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News

Experimental design could reduce need for animal tests

Accounting for environmental changes may be better than trying to control them.

Lucas Laursen

Researchers could cut the use of animals in their experiments by changing the way they analyze their results, according to a study by scientists based in Germany and the United States.

Less standardisation could make animal experiments more reproducible. *Corbis*

In a typical animal experiment, researchers will try to standardize factors such as the animals' genetic backgrounds and laboratory conditions to make it as easy as possible for other researchers to reproduce their results later. Now, a team led by Hanno Würbel at the Justus-Liebig-University in Giessen, Germany, has reanalyzed a study of mouse behaviour by taking such genetic and environmental variations into account, and they got fewer spurious results, or false positives, than the initial study.

In an article in this week's *Nature Methods*[1], Würbel's team argues that initial chemical or drug screenings that include such natural variations in animals could help researchers cut the number of expensive secondary screenings and make their results more reproducible.

"In agricultural [and human] experiments it's absolutely recognized that there is uncontrollable variation," says study coauthor Joseph Garner of Purdue University in West Lafayette, Indiana. "It's only in laboratory animals that we have this draconian idea that we can control all variation."

New analysis

To see whether a different experimental design might work better, Garner, along with Würbel and his student Helene Richter, reanalyzed data from a published multilaboratory mouse behaviour study[2]. They report that analyzing the data from the mice without accounting for different environmental conditions created about 10 times as many spurious results as when they directly compared such mice in what they call a "heterogeneous" experimental design.

Garner says that uncontrollable variations in the conditions from lab to lab may be throwing off the results. He blames interference from environmental factors such as the location of a mouse's cage within a lab, which might introduce additional light, noise or odours that can cause behaviour-changing anxiety.

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In the drug-discovery process, false positives, or drugs that show promise in an initial screening, must be replicated with independent experiments using different animals in other laboratories. Würbel says that cutting down the number of false positives in the initial screening by comparing different strains of mice side-by-side in the same lab could help researchers avoid many of the secondary screenings they currently perform.

"That might be a good thing to do, but I think they would need to show it experimentally," says John Crabbe of the Oregon Health & Science University in Portland.

Back to the bench

Crabbe published a study[3] in 1999 that found that certain mouse behaviours, particularly those thought to be genetically influenced, were easy to replicate from one lab to the next, but others, particularly those involving emotional responses, were more difficult to replicate.

Crabbe argues that problems with replicability also occur in other fields, including biochemistry and physics, and that in practical terms, any provocative experiment "is going to be done again anyhow ... and robust findings will persist".

In an accompanying article in *Nature Methods*[4], neuroscientist and geneticist Richard Paylor, of Baylor College of Medicine in Houston, also says a fresh experiment designed to test Würbel's idea is the "obvious next step".

Würbel says he and his team are already working on such an experiment. "It's impractical to design every experiment as a multilab study," he concedes. "What we need to work out [next] is one or two factors that we can vary within the lab."

References

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