

## IN BRIEF

## TECHNIQUES

## I did it my way

As data analysis approaches become ever more complex — particularly with data-rich technologies such as functional MRI (fMRI) — the differing analytical choices made by different labs have greater potential to yield different outcomes. Here, a raw fMRI data set was allocated to 70 groups for analysis against nine hypotheses. Although each team chose a different analysis workflow that produced substantial variation in rates of reported significant findings, a meta-analysis that grouped information from all teams showed a consensus in activated brain areas. This study highlights the effect of ‘analytic flexibility’ on conclusions drawn from data and the importance of validation and multiple analyses of the same data set.

**ORIGINAL ARTICLE** Botvinik-Nezer, R. et al. Variability in the analysis of a single neuroimaging dataset by many teams. *Nature* **582**, 84–88 (2020)

## PAIN

## Anaesthetizing chronic pain

General anaesthetics (GAs) have analgesic effects that are distinct from their loss-of-consciousness effects, but their mechanisms are unclear. Here, *in vivo* calcium imaging revealed a population of GABAergic neurons in the mouse central amygdala activated by GAs. Optogenetic activation of these neurons produced analgesic-like effects in naive mice and in acute and chronic neuropathic pain models; optogenetic inhibition produced opposite effects. Targeting these neurons might have potential in treating chronic pain.

**ORIGINAL ARTICLE** Hua, T. et al. General anesthetics activate a potent central pain-suppression circuit in the amygdala. *Nat. Neurosci.* <https://doi.org/10.1038/s41593-020-0632-8> (2020)

## SENSORY SYSTEMS

## ‘Seeing’ in the dark

Activity in the mouse visual cortex (V1) changes according to arousal level, but whether this is the case elsewhere in the visual circuit is unknown. The authors imaged calcium activity in retinal ganglion cell (RGC) terminals in the superior colliculus of mice placed on a treadmill to increase arousal. Whether under illuminated or dark conditions, treadmill running produced a change in activity (either an increase or decrease) in around half the terminals monitored. Moreover, activity of RGCs and downstream superior colliculus neurons also showed modulated responses depending on running speed, suggesting that arousal level influences activity from the retina to V1.

**ORIGINAL ARTICLE** Schröder, S. et al. Arousal modulates retinal output. *Neuron* <https://doi.org/10.1016/j.neuron.2020.04.026> (2020)

## SENSORY SYSTEMS

## Light darkens mood

Increased light exposure at night can exacerbate depressive symptoms. Here, increased light exposure at night in mice increased depressive-like symptoms. The authors mapped a retina-to-dorsal perihabenular nucleus (dPHb)-to-nucleus accumbens (NAcc) pathway that was more excitable at night than during the day and found that the resulting increase in activation of the NAcc could underlie the depressive-like behaviours. These findings could have implications for the effects of artificial light and mental health.

**ORIGINAL ARTICLE** An, K. et al. A circadian rhythm-gated subcortical pathway for nighttime-light-induced depressive-like behaviors in mice. *Nat. Neurosci.* <https://doi.org/10.1038/s41593-020-0640-8> (2020)

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mice passively listening to sounds. Spontaneous firing was increased in both regions in mothers compared with naive mice. Neurons in A1 of naive mice preferred USVs over NBN, and this preference was milder in mothers. By contrast, TeA neurons in naive mice showed no preference for USVs versus NBN or UPT, but in mothers these neurons preferred USVs over either control sound, suggesting that the TeA becomes tuned to USVs with the transition to motherhood.

Analysis of the population responses to USVs in the TeA of mothers revealed that neuronal responses were less correlated and showed reduced trial-to-trial

correlation compared with responses in naive mice, implying that TeA responses to USVs become sparser. In line with this, the authors used a decoder classification analysis to show that, compared with the TeA of naive mice, the TeA of mothers was more efficient at decoding USVs than decoding NBN or a UPT.

Together, these results show that the TeA undergoes tuning with motherhood that enables it to better encode behaviourally salient USVs.

Natasha Bray

**ORIGINAL ARTICLE** Tasaka, G. et al. The temporal association cortex plays a key role in auditory-driven maternal plasticity. *Neuron* <https://doi.org/10.1016/j.neuron.2020.05.004> (2020)

through monocular deprivation induced NOVA2 translocation out of the nucleus and reduced E29 inclusion *in vivo*.

What factors regulate NOVA2 localization in response to neuronal inactivity? The authors showed that the nuclear activity of the Ca<sup>2+</sup>/calmodulin-dependent protein kinase CaMKIV increases after chronic TTX treatment and that CaMKIV can interact with and phosphorylate NOVA2 to drive its translocation into the cytoplasm and regulate E29 splicing. Blocking CaMKIV activation prevented the TTX-mediated translocation of NOVA2, confirming the central role of this kinase in the response to inactivity.

Next, the authors considered the mechanisms through which a drop in neuronal activity is detected and relayed to the nucleus to trigger homeostatic changes in alternative splicing. They discovered that chronic inactivity leads to the activation of the voltage-gated calcium channel Cav1 and the translocation of CaM kinase kinase beta (βCaMKK) to the nucleus, where it activates CaMKIV to promote NOVA2 nuclear export.

This signalling cascade is reminiscent of one more usually associated with

neuronal hyperactivity, leading the authors to question how it is activated in the absence of spiking. Optical recordings of spontaneous activity in dendritic spines revealed an increase in spontaneous depolarizations and Ca<sup>2+</sup> transients following chronic TTX treatment. It was discovered that these result from increased surface expression of Ca<sup>2+</sup>-permeable glutamate receptors and can trigger the Cav1–CaMKK–CaMKIV cascade to signal to the nucleus.

This study provides insight into a poorly understood aspect of homeostatic plasticity and shows that such plasticity can employ mechanisms more usually associated with long term potentiation. Many of the molecular factors involved have been linked to neuropsychiatric disorders, suggesting this pathway as a potential source of new therapeutic targets.

Katherine Whalley

**ORIGINAL ARTICLE** Li, B. et al. Neuronal inactivity co-opts LTP machinery to drive potassium channel splicing and homeostatic spike widening. *Cell* <https://doi.org/10.1016/j.cell.2020.05.013> (2020)