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The impact of an ethics committee on animal protection
Josué Lopes Corrêa Neto¹, Cláudio Lorenzo², Mauro Niskier Sanchez³

Abstract
The creation of animal ethics committees in teaching and research establishes a new ethics in relations with non-human animals. The present article carried out a statistical study of data from 390 research protocols evaluated over eight years by a commission at one Brazilian university, to determine if its actions brought about a reduction in suffering and a proportional decrease in the practice of euthanasia. A statistical significance study was carried out using an extension of the Wilcoxon test, seeking to verify a long-term trend of protection procedures, such as lower predicted levels of stress and pain in protocols, more frequent use of anesthesia and sedatives and a reduction in euthanasia. The results were statistically significant for all three of these items, suggesting a concrete effect of animal protection. The method used is proposed as a form of evaluating the use of these procedures by commissions.

Keywords: Ethical review. Bioethics. Animal experimentation. Euthanasia, animal.

Resumo
Influência de uma comissão de ética na proteção de animais
O estabelecimento de comissões de ética no uso de animais em ensino e pesquisa concretiza nova ética nas relações com animais não humanos. Realizou-se estudo estatístico sobre dados de 390 protocolos de pesquisa avaliados durante oito anos por uma comissão em uma universidade brasileira, buscando determinar se essa atuação foi capaz de reduzir o sofrimento e diminuir proporcionalmente a prática de eutanásia. Empregou-se extensão do teste de Wilcoxon para verificar a tendência de procedimentos de proteção como melhor previsão de estresse e dor nos protocolos, uso mais frequente de anestesia e sedativos e redução de eutanásias executadas. Os resultados mostraram significância estatística em todos os três itens, sugerindo efeito concreto na proteção animal. O método utilizado é proposto ainda como forma de avaliar o uso desses procedimentos pelas comissões.


Resumen
Influencia de una comisión de ética en la protección de animales
El establecimiento de comisiones de ética en el uso de animales en enseñanza e investigación concreta una nueva ética en las relaciones con los animales no humanos. Se realizó un estudio estadístico a partir de los datos de 390 protocolos de investigación evaluados durante ocho años por una comisión en una universidad brasileña, buscando determinar si esa actuación fue capaz de reducir el sufrimiento y de disminuir proporcionalmente la práctica de la eutanasia. Se empleó una extensión del test de Wilcoxon para verificar la tendencia de procedimientos de protección, como una mejor previsión de estrés y dolor en los protocolos, el uso más frecuente de anestesia y sedantes, y la reducción en la realización de eutanasia. Los resultados mostraron una significancia estadística en estos tres ítems, sugiriendo un efecto concreto en la protección animal. El método utilizado se propone, también, como una forma de evaluar el uso de estos procedimientos por parte de las comisiones.


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Declaram não haver conflito de interesse.
The use of non-human animals (referred to henceforth as animals) to acquire knowledge and to develop life sciences began in the Antiquity and continued throughout history to the present day. Despite various social movements that campaign against the use of animals in scientific research, their use is still considered absolutely essential to research, especially in the biomedical and veterinary areas. Baumans estimates that between 75 and 100 million vertebrate animals are used per year in research and experiments. Mice and rats are the most used species.

The philosophical discussion about the protection of animals against human exploitation started in a more systematic way only on the 18th century despite the use of animals by Homo sapiens being as old as our earliest ancestors. It was from the emergence of Utilitarianism that the moral consideration of animal rights started to develop. Jeremy Bentham asks a fundamental question to redirect the ethical stance towards animals: “…the question is not, Can they reason? or, “Can they talk?” but, Can they suffer?”

The main philosophical idea developed in the twentieth century by authors such as Russell and Burch, Peter Singer and Tom Regan was the notion that ethics is directed not only to beings capable of thinking (conscious), but to all beings capable of feeling (sentient). The first two authors are responsible for the systematisation of procedures to protect animals used in scientific research, and the last two are considered the main theorists on law and animal liberation. Their work reinforced the need for committees to evaluate the use of animals from an ethical viewpoint. The first committee on animal rights was established at Harvard University in 1907. The impact of the work of the mentioned authors stimulated a widespread dissemination of similar committees at research and educational institutions around the world.

The ethical principles proposed by Russel and Burch, which are still the most used today, are known as the three “Rs”, initials that stand for three guiding principles: replacement, reduction and refinement. They propose, respectively: 1) To replace animal experiments in educational institutions and replace procedures with animals for alternatives whenever scientific or pedagogical objectives can be achieved without their use; 2) to reduce the number of animals used in experiments to the minimum number necessary to fulfil the objectives of the study; 3) Refine the way of conducting scientific experiments to ensure the least possible suffering for the animals involved. This last guiding principle implies the obligation to include in the protocol of an experiment the possibility of pain and distress and to demonstrate the use of minimisation interventions through sedatives and anaesthetics, for example. Other systematisations have been proposed, such as Fagundes and Taha, to determine criteria that define the ethical legitimacy of research with animals through the social and scientific relevance of the expected results.

The practice of euthanasia, considered unavoidable in several experiments with drugs or in surgical procedures, has gained special relevance, and scientists today try to avoid it whenever possible. They also try to regulate its implementation and to allow only forms which are considered humanitarian. The Federal Council of Veterinary Medicine in Brazil published a resolution in 2002 that defines the forms of euthanasia considered ethically acceptable. The use of anaesthetics and sedatives are among the most recommended procedures for a more humanitarian euthanasia, reducing distress and pain.

These systematising ethical proposals address both the planning of procedures and the ethical review of educational and research protocols by members of the Animal Use Ethics Committees (Comissões de Ética do Uso Animal - CEUA) and the formulation of normative documents that seek to guide the work. The issue of protection and welfare of animals involved in educational and research experiments is currently regulated in Brazil by the Law 11794/2008, also known as Arouca Law.

It was the Arouca Law that established and gave legitimacy to the national system of ethical evaluation of animals use despite the fact that committees have appeared in Brazilian institutions well before the promulgation of this law - the CEUA of the Biology Institute of the University of Brasilia (CEUA-IB / UnB) where this study has been carried out, for example, was created five years before the law’s publication. The norm determined the creation of the National Animal Experiments Control Council (Conselho Nacional de Controle de Experimentação Animal - Concea), a normative, advisory and appeals body that is of the Ministry of Science, Technology, Innovation and Communications. The objective is to coordinate scientific procedures with animals in the country, as well as to accredit and monitor the activities of the CEUA in educational and research institutions throughout the country.

The creation of this system has also boosted the production of a national scientific literature both with regard to the operationalisation of CEUAs and the process of revision of protocols by its members. Feijo defines CEUA as multidisciplinary spaces in which one part must discuss ethics regarding animal life and where the human being should be the spokesperson for animals. Miziara and colleagues argue that the review should focus, above all, on the analysis of the special care that animals should receive in experiments, as recommended by Chapter IV of the Arouca Law.
In addition to these authors, the review by Markus \(^\text{14}\) based on information from the National Scientific Electronic Library Online (SciELO) on the subject found 700 articles and a heated discussion on the ethical approach of animal use in research. The review used “animal experimentation” as keyword. This research showed a significant reduction in the use of animals in educational procedures, highlighting the growing preference for alternative methods. These data corroborate a previous review by Diniz et al. \(^\text{15}\), who found that only 1% of the total number of animals involved in protocols evaluated by the CEUA were used for educational procedures.

However, it was not possible to find in the national literature a study that evaluated the tendency to use animal protection procedures caused by the influence of the CEUA. The objective of this article is to make a statistical study about the eight years of CEUA-IB / UnB activity, in order to verify animal species involved in research and the procedures trend to reduce suffering in the protocols evaluated.

### Material and method

A quantitative documentary study was conducted based on the submitted protocol forms evaluated by CEUA-IB / UnB between 2003 and 2010. A total of 390 submission protocol forms for animal research were analysed. The 24,689 animals involved in the protocols examined were categorised as: laboratory animals (rodents); wild animals (small primates, fish, reptiles, amphibians, bats, birds and marsupials); domestic animals (dogs and cats) and livestock (sheep, pigs, goats and horses). Protocols related exclusively to stillborn animals, invertebrates, carcasses and animal organs were excluded. The documents were analysed using two procedures:

1. Quantification of the typology of animals involved in research procedures in the determined period with analysis of the statistical significance of this variation over the years. This procedure was considered essential, since euthanasia and experiments without the use of anaesthetics and sedatives are more frequent when there is a higher proportion of laboratory animals and wild animals in the sample;

2. Study of the statistical significance of trends over time regarding protection procedures such as description in the protocols of prediction of distress and pain as well as the use of respective minimisation techniques such as anaesthetics and sedatives. Another example of protection procedure studied was the significance of the proportional number of euthanasia performed. The study used non-parametric test to analyse the trend in ordinal groups (extension of the Wilcoxon test). The study used Stata software, version 12. Statistical significance was considered when \(p \geq 0.05\).

### Results and discussion

#### Quantity and characteristics of animals and variation statistics

Table 1 shows the categorisation of all animals involved in the researches described in the 390 protocols from the eight years covered by the study.

<table>
<thead>
<tr>
<th>Year</th>
<th>Total per year</th>
<th>Quantitative distribution of animals categories</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Laboratory Animals</td>
</tr>
<tr>
<td>2003</td>
<td>1.932</td>
<td>1.560</td>
</tr>
<tr>
<td>2004</td>
<td>1.701</td>
<td>1.246</td>
</tr>
<tr>
<td>2005</td>
<td>2.856</td>
<td>2.461</td>
</tr>
<tr>
<td>2006</td>
<td>3.522</td>
<td>2.858</td>
</tr>
<tr>
<td>2007</td>
<td>2.894</td>
<td>1.836</td>
</tr>
<tr>
<td>2008</td>
<td>2.794</td>
<td>1.933</td>
</tr>
<tr>
<td>2009</td>
<td>5.115</td>
<td>3.460</td>
</tr>
<tr>
<td>2010</td>
<td>3.858</td>
<td>2.361</td>
</tr>
<tr>
<td>General Total</td>
<td>24.672</td>
<td>17.715</td>
</tr>
<tr>
<td>Percent</td>
<td>100%</td>
<td>71,8%</td>
</tr>
</tbody>
</table>
Laboratory animals, as expected, were the most used among the 24,689 animals involved in the eight years covered by the study. They total 18,083 individuals, what is equivalent to 73.24% of the total number of animals. Wild animals represented 2,706 individuals or 10.96% of the total; 2,230 or 9.03% of the total were domestic animals; and finally, 1,663 or 6.73% of the total were livestock. The first statistical analysis sought to determine if there was a significant variation in the general increase over time of animals involved in researches and showed a trend of increase in the limit of the significance with \( p = 0.051 \).

Then we sought to investigate whether there was a statistically significant variation in the animal typology, since the proportional increase of large animals could imply a greater use of sedatives and anaesthetics or a reduction of euthanasia. This alteration would depend on the variation of animal typology, not on a change of conduct of researchers when implementing procedures of refinement in order to minimise the suffering.

It was observed that the data on the proportional number of animals used according to categories over time show a tendency of a decrease in the number of laboratory animals \( (p=0.051) \), but without any statistically significant increase in the proportion of wild animals \( (p = 0.208) \), livestock \( (p = 0.147) \) and domestic animals \( (p = 0.068) \). The absence of significant variation in the use of animals that are usually less involved in more aggressive experimental practices and are usually more induced to euthanasia confers additional confidence that the results signal a change in behaviour towards the use of animals. This allows to infer that the findings would not be related to the variation of animal typology.

**Statistical significance of the proportion of protection procedures**

The submission form presents data on prediction of pain, distress, surgery, use of sedatives, anaesthetics and euthanasia. The correct filling of this form and the detailed description of those procedures in the protocol are of fundamental importance for the evaluation made by the members of CEUA. A more accurate prediction of distress and pain may demonstrate that the research shows a greater sensitivity to animal suffering and allows CEUA to assess whether procedures to minimise suffering, such as the use of anaesthetics and sedatives, are suitable to the estimate.

The prediction of surgery allows us to evaluate whether sedatives and anaesthetics are being used only when there is surgery, to refine other experiments capable of causing pain and distress, or as a more humane way of inducing euthanasia. Finally, the prediction of euthanasia allows CEUA to evaluate when this procedure is absolutely necessary to the experiment or if the number of animals involved was reduced to the minimum number that would still give significance to the research. Table 2 presents absolute numbers and a percentage of the total number related to each of the description items of the protocols that are important to assess the level of protection.

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Animals</th>
<th>Prediction of Distress</th>
<th>Prediction of Pain</th>
<th>Prediction of Anaesthesia and sedatives</th>
<th>Prediction of Surgery</th>
<th>Prediction of Euthanasia</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>1.932</td>
<td>76</td>
<td>12</td>
<td>1.062</td>
<td>744</td>
<td>1.692</td>
</tr>
<tr>
<td>2004</td>
<td>1.701</td>
<td>206</td>
<td>60</td>
<td>1.256</td>
<td>778</td>
<td>1.426</td>
</tr>
<tr>
<td>2005</td>
<td>2.856</td>
<td>64</td>
<td>80</td>
<td>2.392</td>
<td>1.026</td>
<td>2.851</td>
</tr>
<tr>
<td>2006</td>
<td>3.522</td>
<td>800</td>
<td>451</td>
<td>2.873</td>
<td>1.682</td>
<td>2.989</td>
</tr>
<tr>
<td>2007</td>
<td>2.894</td>
<td>692</td>
<td>624</td>
<td>2.159</td>
<td>1.240</td>
<td>2.282</td>
</tr>
<tr>
<td>2008</td>
<td>2.794</td>
<td>1.137</td>
<td>512</td>
<td>1.644</td>
<td>1.080</td>
<td>1.916</td>
</tr>
<tr>
<td>2009</td>
<td>5.115</td>
<td>2.216</td>
<td>1.884</td>
<td>2.880</td>
<td>1.856</td>
<td>3.552</td>
</tr>
<tr>
<td>2010</td>
<td>3.858</td>
<td>2.481</td>
<td>2.025</td>
<td>2.587</td>
<td>762</td>
<td>2.376</td>
</tr>
<tr>
<td>Total</td>
<td>24.672</td>
<td>7.672</td>
<td>5.648</td>
<td>16.853</td>
<td>9.168</td>
<td>19.084</td>
</tr>
<tr>
<td>Percent</td>
<td>-</td>
<td>31.1%</td>
<td>22.9%</td>
<td>68.3%</td>
<td>37.2%</td>
<td>77.35%</td>
</tr>
</tbody>
</table>

It calls the attention, whilst analysing table 2, that there is a discrepancy between the number of animals expected to be undergoing anaesthesia and surgery and the number of animals with prediction of pain and distress during the first years of CEUA’s activity (2003-2005). In 2005, for example, 2,392 animals were expected to be anaesthetised and 1,026 animals underwent surgery, but distress was predicted for only 64 animals and pain was predicted for only 80 animals. This discrepancy had been progressively reduced and the prediction of distress in 2008 exceeded the prediction of surgery.
This is a strong indication of increased awareness and understanding of researchers about other possible causes of pain and distress in animals in non-surgical procedures. It also seems to indicate a greater responsibility in describing causes of pain and distress in non human animals.

With respect to euthanasia, the table of absolute data and percentages allowed us to assume that there seems to be a tendency to reduce the frequency of euthanasia. At the starting point of the study in 2003, for example, 1,692 out of 1,932 animals predicted euthanasia, what corresponds to 87.6% of the total number of animals, a proportion similar to those of 2004 and 2005. The proportion reached 92.9% of the animals involved in 2005. 1,916 animals out of a total of 2,794 animals were induced to euthanasia in 2008, accounting for 68.6% of the total number of animals. This number went down to 60.7% in 2010.

Graph 1 presents a statistical study related to the predicted proportions of distress, pain, anaesthesia, surgery and euthanasia. The tests confirmed that the prediction of distress and pain in submission forms had a statistically relevant increase over time, with $p = 0.014$ for prediction of distress and $p = 0.012$ for prediction of pain. These data are considered even more relevant by the fact that there was no corresponding increase in the proportion of animals that underwent surgery over the years ($p = 0.284$). Considering how the analysis of protocols shows a certain regularity in the types of other procedures capable of causing pain and distress, these group of data allows to affirm that the quality of prediction description of those factors improved, which leads to believe in a better evaluation of the CEUA of procedures to minimise discomforts and a better adequacy of the number of animals involved in experiments.

Graph 1. Evolution of prediction of distress, pain, anaesthesia, surgery and euthanasia.

Graph 2. Evolution of the relation between absolute numbers of anaesthesia and surgeries

One of the most important findings of this study was to demonstrate that despite the tendency of an increasing number of animals used in research over time, at the limit of significance ($p = 0.051$), this growth has not been due to a greater use of the category of animals that are less involved in procedures that culminate in euthanasia. The proportion of euthanasia’s falling numbers is statistically relevant, with $p = 0.023$. This suggests that CEUA has been fulfilling its role of sensitising the scientific community to the issues regarding animal suffering. The results of the study demonstrate that professionals involved in the projects are more prepared to avoid, whenever possible, suffering, distress, pain and waste of animals in laboratory procedures.

Final considerations

It is recognised that it is not yet possible to do without the use of non-human animals in experiments for the advancement of biomedicine and veterinary medicine. However, the philosophical perspectives that ground the ethical relations between human beings and other sentient animals justify, in our view, the effort to combat unjustified exploitation and to establish norms that seek to eliminate suffering and futile death of animals as well as to eliminate the neglect of those animal’s distress and pain caused by experiments. This should
be done before, during and after educational and research procedures with animals.

The establishment of the system of ethical review of protocols for animal use in Brazil through its central body, Concea, and the various CEUA, is a concrete expression of philosophical perspectives that deal with ethics in relations with animals. It is thus a social protection mechanism for animals submitted to educational and research procedures. In this sense, it is necessary to produce knowledge about the operation and performance of these institutional bodies, both with regard to the education of the scientific community on ethics of animal protection and the concrete consequences of the action of ethical reviews of protocols to reduce suffering and death of animals.

Our findings suggest that there was a close relationship between the work of the CEUA and a raising of community awareness on the matter. The studied period presented improvement and greater frequency of adequate descriptions of the prediction of pain and distress in protocols as well as a more frequent use of anaesthetics and sedatives in nonsurgical procedures what seems to indicate that procedures were more refined. In addition, there was a proportional reduction 8 of animals induced to euthanasia.

Taken from the perspective of the three “Rs” guiding principles, discussed in the introduction of this paper, we can say that the replacement, reduction and refinement of animal use in the studied period increased in the scientific community context where the CEUA-IB/UnB is active.

Although these data can not be applied to the reality of all CEUA actions in Brazil, we believe that we were able to suggest a method to evaluate the tendency of use of protection procedures by a specific scientific community under the influence of the CEUA. It is clear that this first study and its method need to be improved and to include a better control of other variables not evaluated by our study. It also needs to be tested in the future using a larger group of CEUA that will be more representative of the Brazilian context.

Referências


Participation of the Authors
Josué Lopes Corrêa Neto was responsible for the literature review and collaborated in the writing as well as collection and analysis of data. Cláudio Lorenzo formulated the central idea of the article and contributed with data analysis and writing. Mauro Niskier Sanchez defined the variables to be studied, performed statistical calculations, elaborated tables and graphs, drafted the presentation and interpreted results.