Countering the caregiver placebo effect

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Credit: North Carolina State University

How do you know that your pet is benefiting from its pain medication? A new clinical trial design from North Carolina State University researchers could help overcome pet owners' unconscious observation bias and determine whether the drugs they test are effective.

When animals are recruited for clinical trials, particularly for pain medications, researchers must rely on owner observation to determine whether the medication is working. Sounds simple enough, but as it turns out, human and animal behavior can affect the results.

All clinical trials have a "control" – often a set of participants that receive a placebo in place of the medication. In human trials researchers have long struggled with the placebo effect – the psychological impact that the patient's belief in the treatment can have on his or her condition. To get around this, researchers put a lot of effort into developing tools sensitive enough to distinguish between the placebo effect and the medication's "real" effect.

"In veterinary medicine, we're one step removed from the patient, and so we run into what we call the 'caregiver placebo effect,' which is how we refer to a number of factors that result in unconscious influence on owners' responses," says Margaret Gruen, NC State veterinary clinician and researcher. "Merely observing behavior can change it, and any changes in daily routine, like administering medication, will affect the way you relate to that animal and change its behavior." This makes controlling for the placebo effect more difficult, and even the most sensitive detection techniques still have trouble distinguishing between the real and the placebo effect.

Take cats for example. Inscrutable at the best of times, they are also notorious for their reluctance to take medication. So if your cat is participating in a clinical trial for pain medication, both your relationship to the animal and its behavior are going to undergo some pretty significant changes once you start administering medication. And these changes will occur whether or not your pet likes the medication or placebo. That, coupled with your optimism about what the results may be and the fact that you're now closely scrutinizing the cat's every move, can change your responses. "We cannot get away from this," says Dr. Gruen, "so we need to find a way around it."

To do so, Gruen and lead researcher Duncan Lascelles tested a low dose of a drug commonly used for pain management in cats with degenerative joint disease. They started by giving all of the trial participants an initial

two-week placebo to get the animals used to taking the medication. The owners were aware that they were giving placebo during this period. This was followed by a three-week trial, with half of the participants receiving the drug and half receiving placebo, without the owners knowing which was which. Finally, there was a three-week "blinded placebo washout," in which all of the participants were again taking a placebo, but the owners weren't aware of the change.

"The final three-week period is where we were able to get real results about the usefulness of the medication," Gruen says. "During the three week medication trial, all of the owners indicated that their pets improved, which is due to the caregiver placebo effect. But during the washout phase, owners of the cats who had been receiving the medication in the first phase said that their pet's signs of pain were returning, while the owners of cats who had received placebo in the first phase did not notice any change.

"So we were able to circumvent the placebo effect and determine that this medication is effective in cats with degenerative joint disease," Gruen continues. "We understand that this approach will need further investigation, but we believe this design may be useful both in veterinary studies and in human studies where the placebo effect is particularly strong."

Gruen and Lascelles published their new trial design and results in the *Journal of Veterinary Internal Medicine*.

Provided by North Carolina State University