NEURAL CIRCUITS

Making connections in the mouse hippocampus

Bienkowski, M.S. et al. *Nat. Neurosci.* **21**, 1628–1643 (2018)

Not long after moving to southern California to start his postdoc with Hongwei Dong, Mike Bienkowski found himself at a meeting listening to neuroscientists debate the divisions of the hippocampus. At the time, this small area deep in the brain was thought to be functionally divided in two, with a dorsal region responsible for aspects of cognition and information processing and a ventral region involved in emotion and stress responses. Where was the dividing line? "Nobody really knows," says Bienkowski. "Different people had different ideas about how to divide up the hippocampus."

Meanwhile, the results of gene expression studies were starting to suggest that it wasn't quite such a simple split, Bienkowski says. To better understand how gene expression and neural connectivity in the mouse hippocampus contribute to behavior, the field needed a better breakdown.

He started digging into the Allen Brain Atlas, a database with information about over 20,000 genes found in the mouse brain that Dong helped develop during his time at the Allen Institute in Seattle. Rather than evaluating all 258 hippocampal genes one-by-one, Bienkowski and his colleagues looked at multiple gene expression distributions to identify unique patterns. Their approach revealed 20 distinct regions in the mouse hippocampus, not two.

The notion of a dorsal-ventral split was not so far off though.

With their atlas built from gene expression patterns, the team moved in vivo. They used tracer molecules to anatomically outline the neural connectivity within the mouse hippocampus and then conducted a network analysis of the resulting map. They saw just two networks connecting all the different regions.

"That kind of ties it back together," says Bienkowski. "The way we can explain why behaviorists see this dorsal and ventral hippocampus when there's twenty different subregions is because they're wired together as two separate networks."

All of the data behind the team's Hippocampus Gene Expression Atlas plus tools investigate it are available online as part of the larger Mouse Connectome Project, which Dong leads at the University of Southern California. With funding from the NIH Brain Initiative, the lab plans to systematically map the connectivity of the entire mouse brain to the same level of detail that demonstrated for the hippocampus.

It'll then be on to defining specific cell types in the different regions and sub-regions of the brain and translating the results across species, from mouse to rat and larger animals and, eventually, on to humans.

Ellen P. Neff

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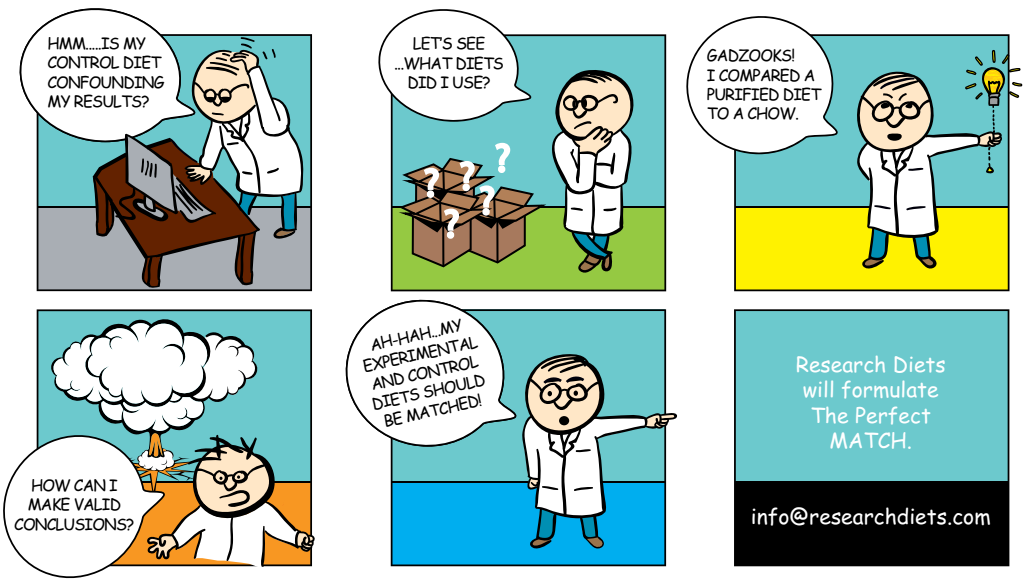

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