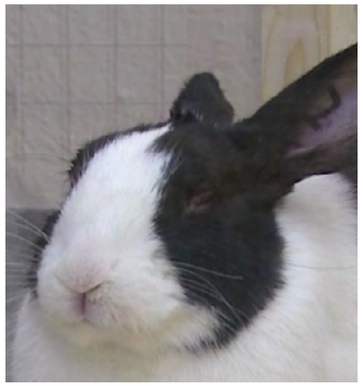
Give Them Two Aspirin…

Researchers push for use of painkillers in lab animals to help them cope with pain

A rabbit that isn't in pain looks at the camera with its ears erect and eyes open. In contrast, a rabbit in pain appears to be wincing with its eyes closed and ears folded back. In the early 1990s, researchers argued that pain killers would greatly benefit lab animals without interfering with research results.

Screenshots courtesy of Paul Flecknell.



Lab animals — like all animals — feel pain. Why then do we not give them analgesics to help with the pain?

This was a question that Paul Flecknell first raised in the late 1970s. At the time, he was a young veterinarian with the UK's Medical Research Council and, rather than delving into the issue, had to focus his research on neonatal physiology. But about a decade later, Flecknell joined Newcastle University as a professor of laboratory animal science and began to develop a research program that explored the issue of pain in lab rodents and the use — or lack of use — of painkillers.

> **"It's a great example of how sharing your research increases its impact."**

Each year more than 7 million research and veterinary procedures are carried out across the world on rodents and rabbits. With research in particular, scientists often hesitate to administer drugs for fear of it interfering with the study's results. But, Flecknell argued, pain could also interfere with results. In 1992, he traveled to Guelph, Ontario on a Canadian Research Fellowship and collaborated with clinical veterinarians who were developing a pain scoring system for dogs and cats. "I was there for three months, which gave me time to talk to those people and others and develop more research ideas," says Flecknell.

When Flecknell returned he began studying tattooing in rabbits — a procedure that is carried out to mark and identify the animal and involves piercing the skin of the rabbit's ear. As a way to measure pain that the rabbit might feel as a result of this procedure, Flecknell and his team measured changes in blood pressure as well as behaviour – was the rabbit wincing or vocalizing, for example. But this process was time consuming; studying changes in each animal's behaviour took at least 10-15 minutes.

Back in Canada, Jeff Mogil, a pain researcher at McGill University in Canada had developed a grimace scale based on changes in facial expressions of mice in pain, and Flecknell decided to apply that approach to rabbits by videotaping them before, during, and after the tattooing procedure. "It's a great example of how sharing your research increases its impact," says Flecknell. "Jeff Mogil published his grimace score online and provided a whole set of illustrations to help others use it."

As part of the effort, Stephanie Keating, then a veterinary anesthesia resident visiting from Guelph, watched hours of footage of the rabbits and concluded they also pull pain faces, similar to what researchers had seen in mice — squeezing their eyes, bulging their cheeks, and scrunching up their noses.

"[Stephanie's] coming to Newcastle was just one of those really fortuitous things," says Flecknell. "She'd wanted to come because we were working on pain and anesthesia, and she was interested in that as a resident. It just happened to coincide with the study, so we got an extra pair of hands. It turned out that she made a major contribution to the study." The collaboration also helped Keating expand her view on pain recognition and treatment. "The experience has guided my interests and shaped my career to this day," says Keating.

In order to score pain in either rodents or rabbits, researchers take multiple photos and pick those that have the animal looking directly at the camera. They look at the eyes, whiskers, cheeks, and ears and score each expression. Researchers then add that up to get the grimace score and, based on the score, might recommend a small dose to help alleviate the pain. As part of the effort, they redo the test to determine if the painkillers they have given the animals have worked.

"We've got a rat and mouse formulary that can provide likely effective doses of analgesics," says Flecknell. "We would predict that potent or morphine-like drugs would be most effective against moderate to severe pain. The nonsteroidals — the aspirin-like drugs — will be better for mild to moderate pain." Flecknell also recommends that researchers use both types of analgesics at once, just as we would for ourselves because of the effectiveness of a multimodal analgesic approach.

One concern that often arises, however, is whether these analgesics interfere with the study results and outcome. According to Flecknell, it depends on the dosage that's administered as well as its duration. "If you just give a short treatment around the time of surgery, it's going to have minimal effects on your animal model," he says. Still, researchers must consider the differences in genetic strains of rats and mice that could affect how much pain the animals express as well as the efficacy of different analgesics.

Over the years, Flecknell has given seminars, conferences, and workshops as well as helped train veterinarians and researchers on the implementation of pain assessment methods. Several agencies and committees have adjusted their regulations regarding use of analgesics to align with the findings and recommendations. Flecknell is also helping develop an e-learning resource, which will outline facial expressions of rodents experiencing pain as well as provide information on drugs and dosage. In addition, researchers are currently exploring the possibility of using facial responses on domesticated and farm animals. "Our argument is that why create models of pain in the lab when you might be able to use some of these natural, larger animal models to study what's going on in a natural setting."

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