

# RESEARCH HIGHLIGHTS

## › RESEARCH IN BRIEF

### He who controls the rats...

Understanding how an animal responds to a treatment is important for drug discovery and development. But it's not practical for a researcher or technician to physically observe the behavior of an experimental animal 24/7, and removing them from their communal cages to take "snapshots" during an experiment can introduce unwanted confounds. A possible solution? Rodent Big Brother, the culmination of a 2011 NC3Rs CRACK It Initiative sponsored by pharmaceutical company AstraZeneca to develop an automated way to continuously monitor rats in the comfort of their home cages.

Using Actual Analytic's Home Cage Analyzer system, Rodent Big Brother combined data from subcutaneous radiofrequency identification, or RFID, transponders with video recordings from high-definition infrared cameras. The system allowed the behavior and body temperature of individually tagged rats to be remotely monitored 24 hours a day for up to 28 days. Details about the development and testing process and the current hardware needed can be found in *PLoS One* (12, e0181068; 2017). Remember rats, big brother is watching.

### Sensing sans synapses

Placozoans don't have brains...nor any semblance of a formal nervous system for that matter. But that doesn't stop these tiny, flat, marine animals from taking gauge of the environment around them. Placozoans glide along surfaces using ventral cilia and pause whenever they come across algae to snack on. How do they know?

A new study has identified an endorphin-like peptide that, when the animal comes in contact with algae (or a researcher injects it nearby), causes a cascading reaction that arrests the cilia and thus movement (*J. Exp. Biol.* 220, 3381–3390). Nearby placozoans will also pause, indicating the signal can reach beyond a single individual. Though the signal can take upwards of a minute to invoke a response, the results reveal how even the simplest of animals achieve intercellular communication.

### Everyone needs a microbiome, right?

Growing evidence suggests that the microbiome has a lot to do with an animal's health. But, there are always exceptions to a rule (*Proc. Natl. Acad. Sci. USA* 114, 9641–9646; 2017). Researchers studying caterpillars investigated the intestinal microbiome of 124 different species in four geographic locations: Costa Rica, the Northeast United States, Arizona, and Colorado. The caterpillars did harbor some microbes, but significantly fewer than the researchers expected to find. What was present mirrored assemblages found on leaves, suggesting the animals' microbiomes reflected lunch rather than a sustained resident community. In a follow-up experiment, the team compared growth and development of wild-harvested *Manduca sexta* caterpillars that were left untreated to those given antibiotics to reduce any gut microbes. A missing microbiome made no difference.

### Closing cleft palates

Oral clefts, structural deformities that occur when tissue in a developing infant's mouth fails to fuse normally, occur in about 1 in 700 births and require reconstructive surgery to correct. Mice are also susceptible to clefts, and many of the genes implicated in palate development in mice also occur in humans. Using the *Pax9*<sup>-/-</sup> mouse model, researchers have identified important signaling pathways and a potential *in utero* treatment (*Development* 2017; doi: 10.1242/dev.157750).

*Pax9* is a transcription factor involved in organogenesis; mice without it develop clefts and will die shortly after birth. Looking at changes in genetic expression in *Pax9* deficient and normal mice, the team saw a relationship with several genes in the Wnt signaling pathway, a highly conserved group involved in embryonic development. Administering a small-molecule Wnt agonist to a pregnant dam greatly mitigated the occurrence and severity of clefts in developing *Pax9*<sup>-/-</sup> pups.

## Genital cortex: a touchy topic

Genital cortex in rats, or the area in somatosensory cortex representing the genitalia, shows a nearly 2-fold expansion during sexual maturity. To investigate possible mechanisms for this timed increase in genital brain representation, scientists from the Bernstein Center for Computational Neuroscience Berlin, Germany, used anatomical methods to measure the size of genital cortex after several perturbations including: ovariectomies and estradiol injections, long-term blockade of activity in neurons of genital cortex, housing with male and female counterparts, and artificial stimulation of genitals by the experimenters (*PLoS Biol* **15**, e2001283; 2017).

Overall, the team found that sexual contact by males (but not females) stimulated growth of the genital cortex, as did artificial touch by experimenters. The ovariectomies and estradiol injections suggested that sex hormones drive genital cortex expansion during puberty, but not maintenance in adulthood. Likewise, chronic blockade of neural activity in genital cortex of females housed with males prevented the expansion of genital cortex expansion and also decelerated vaginal opening in females.

## Monitoring clock-neurons in freely moving flies

Measuring neuronal activity in freely moving animals is a critical area of tool development for systems-level neuroscience. In a recent report (*Proc. Natl. Acad. Sci. USA* **114**, E8780–E8787; 2017), a team at Brandeis University describes a noninvasive method for imaging and manipulation of specific fly neurons and correlating neural activity to real-time behavior. Using optogenetic manipulation of two groups of circadian neurons, the team shows that they can drive sleep or locomotor activity. Calcium imaging of the two groups of neurons also revealed that their activities closely (and oppositely) match sleep-wake cycles in the fly. The team's novel approach to imaging in behaving flies can be an added tool to traditional electrophysiological recordings and calcium imaging using GCaMP.

## Feedback for echolocation in bats

Animals that use echolocation are able to build a mental image of their environment using echo returns from their chirps. But previous research has not established what role audiovocal feedback might contribute to the sounds actively being produced by the echolocating animal. Animals, including nonecholocating animals like humans, use audiovocal feedback from ongoing vocal production to help shape vocalizations. Now, as demonstrated in a recent paper, it appears that echolocating bats use audiovocal feedback as well (*Proc. Natl. Acad. Sci. USA* **114**, 10978–10983; 2017).

Using acoustic jamming signals at precise time-points, the group of scientists demonstrate that echolocating bats can use audiovocal feedback, instead of echo feedback, to help adapt their chirps (or sonar calls). The results also show that the process is very rapid, and can happen on timescales of less than 100ms.

## In vivo monitoring of pH and chloride in neurons

Intracellular chloride and pH play crucial roles in regulating neuronal excitability, and hence, overall neuronal activity. However, methods to simultaneously measure both chloride levels and pH from neurons *in vivo* at a population level with cellular resolution are limited. Using a new two-photon based approach, Sebastian Sulis Sato *et al.* now demonstrate a robust method for capturing simultaneous changes in chloride and pH *in vivo* from neurons in mouse cortex (*Proc. Natl. Acad. Sci. USA* **114**, E8770–E8779; 2017).

The team used a genetically encoded fluorescent protein and multiple imaging and correction methods to make parallel measurements of chloride and pH, validating their approach using well-documented developmental changes in intracellular chloride levels. Overall, the new approach provides an avenue to understand the role of chloride and pH in neuronal processing and circuit dynamics in the intact brain.