IN BRIEF

BEHAVIOR

Sex differences in exploration

Chen, C.S. et al. *eLife* **10**, e69748 (2021)

Our lives are made up of countless decisions for which we often have to choose between sticking with what we know or trying something new. Balancing exploitation/exploration is central to decision-making; too much exploitation makes behavior inflexible, while too much exploration may lead to inefficient decision-making. Exploration is dysregulated in many neuropsychiatric disorders, including conditions that differ between males and females.

A new study used computational modeling approaches to characterize sex differences in a canonical explore/exploit task (the restless two-armed bandit task). Although male and female mice had similar accuracy, they used different explore-exploit strategies during the task. Notably, female mice explored less than males but learned more quickly during exploration. These findings support the use of computational approaches to identify endophenotypes associated neuropsychiatric disorders. *ALB*

https://doi.org/10.1038/s41684-021-00897-7

OBESITY

Screening obesity genes in *Drosophila*

Agrawal, N., Lawler, K. et al. *PLoS Biol*. **19**, e3001255 (2021)

Obesity is a major risk factor for several conditions, including type 2 diabetes. Identifying the genes that regulate human body weight could help identify potential targets for weight-loss therapy. A new study used *Drosophila* to test candidate genes that might be involved in obesity.

First, the investigators performed whole-exome sequencing of individuals with severe obesity to identify several rare homozygous coding variants. Next, they selected a set of human genes with *Drosophila* orthologues and knocked down their expression in flies. Knockdown of 4 out of 24 genes increased adiposity in flies, including *dachsous*, a gene encoding a component of the Hippo signaling pathway. Altogether, these findings support the use of *Drosophil*a to assess the pathogenicity of variants associated with human obesity. *ALB*

https://doi.org/10.1038/s41684-021-00899-5

GUT MICROBIOME

Impact of microbiota on CNS macrophages

Sankowski, R. et al. *EMBO J*. **40**, e108605 (2021)

Immune cells of the central nervous system (CNS) comprise parenchymal microglia and CNS-associated macrophages, including choroid plexus, leptomeningeal and perivascular macrophages (cpMΦ, mMΦ and pvMΦ). While previous work has shown that microbiota controls microglia properties, the effects of gut microbes on CNS macrophages are unknown.

A study combining microbiota manipulation approaches and single-cell RNA sequencing shows that microbiota regulates the numbers and gene expression of cpMΦ under steady-state conditions, but has limited effects on mMΦ and pvMΦ. Upon acute viral infection, the immune response of CNS macrophages was impaired in germ-free mice compared to SPF mice; and in a mouse model of Alzheimer's disease, pvMΦ of mice lacking microbiota showed enhanced amyloid beta uptake. Altogether, these results suggest that microbiota regulates CNS macrophage properties in homeostasis and disease. *ALB*

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INFECTIOUS DISEASE

A new lethal mouse-adapted SARS-CoV-2 for COVID research

Sun, S. et al. *Nat Commun*. **12**, 5654 (2021)

SARS-CoV-2, which relies on cellular receptor angiotensin-converting enzyme 2 (ACE2) to enter host cells, cannot infect standard laboratory mice due to differences in amino acid residues between mouse and human ACE2. In *Nature Communications*, Sun et al. report the generation of a lethal mouse-adapted SARS-CoV-2 for studying COVID-19 pathogenesis in mice.

Varying doses of mouse-adapted SARS-CoV-2 strain MASCp36 — a strain generated by further passaging of previously described MASCp6 — were intranasally inoculated in young, old female and male mice. In infected mice, MASCp36 caused severe respiratory symptoms, massive macrophages and neutrophils infiltration, high levels of proinflammatory cytokines, as well age- and gender-specific responses, resembling the clinical manifestations of severe COVID-19 in humans. *ALB*

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