Beyond the use : the paradox of scientific animal utilization

Ivan Montiel[1, 2, 3]

[1]Institut Pasteur, Université Paris Cité, Department of Neuroscience, F-75015, Paris, France

[2]Sorbonne Université, Collège Doctoral, F-75005, Paris, France

[3]Université Paris-Cité, CNRS, Integrative Neuroscience and Cognition Center, 75006, Paris, France

FENS CARE Writing Competition 2024

"This is the last time I'm doing this." Perfusion of an animal is a deeply dramatic task, an image that seems taken from an Alfred Hitchcock movie. I cleaned the room with some fear because PFA is carcinogenic. A cloud of doubts grew as I washed the equipment, but they all converged into one: Is this necessary? Is my soul being corrupted by so-called scientific curiosity? I filled out thousands of forms with abyssal haste: dosages, times, weights, and so forth. I wrote down all the data as quickly as possible. I just wanted to leave. There was such meticulousness in ending a life, where each note served as a grim reminder of the process. I left the animal facility at a brisk pace.

The anguish wouldn't let me go. I decided to take it step by step, tracing every glimmer of logic I could find in this situation. The silver lining of having a "crisis of scientific vocation" is that, at least in my case, it happens to me in Paris: so many beautiful streets contrast sharply with my awful feelings.

What hurts the most is that last moment when the anesthesia does its job and the animal falls asleep… a dream from which it does not return. That and other thoughts attacked me without any compassion.

Leaving the Pasteur Institute felt like a breath of fresh air, but it was raining outside. It was lightly raining over the city streets. Meanwhile, doubts were heavily raining on me.

I began to remember, to search for the beginning; hunting traces of memories in an attempt to find meaning. Everything led me to the first Thesis Advisory Committee meeting. "I seek to study how the brain allows the storage of new memories while maintaining previous ones," I said. My first thesis committee pressed me in the most

determined and direct manner possible: "Why use animals? Can't you study that with humans or in vitro methods?" I remember replying, "My experimental approach requires mice because one of my objectives is to determine if there is a change in the firing rate of the hippocampus when the animal has to create a new memory. Under these experimental conditions, I cannot use another method." I recall a silence that I wanted to fill with more arguments: "We have used a mathematical model to predict this experiment, and now we need to test it. We will evaluate this hypothesis with a limited number of animals, utilizing previous results obtained in the laboratory."

Now I understand why my advisory committee insisted so much on the use of animals. I have reasons, but are these reasons sufficient?

"Unfortunately, computational or in vitro models are far from achieving accurate data on how the brain generate cognitive processes as complex as memory", I concluded. The vast street of Vaugirard began to be filled with my thoughts and doubts.

Why had this last series of experiments affected me so much? Commitment. That is why. For nearly a month, my weekends revolved around my mice. Throughout that time, I always gave the same answer: "No, no, no. I have a training session tomorrow with my mice. Maybe I am free until 20 h"; "I'd like to, but tomorrow I have a recording session." Family, friends, dates, colleagues, all displaced by a group of mice.

I believe I began to feel attached to those mice. Not too much, because it could influence the interpretation of the results; not too little, because we need to detect if the animal experiences pain, discomfort, fear, or any negative emotion that could affect the results. I think our relationship was characterized by great respect and cordiality; the same attitude one has when receiving family or friends who come to visit.

Remembering those mornings of work with my mice brings a smile to my face. Arriving early, setting a very strict training schedule (always at the same time), preparing everything in advance. I even invented my own rules: never work with animals if I was in a bad mood or stressed.

"Anesthesia, analgesia, future doctors. You have to follow these steps," said Myriam Mattei, the manager of the Pasteur Animal Facility. "Changing every syringe for each injection? Isn't that an expense?" Myriam, very serious, responded: there is no unnecessary expense in animal care. Changing globes frequently, checking water

quality, food, or drugs to administer, and monitoring signs of emotional and physical well-being. You have to make sure that everything is perfect.”

At that moment, I thought, "Come on, Myriam! It feels like we're caring for these mice as if they belonged to the President of France, or worse, to my father-in-law." But truth be told, I appreciated having so many manuals. In Mexico, where I come from, we have similar practices, but the training isn’t as continuous, and having all this systematization makes learning and sharing easier. That's what I liked about Europe. And even though we all fear the animal handling inspector, we all agree on the necessity of their work.

Inadvertently, I had arrived at the Luxembourg Garden. The horrible ghosts of my memory continued to accompany me. Suddenly, I saw a man with his dog: a beautiful Old English Sheepdog. I reflected on the care of pets compared to the care we provide animals for scientific research. I realized that now I place more importance on and am more sensitive to animal welfare.

I remember stopping talking to a cousin once because his dog "accidentally" ate a chocolate cookie. "Do you know what would happen to me if I made that kind of mistake with my mice? I don’t even want to think about it. It would be something very serious."

I saw the man pulling forcefully on the leash of his dog. I wished that the protocols we have for animal care were also followed by pet owners.

In my train of thought, I recalled the statue commemorating the discovery of the rabies vaccine: a child fighting against a fierce and angry dog, which had its small arm between its jaws. "Animal research is necessary," I thought. This and other vaccines, for example, were obtained thanks to studies involving animals. Many lives were saved.

In neuroscience, examples of major discoveries that have changed health and our understanding of the world are plentiful:

Cajal, who worked with bird brains to demonstrate that the brain is not a network and to stablish the modern neuronal theory.[1]

Hodgkin and Huxley, through their studies on squid axons, not only advanced our comprehension of the mechanisms behind propagating action potentials via voltage-gated ion channels, but also established the foundational framework for investigating and analyzing ion channel kinetics.[2]

Rita Levi-Montalcini, who used goodness knows how many mice and chicken embryos to describe the process of cell generation, which would later be called growth factors and now allow us to understand senile dementia, tumors, and nerve and tissue deformities.[3]

However, the study I like the most, because I am a devoted lover of memory, is that of O'Keefe and Moser, with their discoveries on how neuronal cells form a positioning system in the brain and its implications in memory and cognition.[4]

All these discoveries have changed our understanding of nature and human capabilities. They are not the only ones. An army of scientists has always fought against various diseases of the nervous system that cause pain to many people: autism, schizophrenia, Parkinson's disease, amyotrophic lateral sclerosis, and the one that terrifies me the most, Alzheimer's disease.

My first approach to science was with patients suffering from this illness. I saw how Alzheimer's progression consumed their identity and their memories. I experienced the suffering of their families and the helplessness of not having a treatment. We sacrificed a mouse in exchange for a grandfather, a brother, a mother.

Science is also a ritual for caring for and protecting life. How can we not strive to improve and discover better methods and results when someone, somewhere, is waiting for our answers? But what about the animals?

I was so lost in my thoughts that I did not realize I had arrived at the Pantheon: "*Aux grands hommes la patrie reconnaissante".* I then thought that one cannot achieve any distinction without a firm ethical commitment. Furthermore, I recognized that the balance between all the benefits we obtain from using animals in research cannot be achieved without minimizing animal suffering.

The 3Rs make more sense to me than ever: replacement, reduction, and refinement[5]. Everything revolves around that. The mysteries surrounding life, the brain in our case, cannot be studied without that respect, without that care.

Once again, science surprises me. Behind every variable, instrument, participant—behind everything—there is always a reason that goes beyond mere preference or belief.

The view from the Pantheon was imposing. The rain stopped. The majesty of Paris is always indescribable, just like the moments when calm arrives.

My mind replaced intrusive thoughts with more rational ones: Mice, and all species we work with, are held to high standards of care—feeding, stimulation, housing, and continuous medical monitoring, where even the slightest issue or discomfort must be promptly addressed. We do this to achieve good results, but also out of respect for life.

We are still far from completely ceasing to use animals in research. However, we have made significant efforts. By combining mathematical models, in vitro experiments, and even results from other studies, we have succeeded in reducing the number of animals used. I believe that the scientific community should continue to prioritize the replacement and refinement of animal use efforts.

There is no scientific cruelty, but rather a deep desire to understand life—a paradox that I hope the future will resolve as soon as possible.

The Eiffel Tower began to sparkle. “This moment is so beautiful”, I though.

References

[1]Ehrlich, Benjamin, 'Cajal’s Legacy', The Dreams of Santiago Ramón y Cajal (New York, 2016; online edn, Oxford Academic, 1 Dec. 2016), https://doi.org/10.1093/med/9780190619619.003.0001, accessed 3 May 2024.

[2]Catterall, W. A., Raman, I. M., Robinson, H. P., Sejnowski, T. J., & Paulsen, O. (2012). The Hodgkin-Huxley heritage: from channels to circuits. The Journal of neuroscience : the official journal of the Society for Neuroscience, 32(41), 14064–14073. https://doi.org/10.1523/JNEUROSCI.3403-12.2012

[3]Chao, M. V., & Calissano, P. (2013). Rita Levi-Montalcini: in memoriam. Neuron, 77(3), 385–387. https://doi.org/10.1016/j.neuron.2013.01.019

[4]Sugar, J., & Moser, M. B. (2019). Episodic memory: Neuronal codes for what, where, and when. Hippocampus, 29(12), 1190–1205. https://doi.org/10.1002/hipo.23132

[5]Fenwick, N., Griffin, G., & Gauthier, C. (2009). The welfare of animals used in science: how the "Three Rs" ethic guides improvements. The Canadian veterinary journal = La revue veterinaire canadienne, 50(5), 523–530.