Animal Models in Neuroscience: What is the "Culture of Care"?

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In situations where animal models (AMs) are necessary, as in the field of neuroscience, a strong culture of care must be supported and established. The pivotal question remains: how can we uphold a robust "culture of care"? In the multifaceted domain of neuroscience research, AMs traverse a spectrum shaped by conflicting viewpoints, anthropocentrism and pathocentrism, where established scientific norms intersect with ethical deliberations. Anthropocentrism, representative of conventional scientific approaches, may prioritize scientific goals potentially to the detriment of animal welfare. Conversely, pathocentrism places significant importance on the ethical treatment and well-being of AMs. This divergence of approach prompts the imperative development of a robust culture of care framework within research institutions, advocating for animal welfare, ethical responsibility, and adherence to regulatory standards. In this review, we refer to a European view of animal care, discussing internationally valid concepts that find rebuttal in the current European legislation. This review meticulously analyzes the many facets of the culture of care, particularly for neuroscience studies involving AMs, illustrating the principles, practices, and collaborations critical to overcoming ethical expectations. This commitment increases credibility and builds trust in the public and research spheres, underscoring the critical importance of a culture of care in the ethics of neuroscience research.

animal welfare   3Rs   ethical responsibility   research community   neuroscience research

Exploring the human brain and nervous system (NS) represents one of scientific inquiry's most intricate and promising frontiers [1][2][3]. In this area, neuroscience research often relies on animal models (AMs) to unravel the complexities of neural function, behavior, and disease mechanisms [3][4][5]. However, ethical considerations surrounding using AMs in research have attracted increasing public and research community attention [6][7]. To navigate this moral landscape effectively, institutions engaged in research using AMs must adhere to a comprehensive culture of care framework [8]. The concept of a "culture of care" within the context of utilizing animals in scientific research pertains to the organizational environment that fosters continuous improvement in various aspects: animal care and welfare, the well-being of staff engaged in the animal care and use program, scientific quality, openness, and transparency [9]. While European Directive 2010/63/EU on protecting animals for scientific purposes does not explicitly mention "culture of care," it underscores the importance of fostering a "climate of care" within animal welfare bodies (AWBs), as indicated in Recital 31 [9]. Although not expressly stated in the directive, guidance documents from the European Commission, member states, and stakeholders refer to the significance of a culture of care. For instance, the Education and Training Framework promotes a "Culture of Care" among staff at all levels. Additionally, guidance on inspections and enforcement incorporates the concept of a culture of care, offering insights into factors influencing its determination and leveraging inspectors or inspections to promote it. A culture of care transcends mere compliance with legal requirements [9]. It encompasses an

organizational culture that values and supports compassionate and respectful behavior towards animals and colleagues. Everyone involved in animal studies, from those directly conducting research to animal facility management, planners, engineers, biologists, chemists, statisticians, project leaders, and senior leaders, is responsible for cultivating a culture that emphasizes ethical practices and continuous improvement [9][10][11][12]. Within this context, addressing the expectations of the public, who rightly advocate for ethical animal treatment, and meeting the stringent ethical standards set by the research community become imperative for these institutions [13]. This review explores the multifaceted dimensions within a culture of care framework [14][15]. Specifically tailored to neuroscience research involving animal subjects, this review delineates the principles, practices, and collaborations essential to meeting and exceeding the ethical expectations of the public and the research community [6][7].

From transparent communication to continuous improvement, welfare-centric practices, and collaborative education, this review delves into the intricacies of fostering ethical excellence within neuroscience research [16].

Ethical Considerations: Prioritizing Animal Welfare and Scientific Progress

The interface between animal welfare and research necessitates a delicate balance between scientific progress and ethical responsibility [16][17]. Animal welfare refers to the appropriate condition of a species based on science and ethics. It encompasses multifaceted considerations, from the initial stages of experimental design to the implementation of procedures and the overall well-being of animal subjects [18][19]. Ensuring animal welfare involves providing optimal living conditions that mimic natural environments tailored to the species' behavioral and physiological needs [10][19]. Enrichment strategies, such as cognitive stimulation and social interactions, are integrated into housing environments to promote mental well-being and prevent boredom or distress [11][16][20]. The PREPARE Guidelines (https://norecopa.no/prepare, accessed on 15 December 2023) are pivotal to guiding researchers toward a meticulous and ethically sound approach [21]. They emphasize not only the scientific rigor but also the ethical responsibilities towards animal subjects [18][22][23]. These guidelines advocate for reducing animals used in experiments, refining procedures to minimize pain or distress, and replacing new alternative models (NAMs) wherever feasible [24][25]. Researchers navigate ethical considerations by continually refining methodologies and embracing innovative technologies to reduce the reliance on AMs [13][22][26]. Techniques such as non-invasive imaging or in vitro models offer alternatives that minimize the need for animal subjects, promoting ethical practices while advancing scientific knowledge [19][20]. Moreover, fostering a culture of care within research centers should be an institutional commitment to the ethical treatment of animals [10][14][27][28][29]. This involves comprehensive training for researchers, veterinarians, and support staff, ensuring they understand and adhere to ethical animal handling and experimentation guidelines [30][31]. The ethical landscape within research involving animals encapsulates a collective commitment to upholding rigorous scientific standards while prioritizing the welfare of sentient beings [10][19].

Ethical Paradigms: Anthropocentrism and Pathocentrism Examined

In the dynamic landscape of scientific research, AM utilization navigates a spectrum influenced by opposing perspectives, anthropocentrism and pathocentrism, where traditional scientific paradigms clash with ethical considerations [32][33]. Anthropocentrism, often reflective of traditional scientific practices, might prioritize achieving scientific objectives at the potential expense of animal welfare [34][35][36]. It ensures that the animals involved are treated ethically and compassionately throughout the research process, acknowledging their capacity to experience emotions and sensations [34][35][36]. Pathocentrism in scientific research ensures ethical standards and yields more reliable and translatable results. Within a pathocentric framework, researchers embracing animal experimentation must initially assess its indispensability [37][38][39][40]. Can valuable insights be derived from robust meta-analyses, probabilistic computational tools, or NAMs [41]? However, it is crucial to acknowledge that scientific inquiry frequently demands exploration beyond cellular or molecular levels, necessitating more intricate investigations [38][39][40][41][42]. When the trajectory of research mandates animal experimentation, the paramount concern for the researcher becomes prioritizing the welfare of these subjects [38][39][40][41][42]. By emphasizing the well-being of AMs, researchers reduce confounding factors such as stress-induced responses that might skew experimental outcomes [38][39][40][41][42][43]. Moreover, ethical research practices often contribute to better animal health, reducing variables that might interfere with neurological studies [37][42]. Adopting pathocentrism does not necessarily hinder scientific progress; instead, it encourages researchers to refine methodologies, explore alternative approaches, and create enriched environments for AMs [37][42]. Pathocentrism and the culture of care shape the ethical landscape of using AMs in scientific research [44][45]. Pathocentrism, by recognizing the intrinsic value and conscious nature of AMs, advocates for their ethical treatment, emphasizing the reduction in distress and promoting their overall well-being throughout the research process [44][45]. This ethical standpoint aligns with the culture of care, fostering an environment where researchers prioritize animal welfare by implementing refined methodologies, providing enriched environments, and continuously evaluating protocols to minimize discomfort and stress for the AMs involved [44][45]. The culture of care embodies a collective commitment within research institutions to uphold stringent ethical standards, training researchers in handling and fostering an ethos that values the ethical treatment of animal subjects [39][42]. Pathocentrism and the culture of care establish an ethical framework that advances scientific knowledge in the research community, acknowledging their intrinsic value and promoting ethical responsibility [42][46][47].

Synergizing Ethical Compasses: Comparing the Five Freedoms and the Five Domains

The five freedoms framework embodies essential principles guiding ethical treatment of animals involved in scientific studies [48][49]. Freedom from hunger and thirst, discomfort, pain, and distress, and the ability to express natural behaviors hold profound implications in experiments [48][49]. AMs must have access to fresh water and a diet that maintains health and vigor, meeting their nutritional needs [50]. AMs should have a suitable environment that offers shelter and living conditions that avoid discomfort [50][51][52]. This includes appropriate resting areas, protection from adverse weather, and clean living spaces [50][51][52]. Measures should be in place to prevent or rapidly diagnose and treat injuries or diseases to minimize suffering [50][51][52]. AMs should have sufficient space and suitable conditions to exhibit natural behaviors characteristic of their species [50][51][52]. This includes providing opportunities for social interactions, exploration, and activities that allow them to express their innate behaviors [50]

[51][52]. The environment and handling should not induce mental suffering or distress in AMs [50][51][52]. Integrating these principles into a broader culture of care within research institutions elevates their significance [27][28]. The culture of care fosters an environment where these freedoms become embedded in the institutional ethos, influencing the practices and behaviors of researchers and staff [13][28]. It emphasizes creating enriched environments that cater to the animals' needs, refining methodologies to minimize distress and prioritizing their welfare throughout the research process [14][29]. This approach ensures that research upholds ethical standards, minimizing potential suffering for AMs while fostering a commitment to responsible and compassionate scientific inquiry [14][29].

In 1994, Professor David Mellor and Dr. Cam Reid introduced a novel model, transforming the established five freedoms into "five domains" to systematically assess and grade the severity of welfare compromise in various aspects: nutrition, environment, health, behavior, and mental state/experiences [53][54][55]. This approach distinguishes between the physical and functional factors affecting an animal's welfare and the overall mental state arising from these factors [53][55]. Widely embraced over the past two decades, this paradigm has become a valuable tool for evaluating the welfare impacts of research procedures, pest control methods, and other animal life interventions [53][54][55].

While both the five freedoms and five domains frameworks share the same core elements, the latter delves more deeply into the mental state of animals, recognizing that an emotion or subjective experience may accompany every physical aspect influencing welfare [53][54][55]. This nuanced exploration reinforces that emotional needs are as significant as physical needs for animals (**Figure 1**)
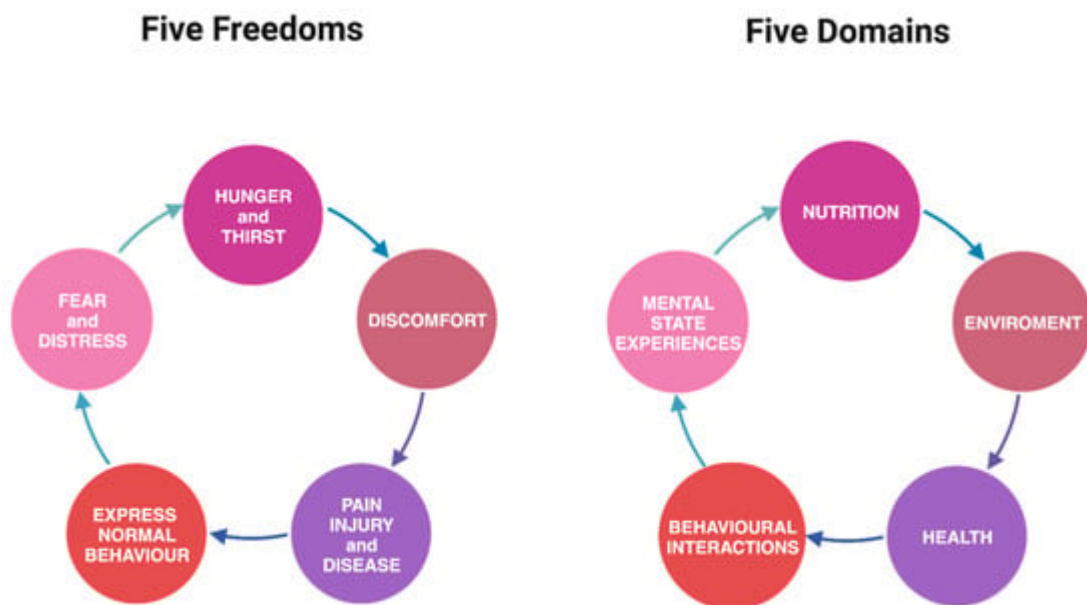

Figure 1. Comparison of five freedoms and five domains versus one another.

A notable strength of the five domains framework lies in its clarity, emphasizing that merely alleviating negative physical or mental states does not necessarily guarantee positive welfare; it may, at best, achieve a neutral state.

True good welfare for animals goes beyond the mere resolution of negatives [53][55].

Ensuring animals lead a "good life" involves providing opportunities for positive experiences, including anticipation, satisfaction, and satiation. Caretakers must create environments that encourage animals to engage in rewarding behaviors [53][55]. This shift in perspective forms the foundation of the five domains model, which integrates positive welfare states into its assessment, extending beyond the traditional focus on minimizing negatives [53][55].

Therefore, the five domains model serves as a comprehensive evaluation tool for assessing the welfare of individuals or groups of animals, prioritizing mental well-being and emphasizing the importance of facilitating positive experiences, thus expanding our considerations beyond the original five freedoms [53][55].

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