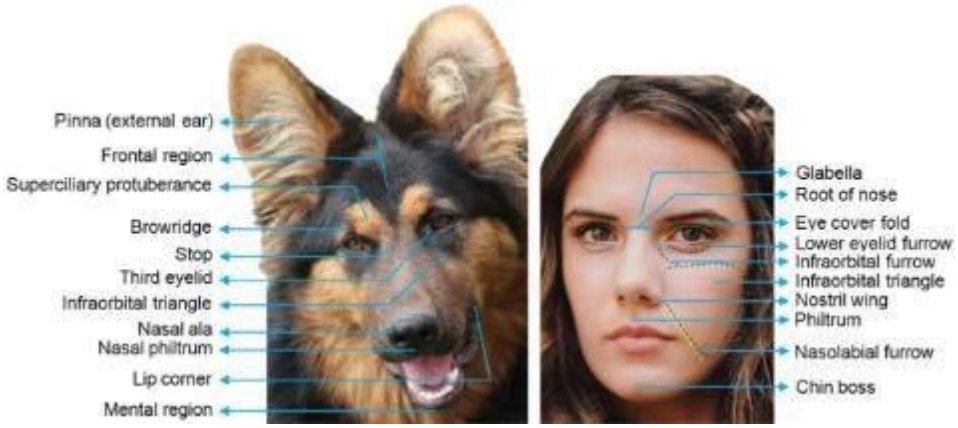


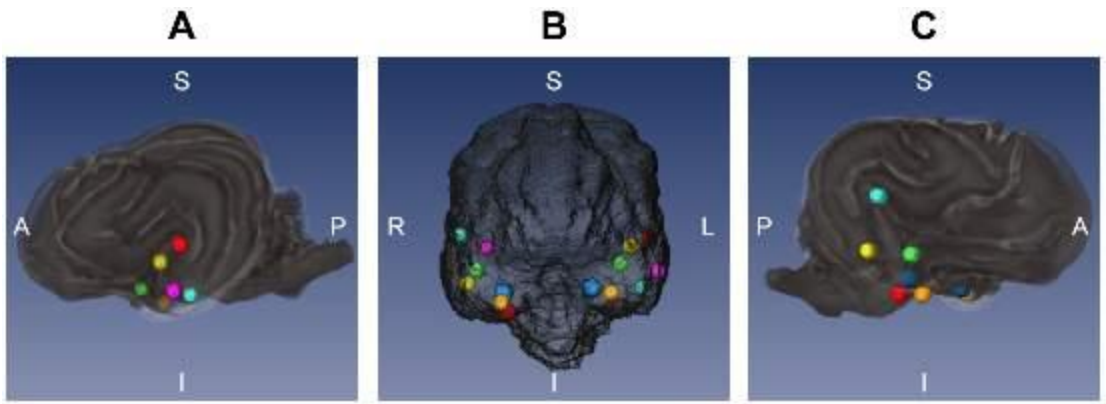
当狗看情绪价值为正的刺激（例如主人）时，摇尾幅度向右偏高。另一方面，在出现负面情绪刺激（如表现出明显激动行为的陌生犬）时，尾巴摆动出现左侧偏向。

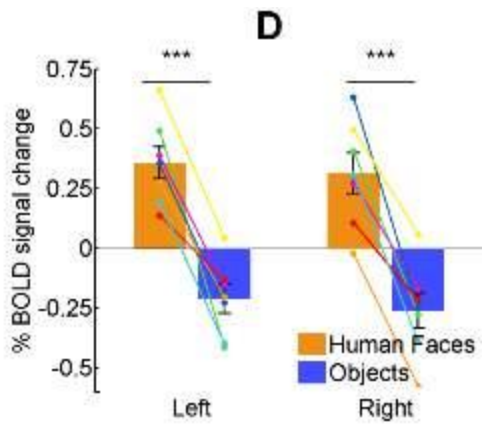
Quaranta A. et al. Curr Biol. 2007.

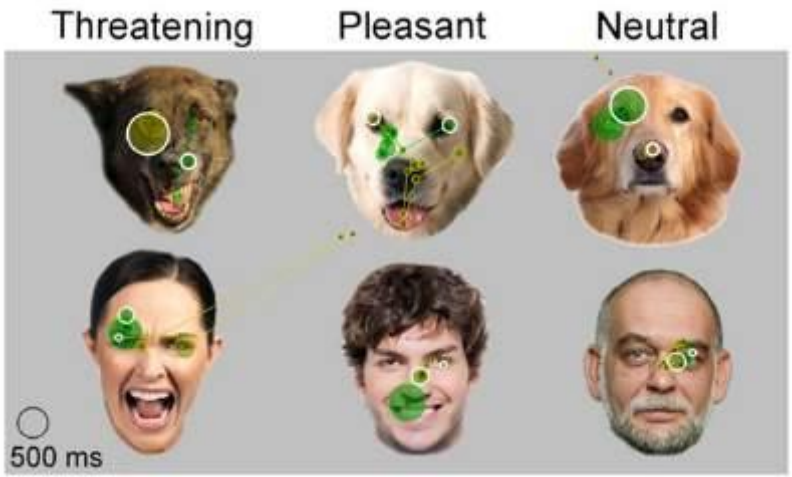
Visual perception of emotion cues in dogs

面部情绪识别（FaBER）机制







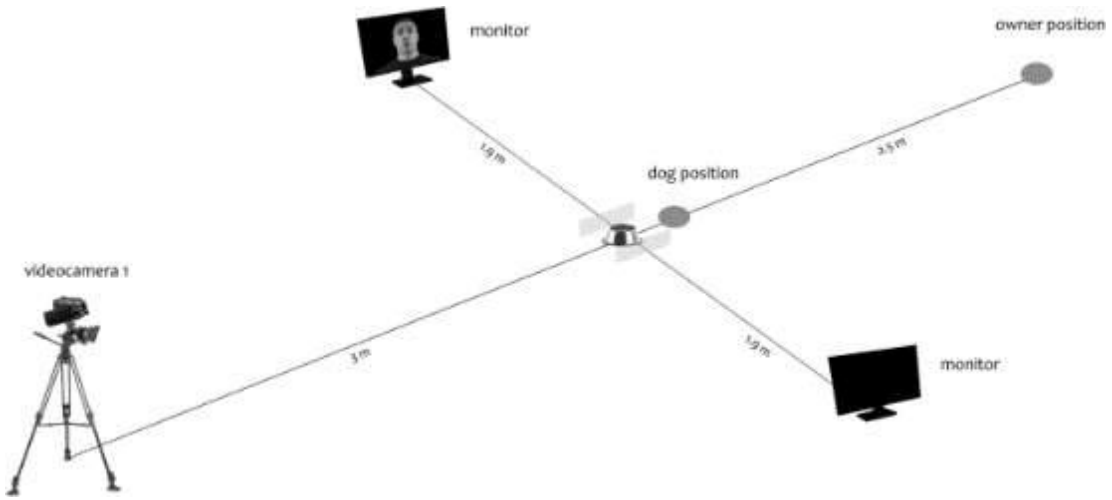


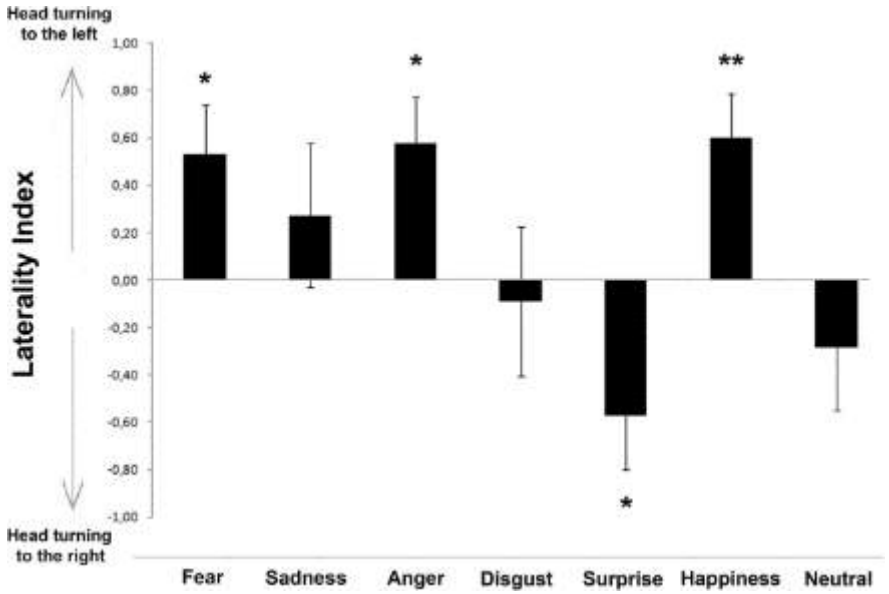
狗的大脑颞叶皮层具有一个可区分面部的处理区域

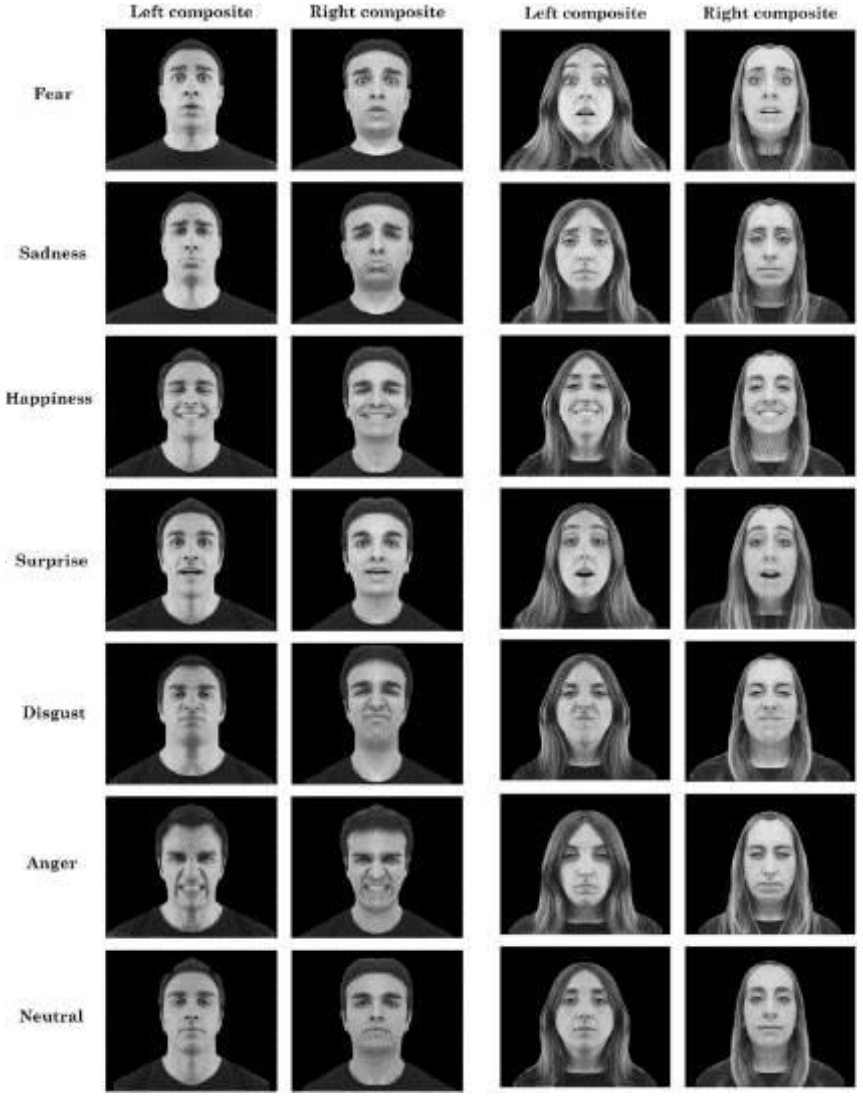
Cuaya LV. et al. PLoS One. 2016.

Thompkins AM. et al. Learn Behav. 2018 .

Visual perception of emotion cues in dogs



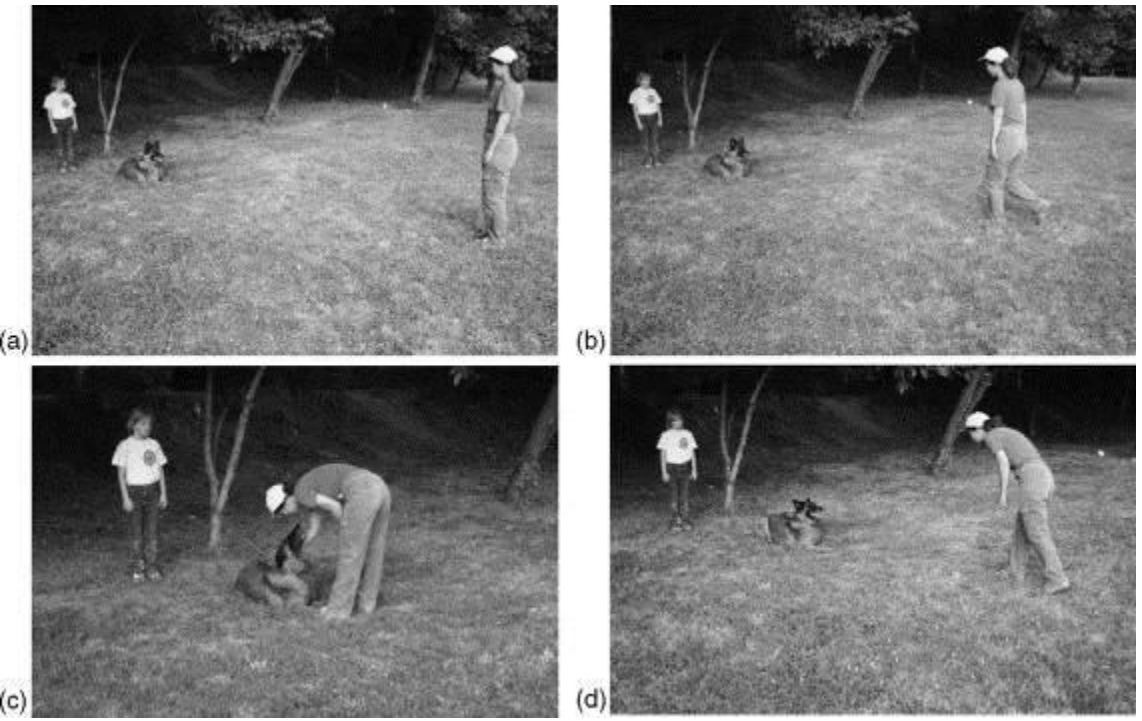




左侧转头反应表明在处理这些情绪刺激时，右半球表现出主导活动。右半球在愤怒和恐惧刺激的视觉分析中普遍激活

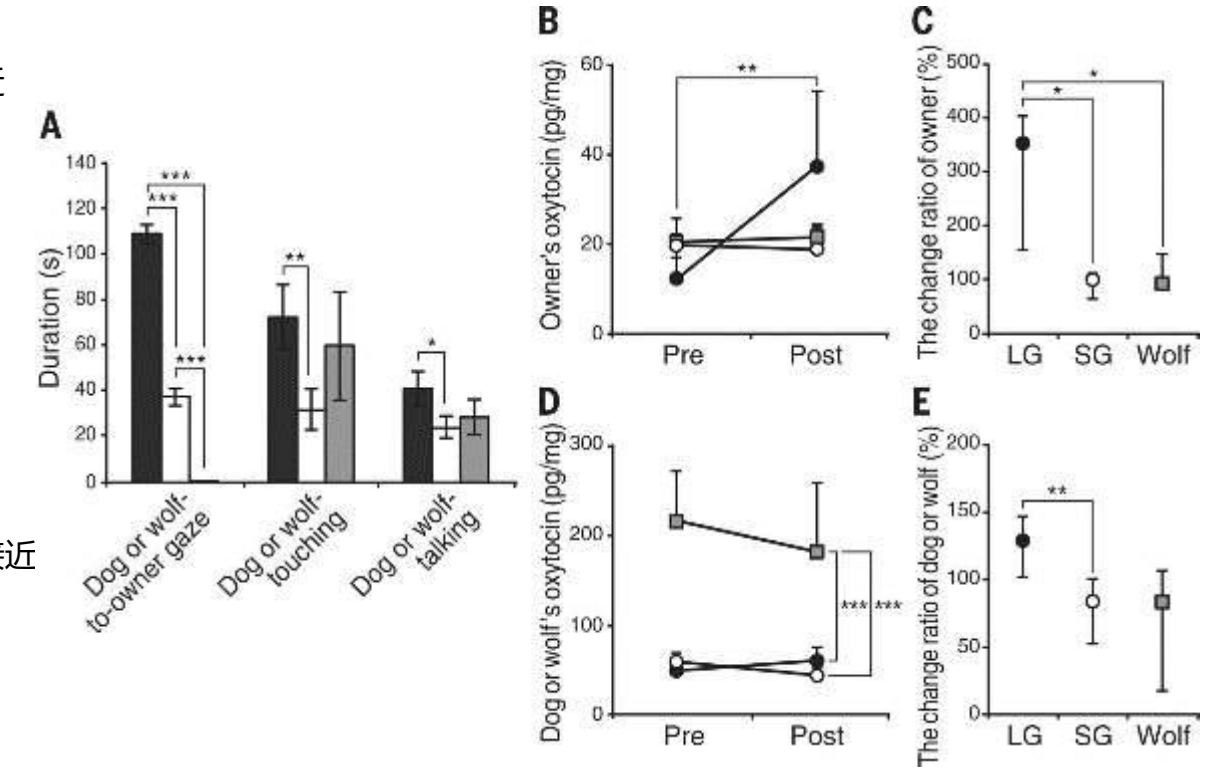
Siniscalchi M. et al. Learn Behav. 2018.

Visual perception of emotion cues in dogs



友好接近

威胁性接近

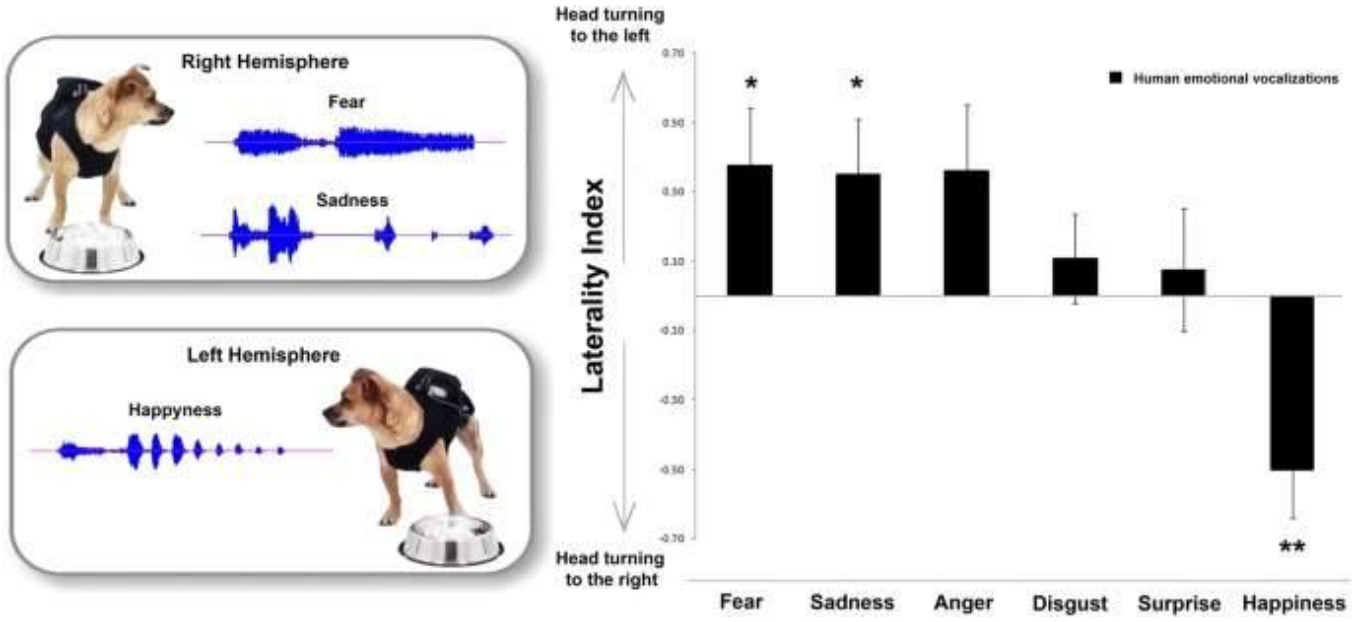


gaze， body position, gestures, head orientation

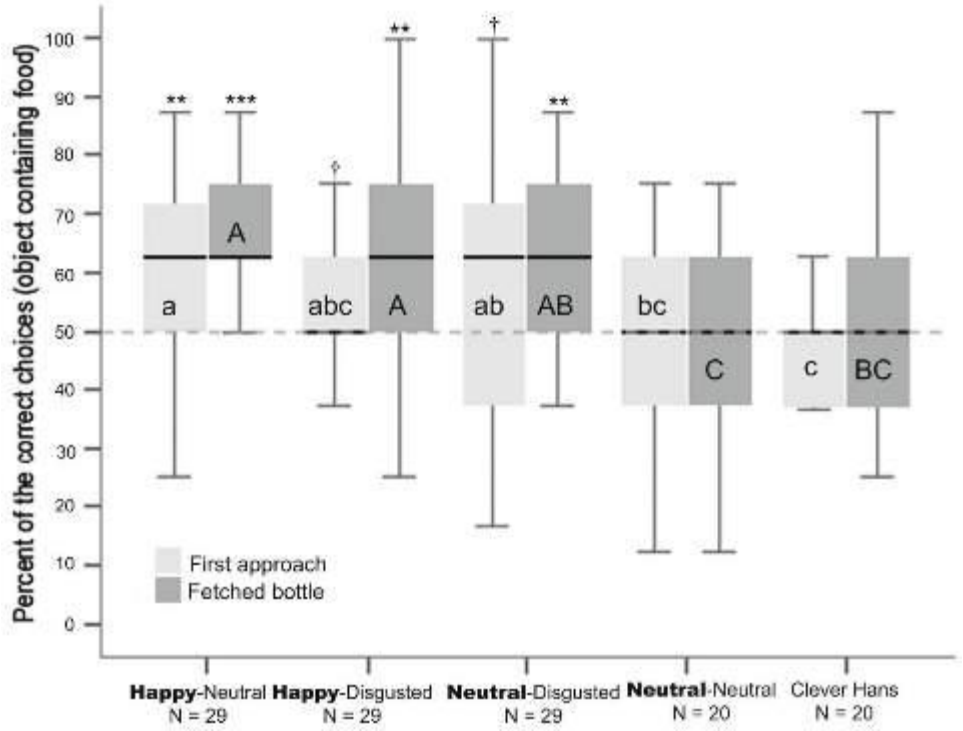
凝视（目光交流）会触发主人释放催产素，促进人与犬的互动和情感联结，从而在人与犬体内形成催产素系统的正反馈循环。

Miho Nagasawa et al. Science. 2015.

Auditory senses in dogs’ recognition of human emotions



犬对人类情绪性发声的侧化行为反应

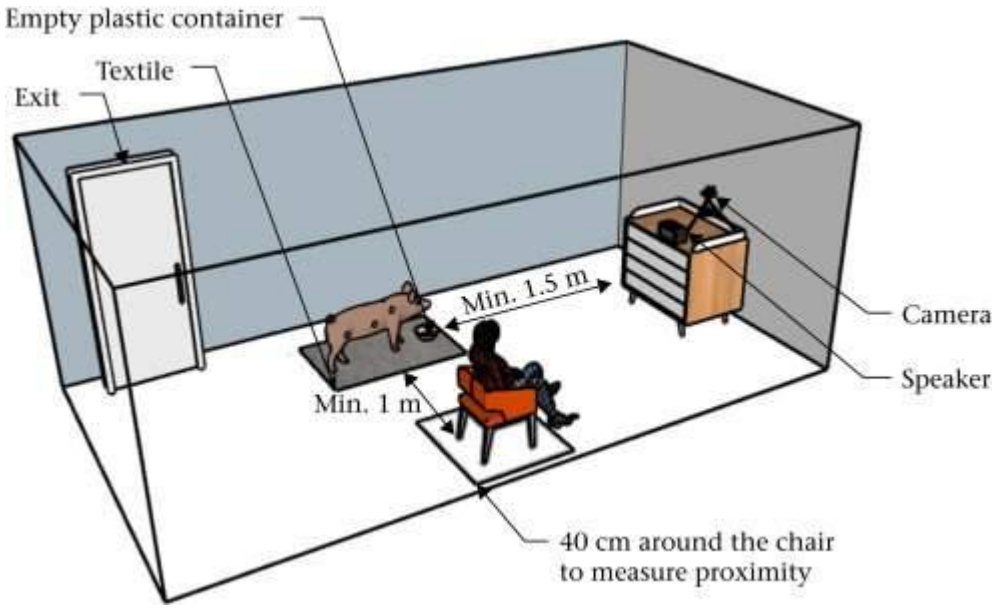


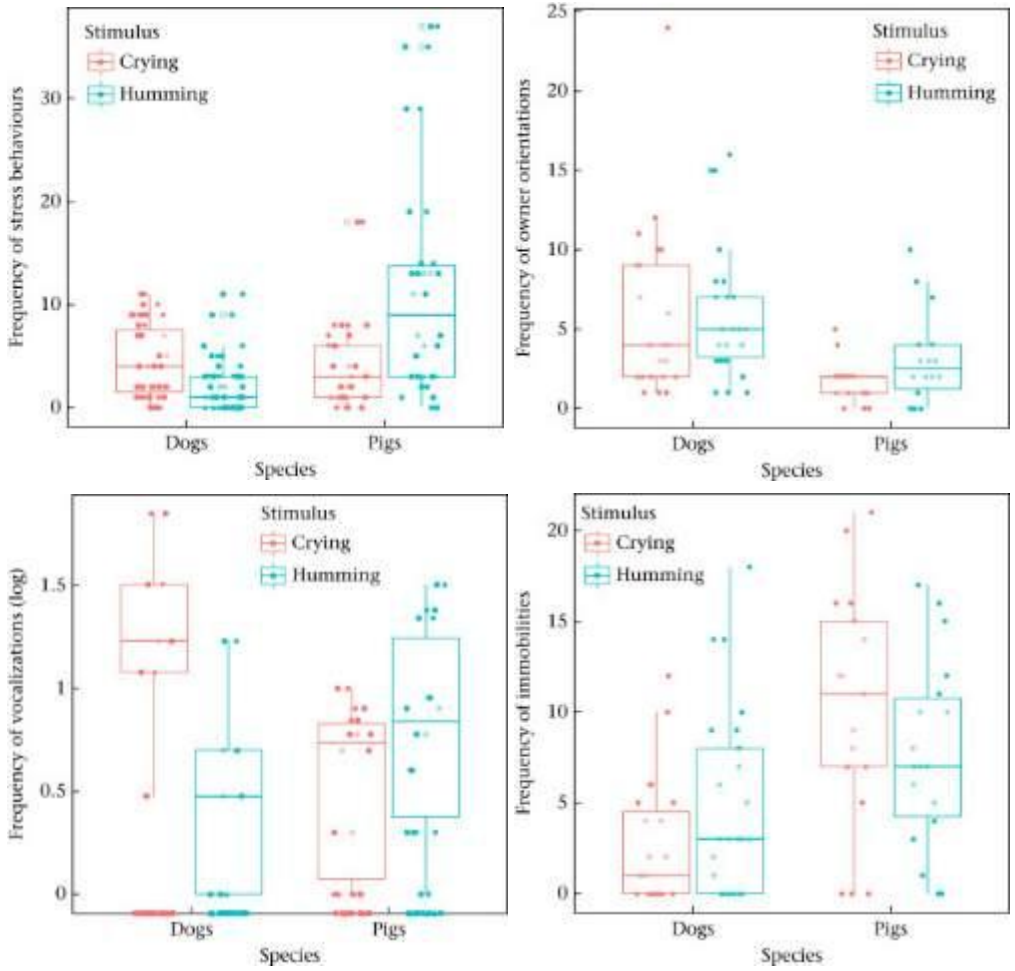
狗可以根据人类的听觉情绪线索改变反应

Siniscalchi, M. et al. Sci Rep. 2018.

Turcsán B. et al. Anim Cogn. 2015.

Auditory senses in dogs’ recognition of human emotions

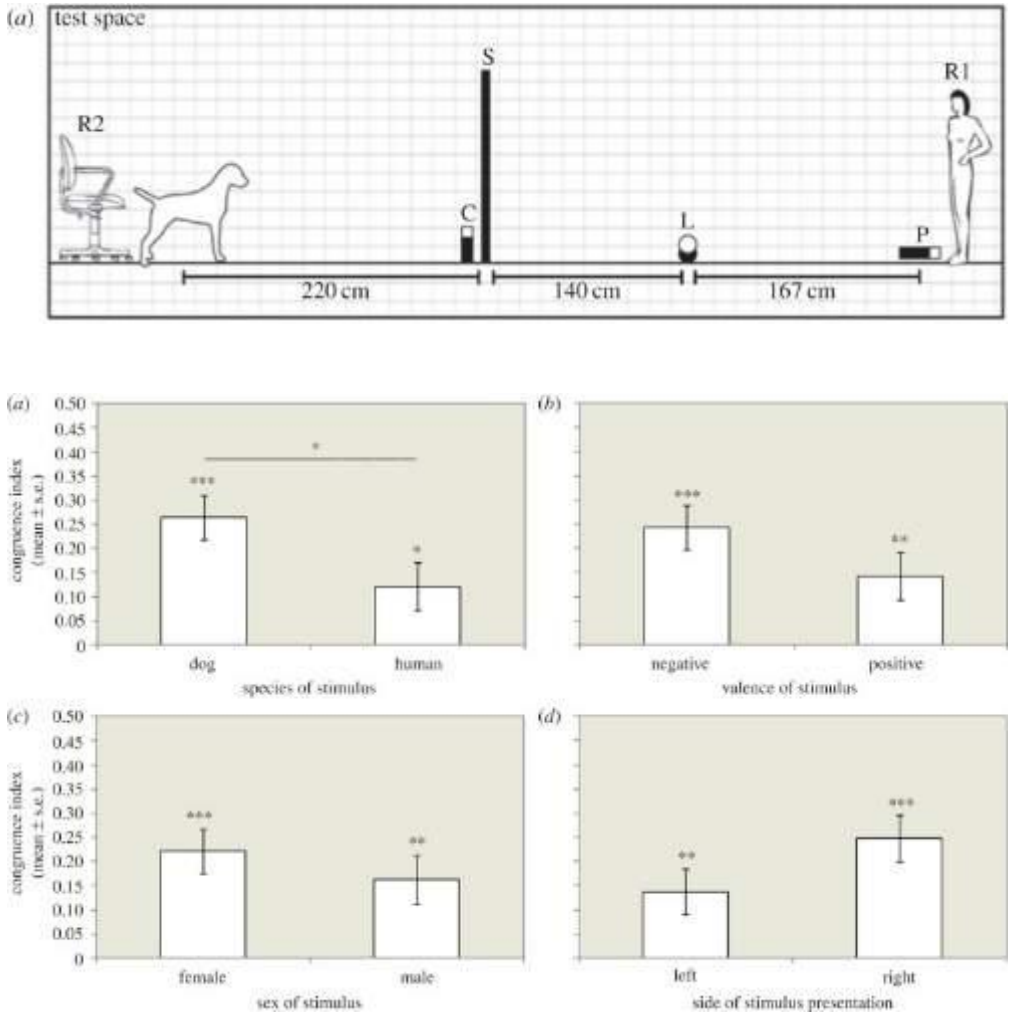


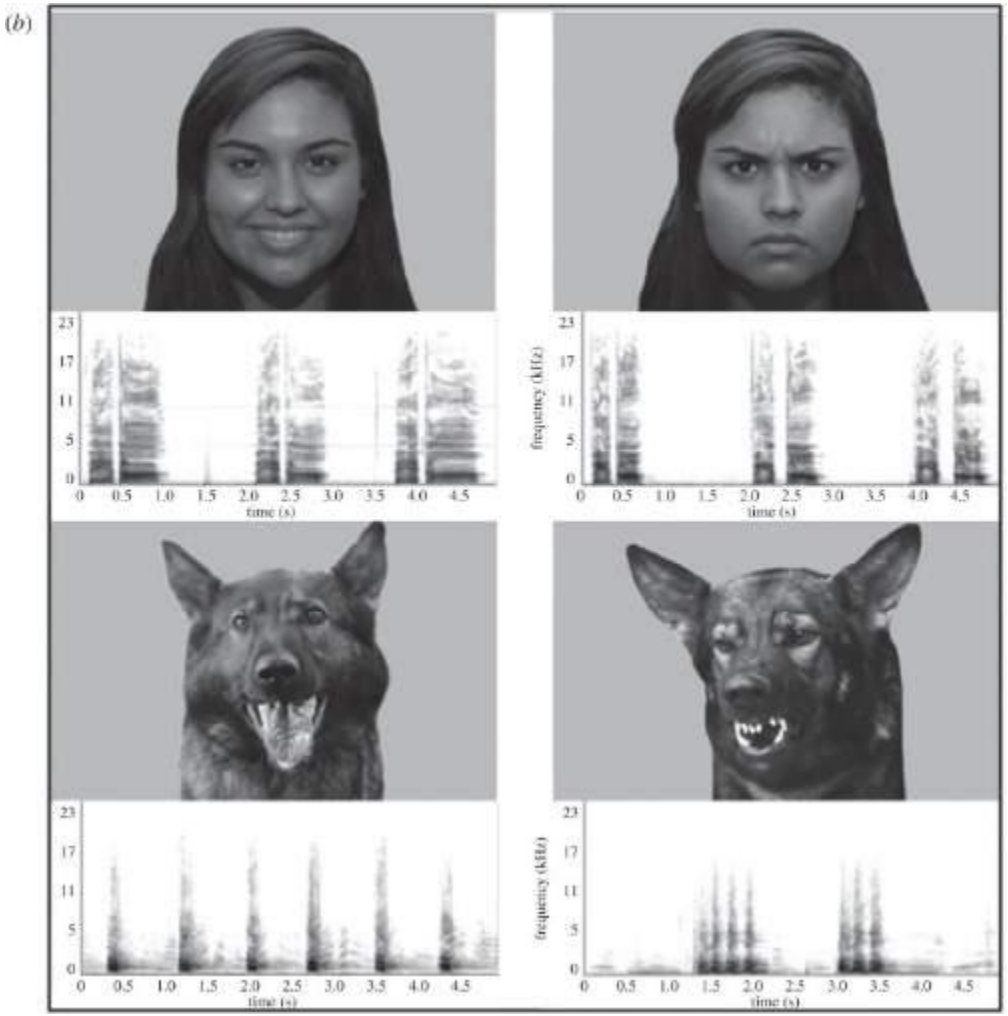


当狗听到人类哭泣时，其表现出更高的应激行为，说明其处于负面情绪状态。
狗能区分负面的人类声音。

Paula Pérez Fraga. et al. Animal Behavior. 2024.

Dogs integrate human visual and auditory emotional cues cross-modally

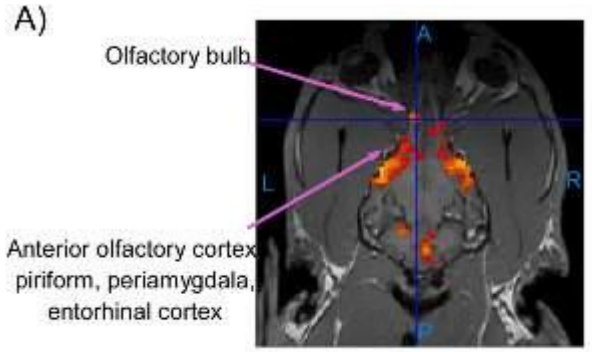


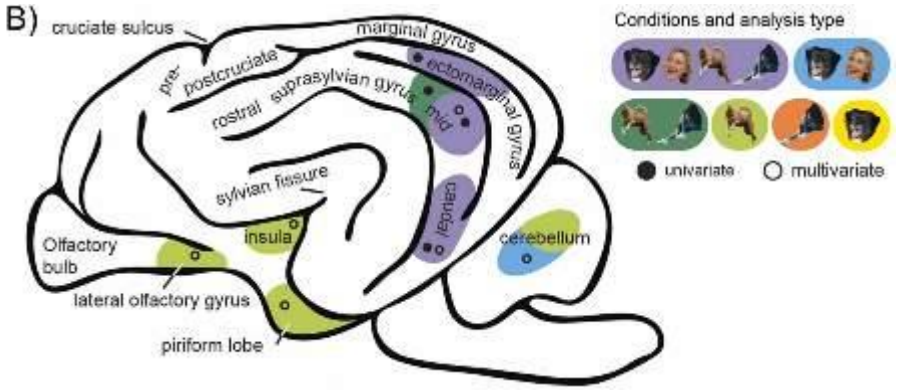


家犬能够通过听觉和视觉输入获取犬类与人类的情感信息，并将其整合为对情绪的连贯感知

Albuquerque N. et al. Biol Lett. 2016.

Olfaction in the perception of emotion in dogs

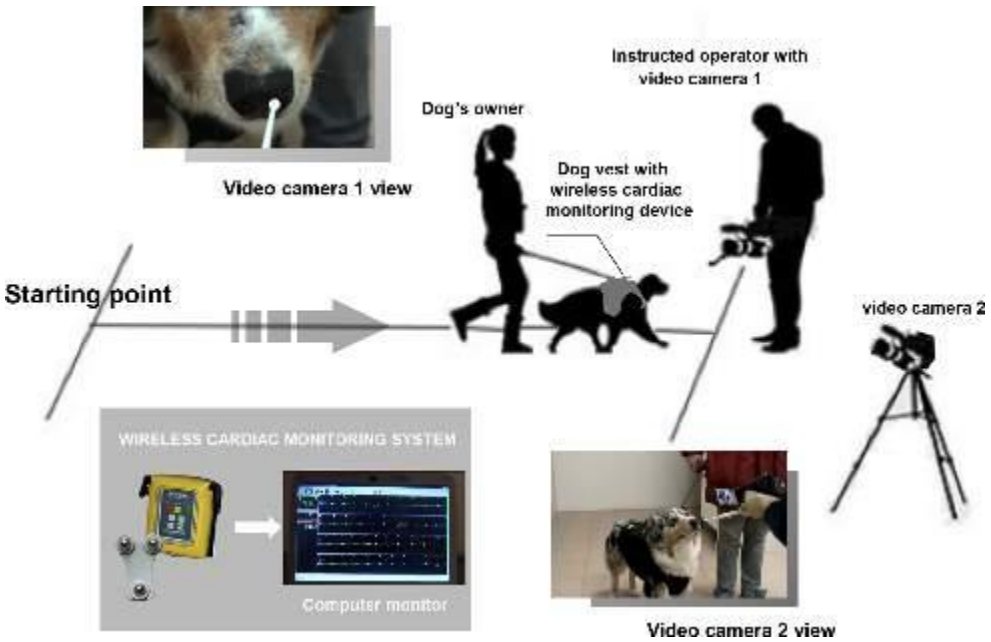


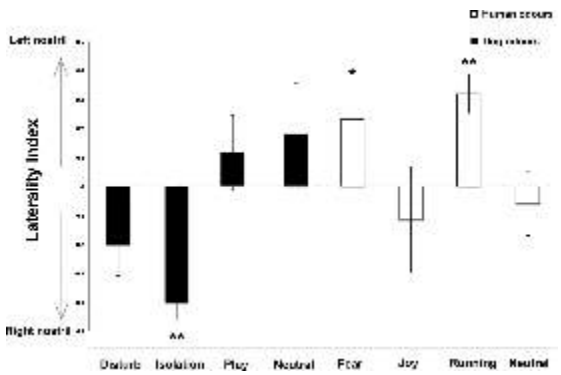


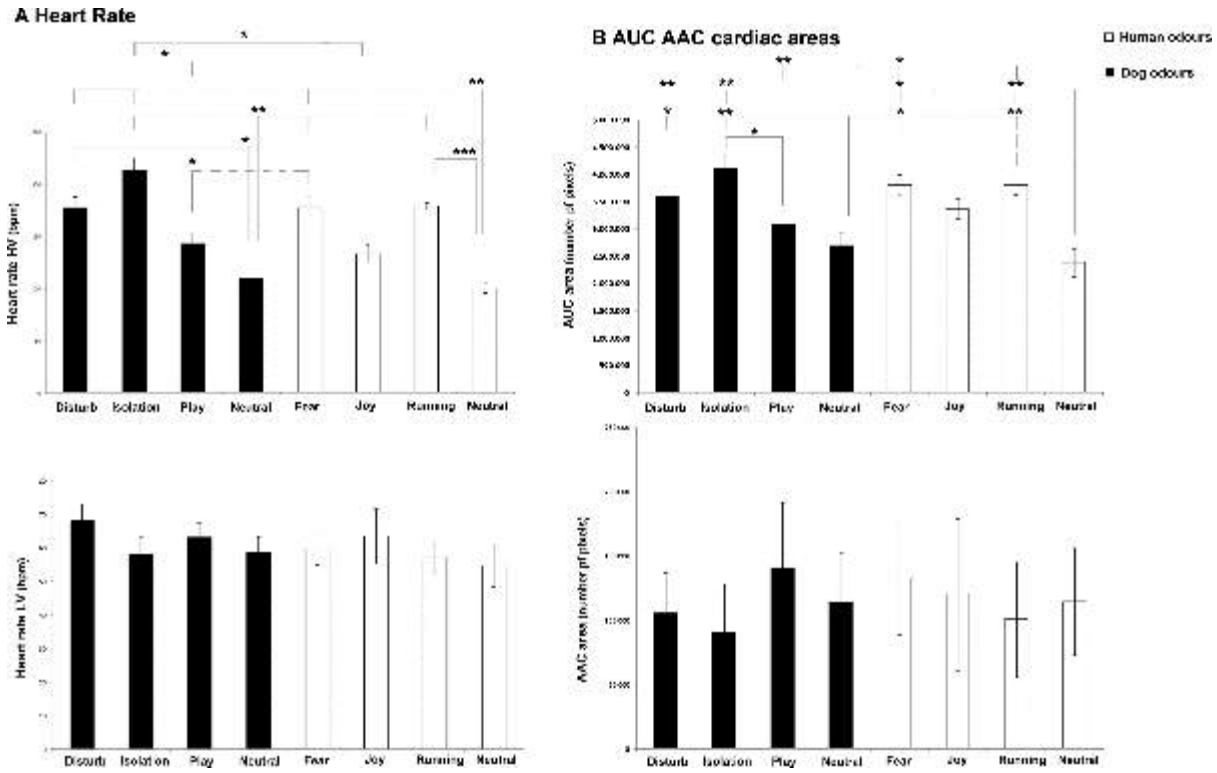
犬鼻的嗅上皮中除支持细胞和基底细胞外，还含有约2.5亿个嗅觉细胞，该上皮覆盖面积约18至150平方厘米。

Berg P. et al. Neurosci Biobehav Rev. 2024.

Olfaction in the perception of emotion in dogs

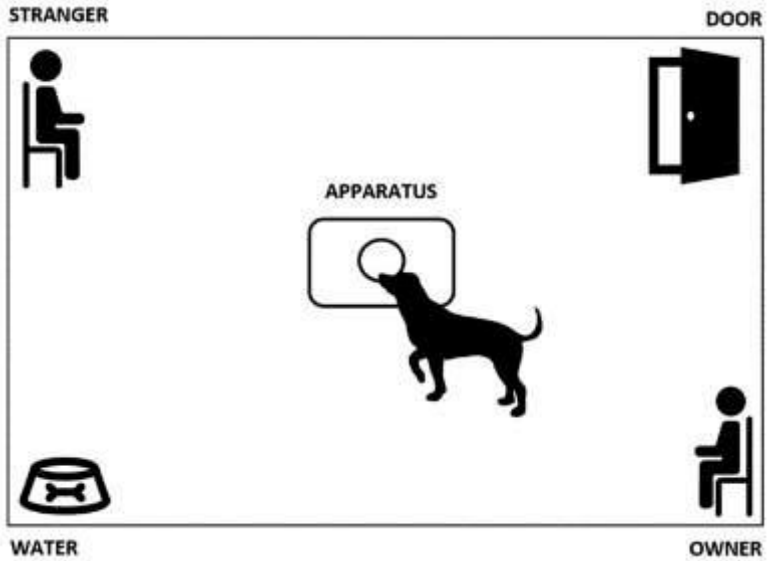




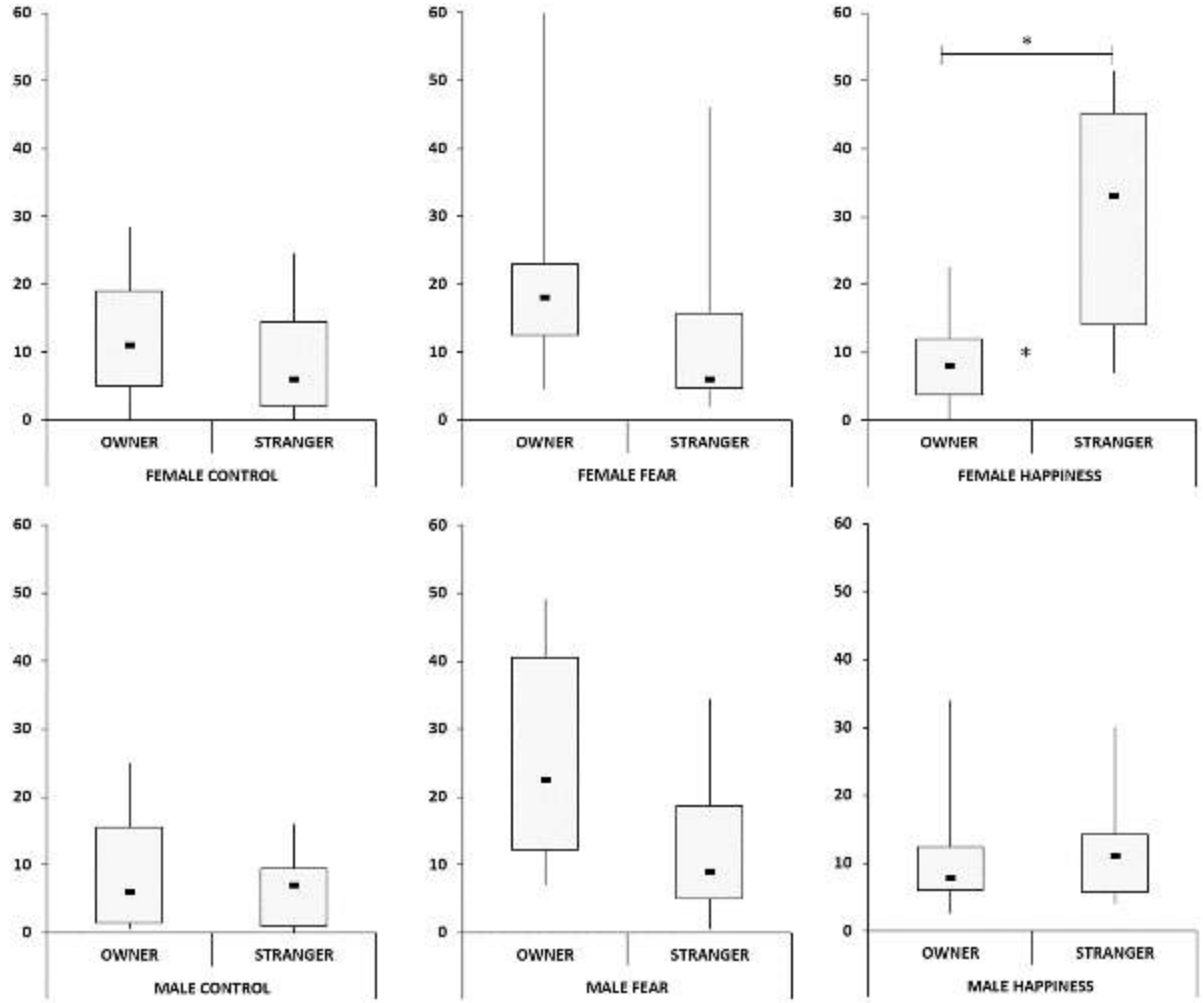


犬类在不同情绪状态下对同种（犬类）和异种（人类）气味表现出不同的行为和生理反应性。

Marcello Siniscalchi et al. Behav Brain Res. 2016.

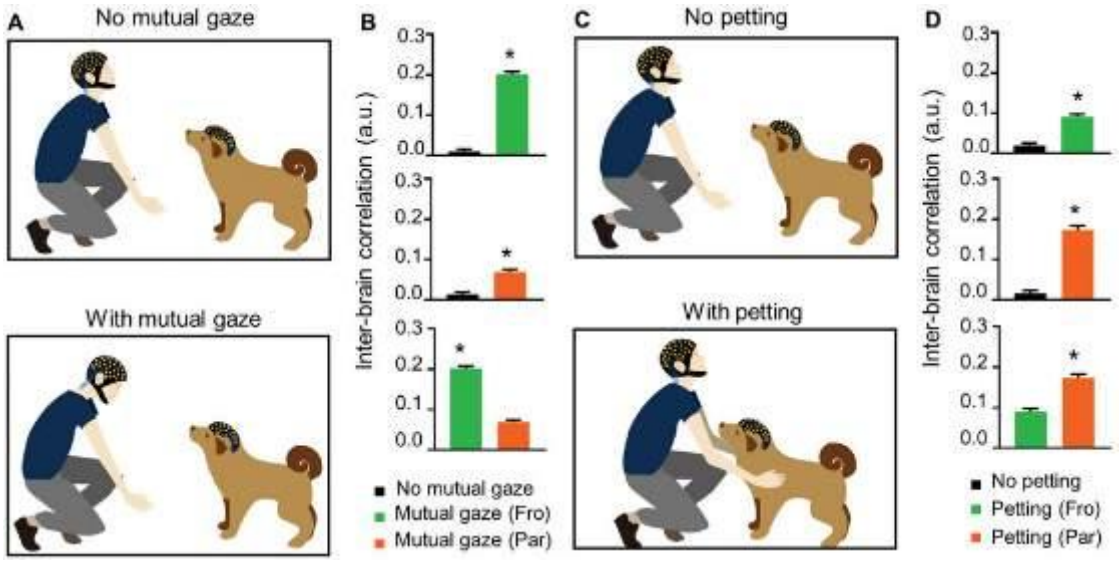


暴露于人类快乐化学信号下的狗在行为反应中存在性别差异

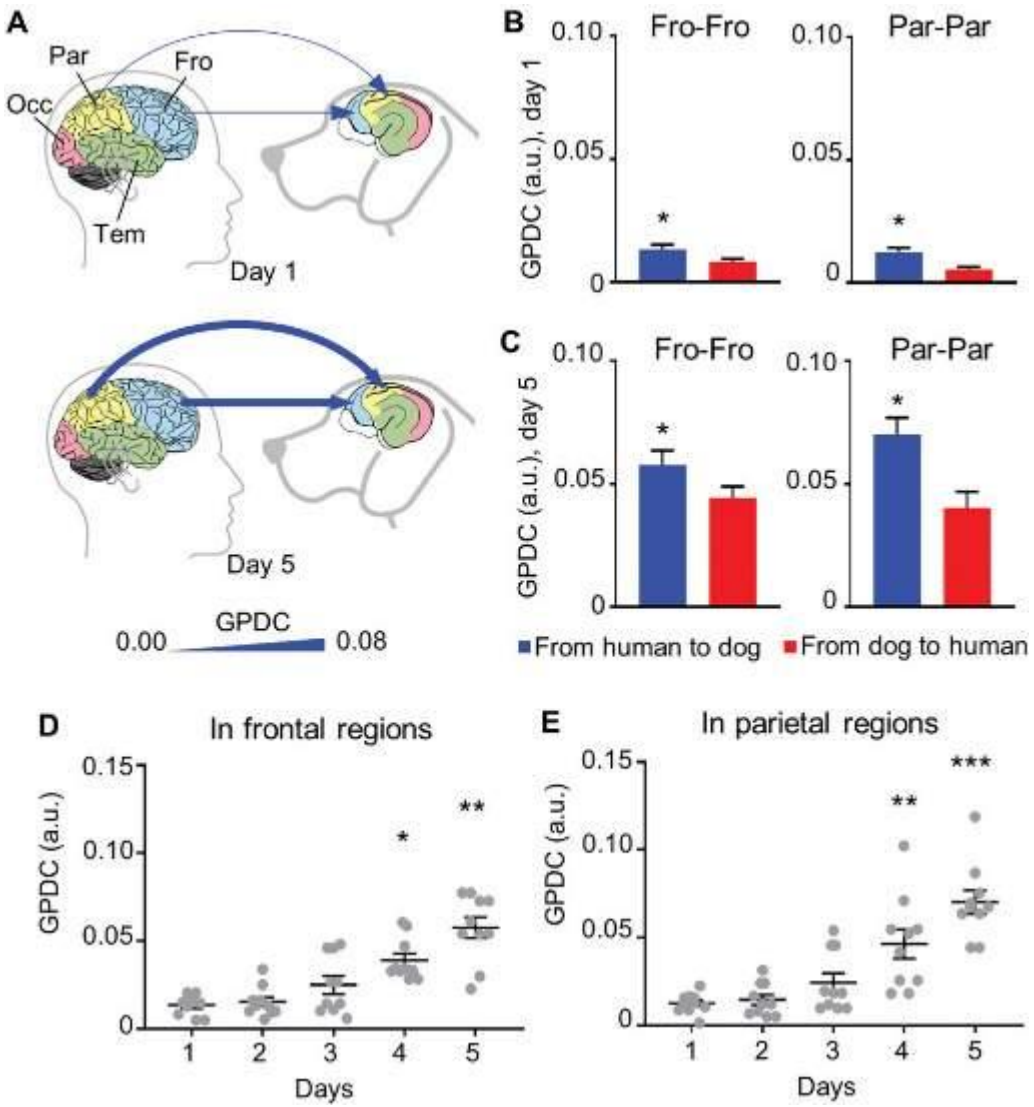


Biagio D'Aniello et al. Anim Cogn. 2021.

The Interacting of Human and Dog Emotions



人类与狗交流时，关键区域的大脑活动可以同步



Wei Ren et al. Adv Sci (Weinh). 2024.

Summary

- Dogs have brain structures that generate emotions and can detect emotions through multiple indicators.
- Dogs can use their vision, hearing and smell to sense emotional cues.
- There is a mutual influence between dogs and human emotions.

PART 3:

Canine Model and Typical Disease Research

王红蕾

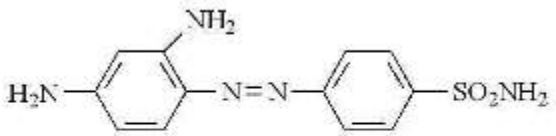
11/26/2025

Why do we need canine models in pharmacology?

The beginning of forced animal experiments is Elixir Sulfanilamide Incident (磺胺酏事件)

Gerhard Domagk
（1895-1964）

1937年，药剂师瓦特金斯通过实验发现，磺胺可以很好地在二甘醇中溶解。



百浪多息

1937

Elixir of Sulfanilamide, containing the poisonous solvent diethylene glycol, kills 107 persons, many of whom are children, dramatizing the need to establish drug safety before marketing and to enact the pending food and drug law.

1938

The Federal Food, Drug, and Cosmetic (FDC) Act of 1938 is passed by Congress, containing new provisions:

- Extending control to cosmetics and therapeutic devices.
- Requiring new drugs to be shown safe before marketing-starting a new system of drug regulation.
- Eliminating the Sherley Amendment requirement to prove intent to defraud in drug misbranding cases.
- Providing that safe tolerances be set for unavoidable poisonous substances.
- Authorizing standards of identity, quality, and fill of container for foods.
- Authorizing factory inspections.
- Adding the remedy of court injunctions to the previous penalties of seizures and prosecutions.

Under the **Wheeler-Lea Act**, the Federal Trade Commission is charged with overseeing advertising associated with products otherwise regulated by FDA.

There are a series of regulatory requirements for animal testing of drugs in China


国家食品药品监督管理总局 CFDA
China Food and Drug Administration

《药物非临床研究质量管理规范》（国家食品药品监督管理总局令第34号）

2017年08月02日 发布

国家食品药品监督管理总局令

第34号

《药物非临床研究质量管理规范》已于2017年6月20日经国家食品药品监督管理总局局务会议审议通过，现予公布，自2017年9月1日起施行。

局长 毕井泉

2017年7月27日

第二章 基本制度和要求

第十条 申请人在申请药品上市注册前，应当完成药学、药理毒理学和药物临床试验等相关研究工作……申请药品注册，应当提供真实、充分、可靠的数据、资料和样品，证明药品的安全性、有效性和质量可控性。

GLP内容包括但不限于：

伦理审批、

实验动物生存及试验环境监控、

避免相互污染

……

How do researchers select appropriate animal species for toxicology experiments?

相关指导原则对动物种属选择的要求

指导原则	要求摘要
ICH M3 (R2)	至少两种哺乳动物(一种非啮齿类动物)。
ICH S1B	在没有明确证据支持某一物种的情况下，建议选择大鼠。
ICH S2 (R1)	大鼠和小鼠都被认为适合用于骨髓微核试验
ICH S5 (R3)	DART 试验的物种选择概述了选择大鼠、小鼠或家兔的一般原则
ICH S6 (R1)	第 3.3 节和附录 2.1:概述了使用相关物种和确定相关性的一般原则
ICH S7A	应提供选择特定动物模型或测试系统的理由
ICH S7B	应该选择并证明最合适的体内试验系统和物种
ICH S8	与观察到不良免疫效应的一般毒性试验一致
ICH S9	通常包括啮齿类动物和非啮齿类动物
ICH S11	第 3.3 节:动物试验系统选择概述了在选择相关物种时应考虑的因素。
EMEA/CHMP/SWP/ 28367/07 (R1)	第 6.1 节:描述了证明动物模型相关性的适当试验。

国际协调会议（ICH）和欧盟

小分子药物毒性实验遵循原则

啮齿类：
SD大鼠

非啮齿类：
比格犬

Beagle is the common breed of experimental canine

比格（Beagle）犬:

又称米格鲁猎兔犬，源于英国。体型小，体长30-40厘米，体重7-12公斤，多为黄、黑、白三色，性情温和，易于驯服。

Why beagle?

- **Medium build**
- **Genetic stability**
- **Reproductive advantages**
- **Non-aggressive**
- **Outgoing personality**

Canine models drive medical breakthroughs.

Bell-Magendie law reveals the functional division between sensory nerves and motor nerves.

In the early 19th century

Charles Bell
(1774-1842)

Dr Francois Magendie
(1783 - 1855)

RECHERCHES

PHYSIOLOGIQUES ET CLINIQUES

LIQUIDE CÉPHALO-RACHIDIEN

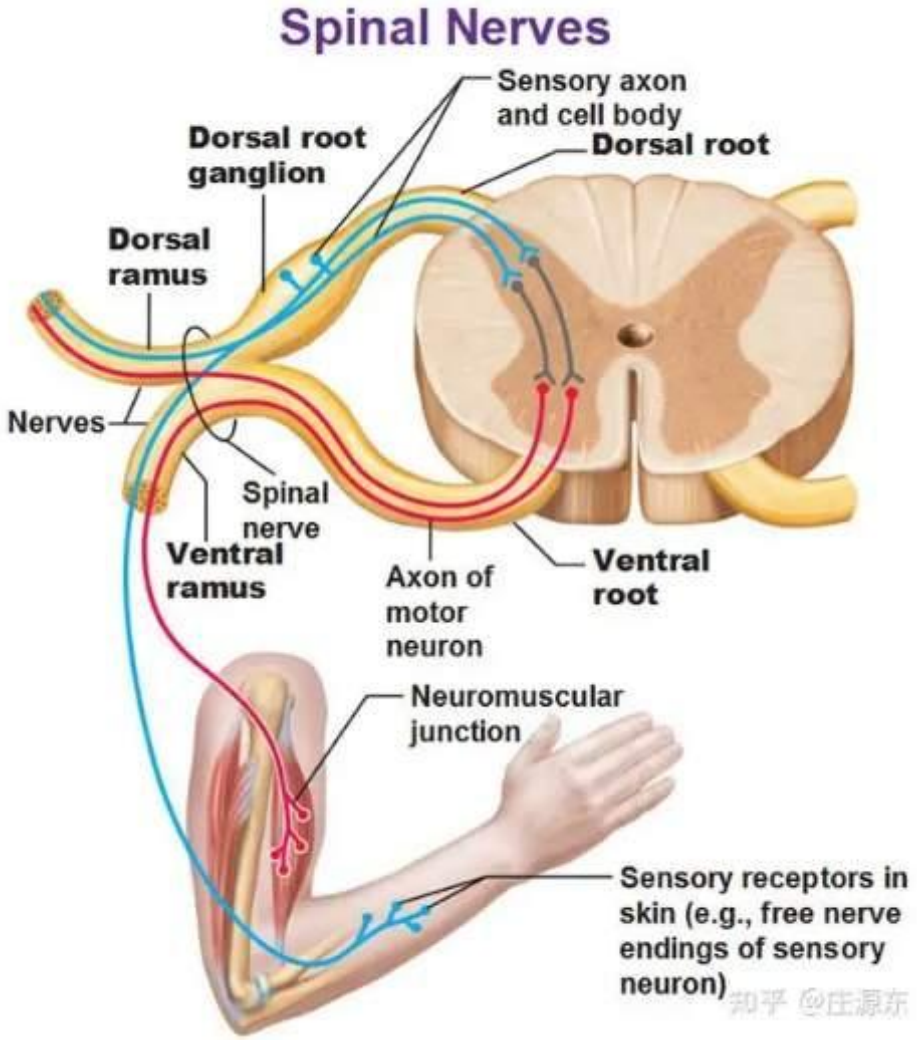
CÉRÉBRO-SPINAL,

Par F. MAGENDIE,

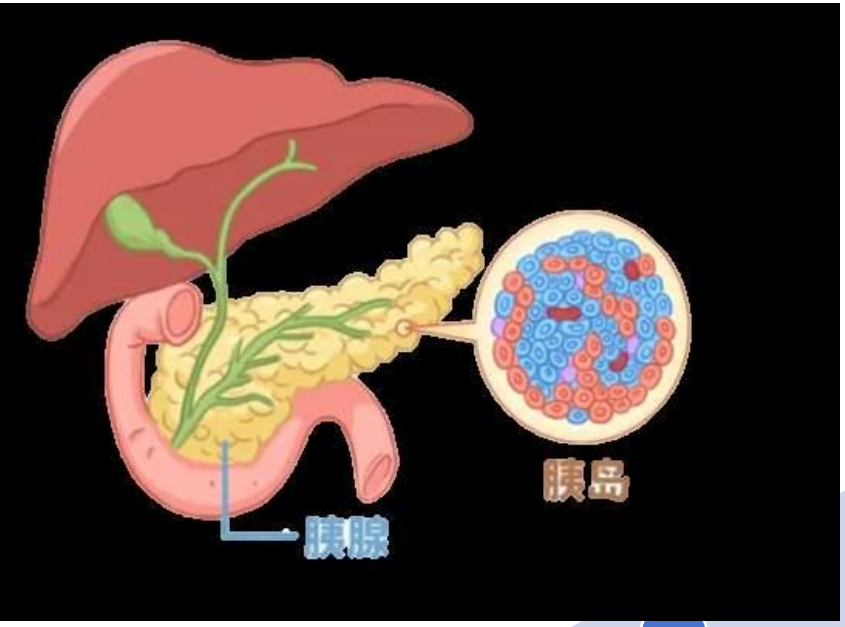
PARIS,

LIBRAIRIE MÉDICALE DE MÉQUIGNON-MARVIS FILS,

1842



The history of insulin discovery



1869

Paul Langerhans

Discovered “islets of Langerhans”

1920

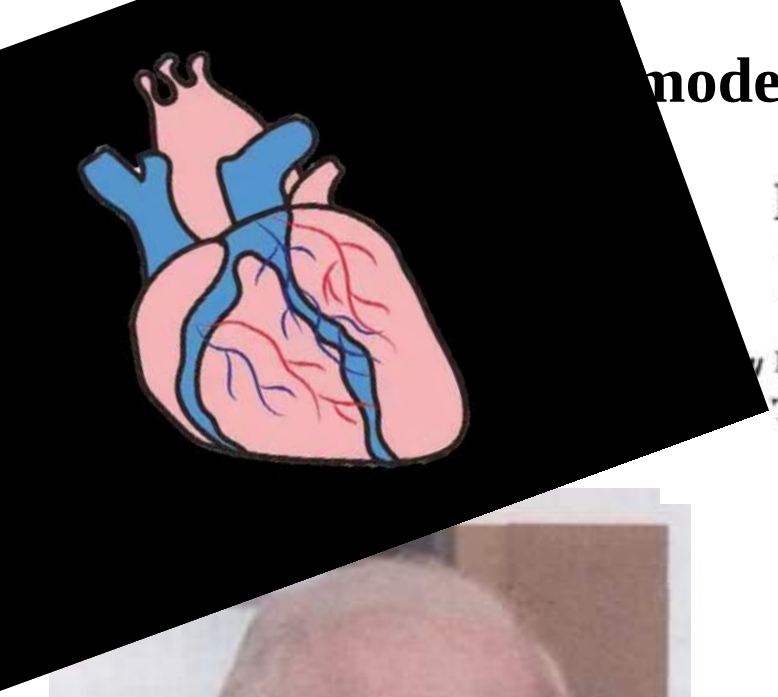
Banting thought that ligating the pancreatic duct of the dog, allowing it to survive until the acini has degenerated and only the islets remained.

1921

Dr. John James Rickard Macleod provided Banting and Best with the surgical methods and assisted in the operation of the first dog.

Frederick Grant Banting (1891–1941, right), Charles Herbert Best (1899–1978, left) and experimental dog on the roof of the medical building of the University of Toronto. Picture: F. G. Banting Papers, Thomas Fisher Rare Book Library, University of Toronto

models promote the treatment of myocardial infarction



Eugene Braunwald
(1929~)

Factors Influencing Infarct Size Following Experimental Coronary Artery Occlusions

y Peter R. Maroko, M.D., John K. Kjekshus, M.D., Burton E. Sobel, M.D.,
Tan Watanabe, M.D., James W. Covell, M.D., John Ross, Jr., M.D.,
and Eugene Braunwald, M.D.

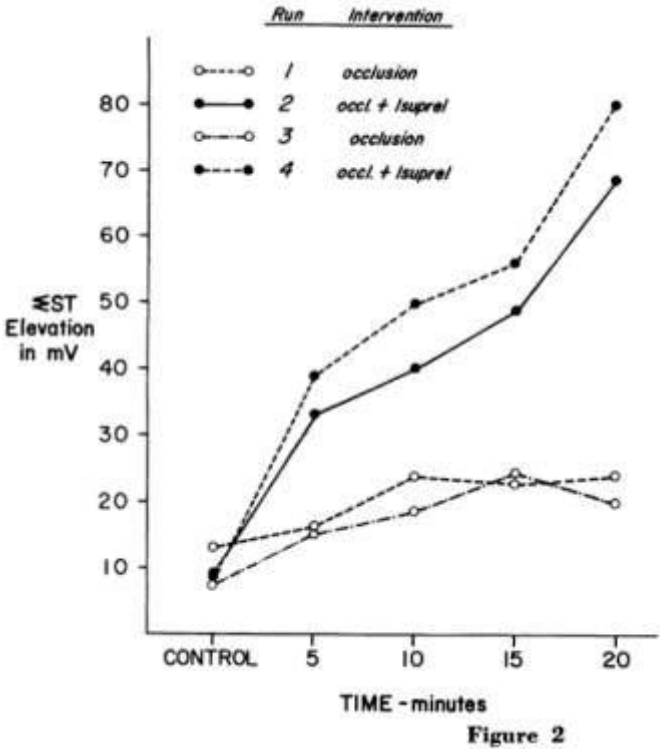
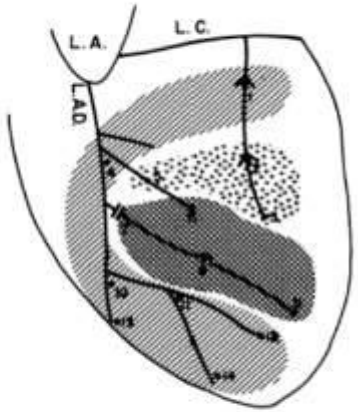


Figure 2



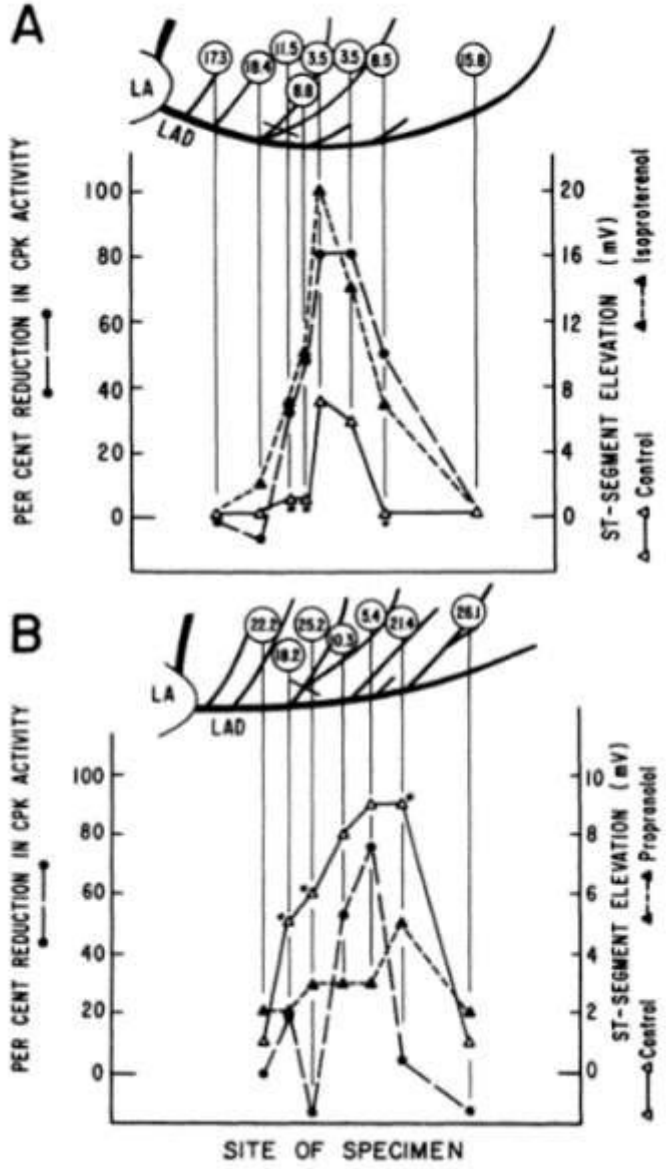


Figure 10

心外膜S-T段抬高幅度（作为急性缺血损伤的指标）和24小时后心肌肌酸磷酸激酶（CPK）活性下降（作为心肌细胞坏死的指标）来量化损伤程度

PETER R. et al., Circulation, 1971

The contribution of the night-blind puppy

Swedish Briard dogs
伯瑞犬

Genomics **57**, 57–61 (1999)
Article ID geno.1999.5754, available online at http://www.idealibrary.com on IDEAL®

Retinal Dystrophy of Swedish Briard/Briard–Beagle Dogs Is Due to a 4-bp Deletion in *RPE65*

Andres Veske,* Sven Erik G. Nilsson,† Kristina Narfström,‡ and Andreas Gal*,[1]

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Received September 23, 1998; accepted January 11, 1999

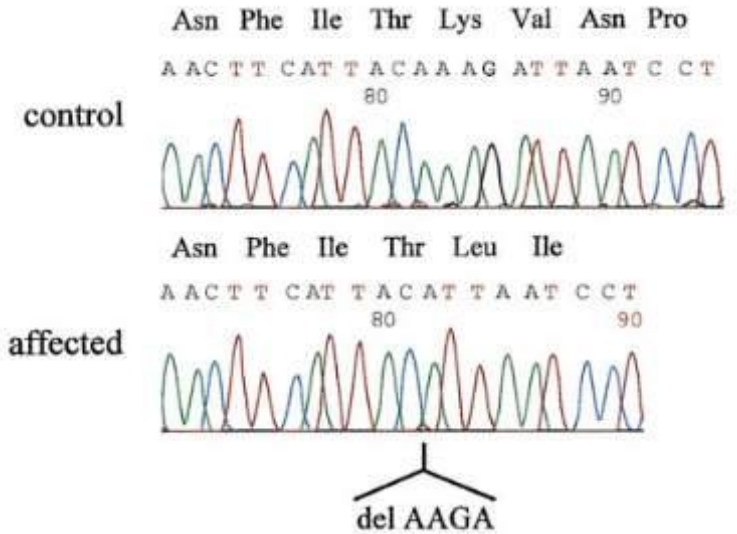


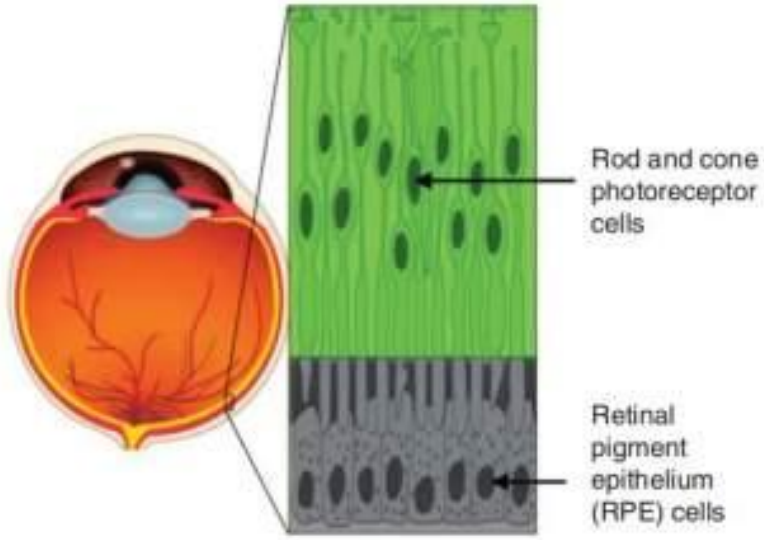
FIG. 3. Direct sequencing of a 135-bp genomic PCR fragment of the canine *Rpe65* gene. Nucleotide and predicted amino acid sequence of an unaffected **(top)** and an affected animal **(bottom)** is shown.

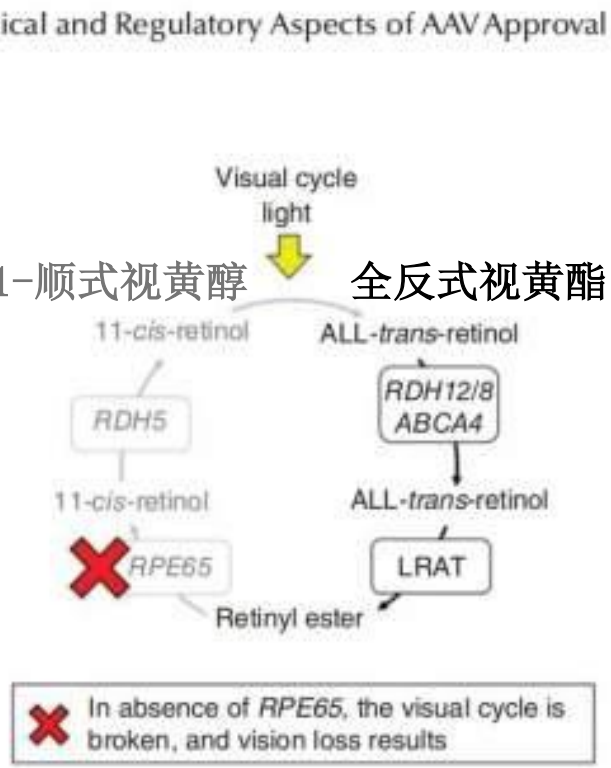
Narfstrom, K, Wrigstad, A, Nilsson, SEG. *Br J Ophthalmol*, 1989

Andres Veske, et al, Genomics, 1999

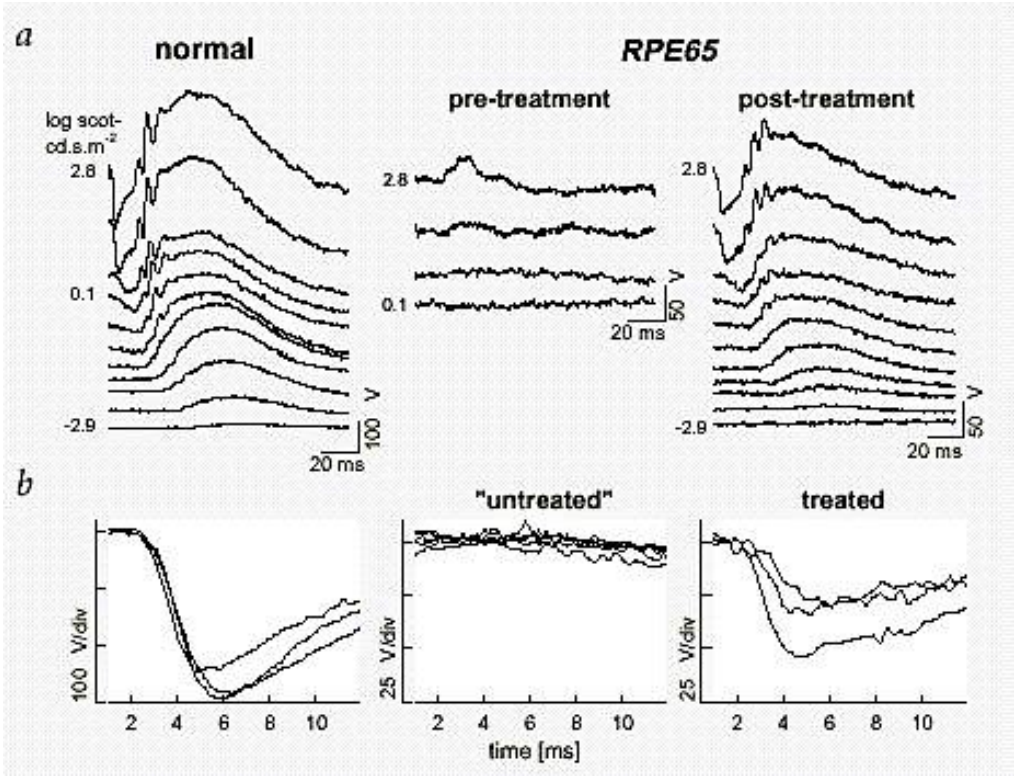
Briard dogs help develop the first AAV gene therapy product

莱伯氏先天性黑蒙症(Leber's congenital amaurosis, LCA)





11-顺式视黄醇 全反式视黄酯



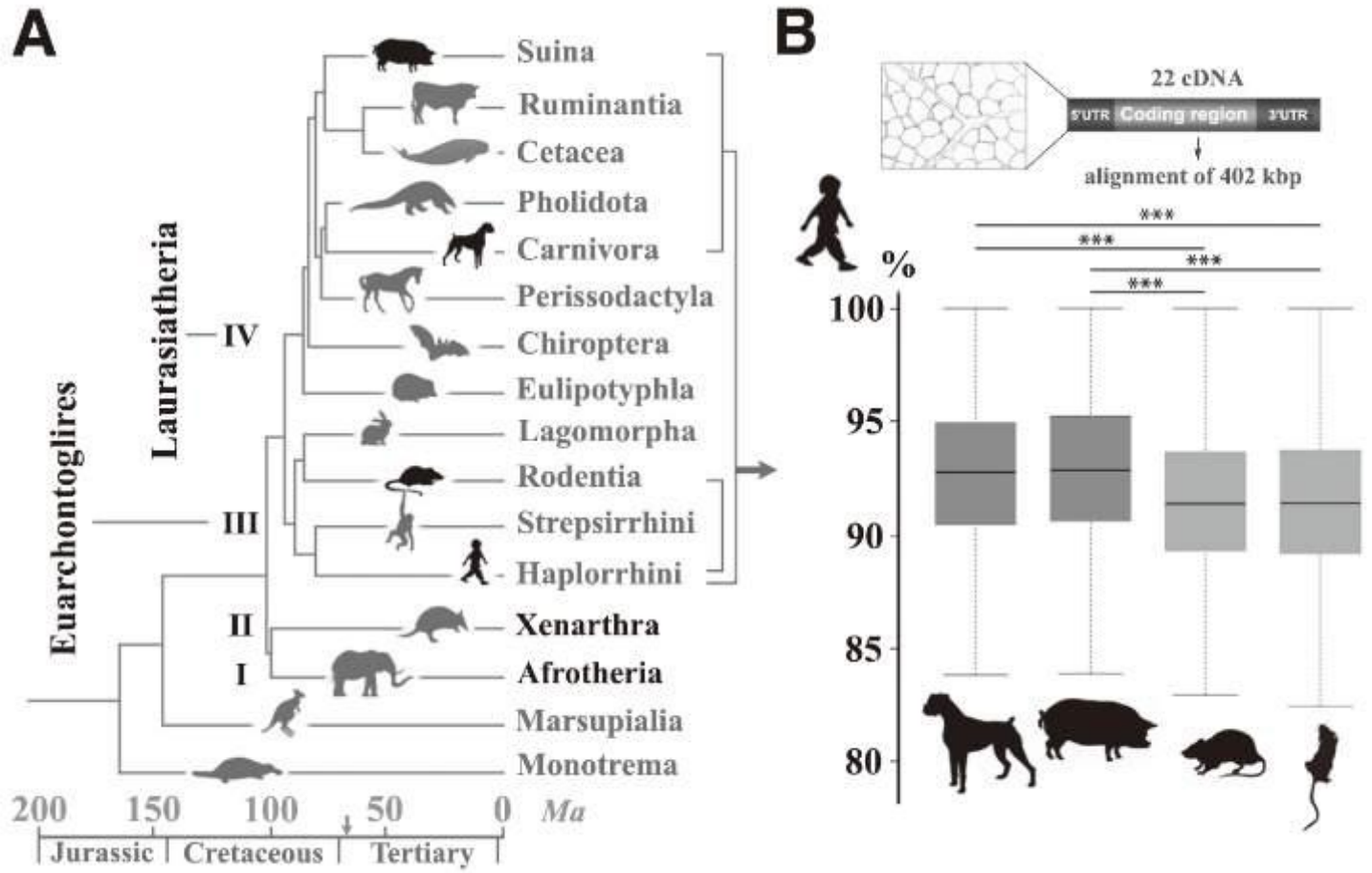
Acland, G., *et al. Nat Genet,* 2001

Kristina Narfström, et al., *Invest. Ophthalmol. Vis. Sci.* 2003

Reape KZ et al., *Cold Spring Harb Perspect Med*. 2023

Animal testing for drugs in the future

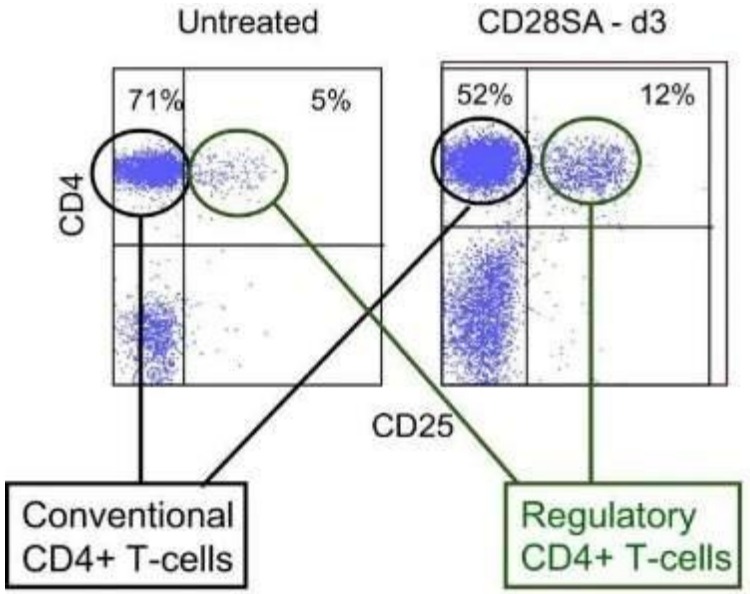
From faithful companion to scientific partner

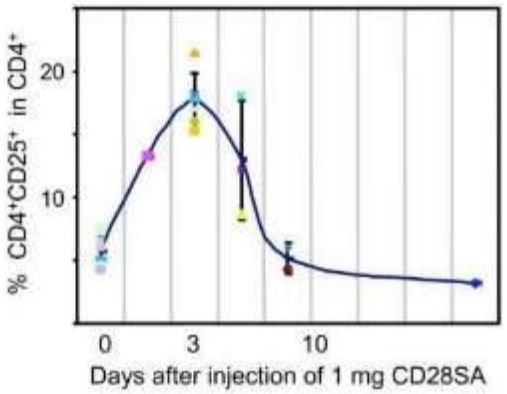


Inès Barthélémy, Christophe Hitte and Laurent Tiret, *Journal of Neuromuscular Diseases*, 2019

TGN1412: From Discovery to Disaster

Northwick Park Hospital, London
3/13/2006
First in man phase 1 trial





TGN1412 was thought to be useful for disease related to low numbers of activated T such as B-cell lymphoma or for treatment of autoimmune diseases such as rhematoid arthritis (风湿性关节炎).

Attarwala H., J Young Pharm. 2010

FDA has announced the gradual removal of the requirement for animal testing for drugs.

An official website of the United States government Here's how you know

U.S. FOOD & DRUG ADMINISTRATION

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Home / News & Events / FDA Newsroom / Press Announcements / FDA Announces Plan to Phase Out Animal Testing Requirement for Monoclonal Antibodies and Other Drugs

FDA NEWS RELEASE

FDA Announces Plan to Phase Out Animal Testing Requirement for Monoclonal Antibodies and Other Drugs

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More Press Announcements

For Immediate Release: April 10, 2025

Today, the U.S. Food and Drug Administration is taking a groundbreaking step to advance public health by replacing animal testing in the development of monoclonal antibody therapies and other drugs with more effective, human-relevant methods. The new approach is designed to improve drug safety and accelerate the evaluation process, while reducing animal experimentation, lowering research and development (R&D) costs, and ultimately, drug prices.

Content current as of:
04/10/2025

Regulated Product(s)
Biologics
Drugs

New Approach Methodologies (NAMs)：

1. In Vitro Human-Derived Systems (Organoids and Microphysiological Systems)
2. In Silico Tools and Computational Modeling
3. Other Innovative Platforms

Summary

- The development of mandatory drug toxicity tests has lasted for 87 years.
- The beagle is a conventional animal model for toxicity experiments of small molecule drugs.
- The beagle is the most commonly used experimental dog due to its breed advantages.
- Canine models play a vital role in driving progress in neuroscience and the treatment of conditions such as diabetes, myocardial infarction, and vision loss.
- In the future, new methods for assessing the safety of drugs need to be sought in order to enhance animal welfare and human safety.

Thanks!