The Ethics of Using Animal Models to Study Treatment of Phantom Pain

To the Editor—It has been known for some time that transecting certain animals' sciatic and saphenous nerves can, after a latent period, provoke them to attack and devour their toes and feet. The basis of this phenomenon of "autotomy" (literally, eating oneself) is believed by many (including the authors of the recent article on this subject published in ANESTHESIOLOGY) to be "painful or dysesthetic sensations referred to the denervated limb and represent[ing] a behavioral model of phantom limb pain or anesthesia dolorosa."

As the director of a pain clinic, I have, on many occasions, been moved by the lamentations of my patients with peripheral neuralgia. I am in favor of scientific investigation into this problem and, in fact, am personally directing two research projects (one in humans, the other in animals) aimed at finding new solutions to this important clinical problem. Limits should be placed, however, on how much suffering we inflict on animals during our exploration of ideas that may eventually benefit humans. Anesthesiologists, specialists in alleviating pain, have, I believe, a special obligation to help set such limits. Inflicting laboratory animals with prolonged, inescapable pain leading to self-mutilation breeches our obligation to conduct humane research. We must find other means to achieve our ends.

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In Reply—We have much sympathy for Riopelle's views, for we too have been touched by the suffering of amputees with intractable phantom limb pain. We have been frustrated by our inability to relieve their anguish and distress, and we are disillusioned with our colleagues who do not take seriously the reports of amputees who continue to suffer with phantom limb pain that is identical to the pain they experienced in their limb before amputation. That animals show behavioral evidence of persistent injury-induced central neural activity in the absence of any experience of the injury in the awake state strongly suggests that, among amputees, the similarity in the sensory component of pain before and after amputation does not depend on conscious awareness at the time of injury.

The ethical and moral boundaries involved in studying chronic pain in animals have been debated in the past and continue to be a source of concern for the scientific community as well as the public at large.1-3 The International Association for the Study of Pain (IASP) has outlined ethical guidelines for investigations of pain in conscious animals.4 The autotomy model falls within IASP guidelines and is commonly used as an animal model of phantom limb pain and anesthesia dolorosa.

Our use of this procedure was based not only on its appropriateness as an animal model of neuropathic pain, but also on the degree to which it is ethically acceptable. It is important to note that the rats do not feel pain as a result of their biting, because the entire paw has been denervated and therefore is insensitive to stimulation. Furthermore, the rats do not show signs of severe suffering; they eat, gain weight, groom, and engage in sexual behavior in a normal manner. It has been suggested that in this model, rats are not subjected to severe prolonged pain, but rather to mild dysesthesias combined with occasional brief attacks of more intense pain.5 The lack of behavioral signs of severe suffering, combined with the potential benefits of such research to our understanding of pain mechanisms and therapy, points to the justification of such investigations from an ethical standpoint. As an additional ethical consideration, and as described in the paper, the rats were killed within 5 days of autotomy onset. We cannot advance our understanding of these disorders and improve available treatments for chronic pain sufferers without appropriate animal models.

Our decision to submit the paper to ANESTHESIOLOGY was motivated by a desire to address anesthesiologists—specialists who have much to offer patients about to undergo amputation. The clinical implications of our study are clear. First, pain should be relieved prior to amputation. If there is pain in the limb before amputation, there is a good chance that it will persist after amputation (or at least contribute to increased phantom limb pain intensity). Second, just as a preamputation lesion may persist as a phantom pain "memory" and cause the patient continued suffering and distress, the effects of cutting tissue, nerve, and bone during the amputation may persist as well. The use of a general anesthetic does not protect the patient adequately from the surgical trauma because these effects are independent of conscious awareness. Preoperative regional anesthesia should block the surgically induced central neural changes from contributing to postoperative phantom limb pain and stump pain.

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