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Introducing individual sentience profiles in nonhuman primate neuroscience research

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ARTICLE INFO	A B S T R A C T
<i>Keywords:</i> NHP neuroscience research Translational neuroscience Animal welfare Animal sentience	The Animal Research Declaration is committed to establishing cohesive and rigorous ethical standards to safe- guard the welfare of nonhuman primates (NHPs) engaged in neuroscience research (Petkov et al., 2022 this issue). As part of this mission, there is an expanding dialogue amongst neuroscientists, philosophers, and poli- cymakers, that is centred on diverse aspects of animal welfare and scientific practice. This paper emphasises the necessity of integrating the assessment of animal sentience into the declaration. Animal sentience, in this context, refers to the recognized capacity that animals have for various kinds of subjective experience, with an associated positive or negative valence (Browning and Birch, 2022). Accordingly, NHP neuroscience researchers should work toward instituting a standardised approach for evaluating what can be termed "individual sentience pro- files," representing the unique manner in which an individual NHP experiences specific events or environments. The adoption of this novel parameter would serve a triad of indispensable purposes: enhancing NHP welfare throughout research involvement, elevating the quality of life for NHPs in captivity, and refining the calibre of recently externed.

1. Introduction

Non-human primate (NHP) research is fundamental to translational neuroscience: non-human primates share with humans many neurological processes and functions, and, as a consequence, they also develop many of the same diseases and dysfunctions (Mitchell et al., 2018; Lear et al., 2022). NHP neuroscience research findings can improve both nonhuman and human quality of life. Furthermore, NHPs are frequently the only relevant animal models because of their genetic, physiological, and behavioural similarities to humans (Harding, 2017).

NHP neuroscience research needs unity of ethical standards across nations in order to facilitate international collaborations. It is also critical to educate researchers in different disciplines who contribute to neuroscience research to be familiar with such ethical standards (Beauchamp and DeGrazia, 2019; DeGrazia, 2020). There are, however, a number of challenges to face. At present, there are no common ethical and regulatory frameworks. This is because ethical standards are culture-specific, and this makes it difficult to determine who should be entitled to define them. Nevertheless, several criteria, such as minimising unnecessary experiments and promoting inter- and intra-national collaboration to reduce replication redundancy, are widely recognized (Brønstad et al., 2016). Furthermore, there is a growing commitment among countries conducting NHP neuroscience research to converge on a common set of ethical standards of practice (see, Hartig et al., 2023 current issue) since, above all, it is important to recognize that improved animal welfare correlates with better scientific outcomes (Tannenbaum, 2017).

To serve this purpose, the Animal Research Declaration is committed to establishing cohesive and rigorous ethical standards to safeguard the welfare of nonhuman primates (NHPs) engaged in neuroscience research (Petkov et al., 2022 this issue).

The declaration is built upon a combination of principles already present in the Basel Declaration on Animal Research (https://animalrese archtomorrow.org/en) and integrates additional ethical principles influenced by the Helsinki Declaration on Human Medical Research (Goodyear et al., 2007).

The Basel Declaration has over time established principles ensuring a broad scope of animal welfare considerations as part of responsible and effective scientific practice (Prescott and Lidster, 2017). It also fostered transparency and public engagement while increasing awareness among educators (Mendez et al., 2022).

To support this mission, neuroscientists are in continuous and

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growing dialogue with philosophers, educators, and policy-makers, on a variety of subject matters concerning animal welfare in relation to scientific practice (Birch, 2022; Rollin, 2006).

An essential facet not yet integrated into the Animal Research Declaration, is *animal sentience*: the capacity that animals have for various kinds of subjective experience. In this paper, I argue for the utility of setting up unified standards for measuring it in animals that are involved in biomedical research and translational neuroscience.

The possibility to include animal sentience as a key principle for establishing common ethical standards is especially relevant when we analyse this concept in its narrow sense as the capacity that animals have for ascribing a positive or negative valence to their subjective experiences (Browning and Birch, 2022). Ascribing valence to one's own experience is not only determined by the type of experience one animal may be subject to but also by the *individual sentience profile* ascribed to the specific animal. Accordingly, an individual sentience profile can be defined as the specific way in which a specific individual experiences a specific event or environment.

Sentience is often viewed as a determinant of moral status (Kriegel, 2019; Nussbaum, 2007; Schukraft, 2020; Singer, 1977). Despite empirical uncertainties, NHP neuroscience researchers should adhere to precautionary principles of protection legislation where there is credible evidence of sentience (Browning and Veit, 2020; Birch, 2017). Against radical forms of epistemic pessimism, sentience remains a necessary and sufficient condition for ascribing moral status to animals (Dung, 2022), and hence critical for developing robust welfare standards (Sneddon et al., 2014; Jaworska and Tannenbaum, 2021).

In NHP neuroscience research, there are compelling reasons to recognize and incorporate individual sentience profiles in defining ethical standards. This is feasible given the advanced knowledge we have of NHPs' behaviour and cognition (Matsuzawa, 2008; Strier, 2021; Schwartz and Beran, 2022).

In what follows, I will first explain what individual sentience profiles add to animal sentience as currently understood in the literature; subsequently, it will be suggested that the adoption of this novel parameter would serve a triad of indispensable purposes: enhancing NHP welfare throughout research involvement, elevating the quality of life for NHPs in captivity, and refining the calibre of research outcomes.

2. Animal sentience and individual sentience profiles

The Cambridge Declaration on Consciousness (Low et al., 2012) crystallised a scientific consensus that humans are not the only sentient beings and that many other creatures, particularly NHPs, possess neurological structures complex enough to support conscious experiences, that is sentience in the broader sense.

There is a consensus among animal welfare scientists about the fact that sentience can be tracked in many different species (Godfrey-Smith, 2016). This is especially clear in the case of NHPs. What there isn't enough clarity about is whether ascribing sentience to NHPs suffices for them to be treated ethically in neuroscience research. However, as I will explain, there are reasons to think that mere recognition that NHPs are sentient, in the broad sense, is not sufficient for ensuring ethical treatment.

Biomedical research and translational neuroscience do acknowledge a high level of sentience to NHPs (Prescott, 2020). But neuroscientists should go further and aim to define parameters to assess the capacity for valenced experiences (i.e., sentience in the narrow sense) among animals involved in neuroscientific research. This would mark a notable advancement in the establishment of shared and unified ethical principles in NHP neuroscience research (see Browning and Veit, 2022).

Partly stimulated by this concern, in recent years, the interdisciplinary debate about animal consciousness moved from asking what degree of sentience a given animal species has (Tardif et al., 2013), to what form sentience takes in that given animal species (Dung and Newen, 2023). This shift acknowledges that behavioural expressions of sentience vary across species due to distinct neurological foundations. Such variations are also observed among NHP species. To assess if an animal species is more or less sentient in comparison to others is to fail to appreciate that sentience doesn't manifest itself in the same form in every species (in fact, it has been argued that it doesn't even manifest itself in the same way within individuals of the same species, as will be discussed in section 3). Accordingly, a proposal has been advanced for how to assign consciousness profiles to different species, called the multidimensional framework for the study of consciousness (Birch et al., 2020), building on a previous proposal concerning human consciousness (Bayne et al., 2016).

While there is a consensus that NHPs are sentient beings (in the broad sense), there isn't a consensus about whether sentience should be measured on a scale of intensity or according to the assignment of species-specific profiles, as suggested by the proponents of the multidimensional framework. In the future, we may see the majority of NHP neuroscience research favouring this novel proposal. In the meantime, we can take the discussion a step further: recognizing NHPs as sentient beings in the narrow sense. This means ascribing NHPs the capacity to attribute a positive or negative valence to their subjective experiences. In Birch et al. (2020) this dimension of subjective experience is defined as 'evaluative richness'. As they explain, all affective responses possess either positive or negative valence. Valence serves as a common evaluative measure that influences affect-based decision-making. NHPs are likely to exhibit variation in the richness of their experiences and valence is a particularly useful concept for understanding this variation.

This is not to suggest that NHP neuroscience researchers should employ negative reinforcement, but rather that they may appreciate that the same experience (e.g., a certain experimental set-up, specific living conditions, foods, or companionship) may be valued differently by different individuals. Accordingly, where applicable, researchers should alter elements that carry negative valence for the animals. Understood in these terms, sentience as valenced experience becomes a key principle to be acknowledged in the Animal Research Declaration, which is not going to be a static set of principles. On the contrary, it is supposed to be regularly updated to keep up with advances in science, and bioethics especially. Accordingly, researchers should develop ways to recognize how experiences are valued by NHPs, through a combined analysis of the neurological substrates and of the behavioural and communicative manifestations observable in NHPs collaborating in neuroscience research (see Browning, 2022, for a proposal).

Additionally, I suggest, it is crucial to introduce the concept of 'individual sentience profiles' to the existing guidelines. This means recognizing that individual NHPs have unique ways of experiencing events or environments and assigning specific values to those experiences. Each individual experiences a specific event or environment in a specific way and ascribes a specific valence to that specific experience. This means that what an NHP individual may attribute positive valence to, another NHP individual may attribute negative valence. These differently valued experiences may refer to the same experimental procedure or living environment. One individual may display discomfort towards a certain experimental procedure, whilst another may display engagement. Similarly, one individual may appreciate a certain type of food, whilst another may find it repelling. While positive reinforcement procedures have partly addressed these concerns, there is no systematic approach for profiling valenced experiences at the individual level. In addition to the development of sensitive and ethically-driven experimental procedures, and the construction of species-specific living conditions, NHP researchers should assign individual sentience profiles to each one of the NHPs that they are collaborating with, in order to improve their overall quality of life. This means getting to know the animal and acknowledging that what may be valued positively by one, may be valued negatively by another. It is documented that NHPs show individual differences in their behavioural and physiological responses to experimental challenges and caretaking procedures (Boccia et al., 1995; Izzo et al., 2011; Manteca and Deag, 1994). Even if dedicating resources to profiling sentience in such a narrow manner is inevitably time-costly, it may result in less need for rehabilitation and other aftercare post-experimentation recovery measures. Individual sentience profiles can be not only a key ingredient in the design of ethical principles but also a tool to improve the quality of research findings, and finally, a resource to make research more cost-effective.

In the following section, I will discuss how the present proposal resonates with what can be done to balance the pursuit of welfare and optimal experimental results.

3. The challenges of setting standards for measuring individual sentience

The challenges involved in establishing standards for measuring individual sentience in animals are closely tied to both the pursuit of animal welfare and the optimization of experimental results.

The scientific debate on animals' capacity for valenced experience has been constrained by a lack of quantifiable measures. Reasons for overcoming the challenges of setting up unified standards for measuring individual sentience are at least of two types. One pertains to the pursuit of animal welfare, and one concerns the pursuit of optimal experimental practice.

Let's discuss welfare first and optimality second to appreciate how tight is their relationship with each other, and how useful to both outcomes is the notion of sentience in the very narrow sense of individual valenced experience.

3.1. Balancing the pursuit of welfare and optimal experimental results

Welfare researchers widely recognize the ethical justification for discussing the potential for subjective experiences in other species (e.g., Goodall, 1986; de Waal, 2006; Broom, 2010; Panksepp, 2011). In particular, evaluating the psychological component of welfare, referred to as "psychological well-being," in animals that cannot directly communicate their feelings poses a significant challenge in animal welfare research (Russell and Burch, 1959; Dawkins, 2017). Here we can leave aside the disagreements about whether or not subjective experience can be measured scientifically (Dung, 2022) and whether measuring welfare depends on measuring sentience or not (Dawkins, 2017, 2021).

If NHPs are considered capable of evaluating their subjective experiences, there are reasons to assume that they are capable of evaluating their well-being as well. Browning (2022, 2023) outlines a proposal for how the subjective experience of welfare can be measured. There are three primary measurement scales – ordinal, interval and ratio that can be used to evaluate valenced sentience according to specific experimental settings and techniques (Stevens, 1951).

Ordinal scales, for instance, can be beneficial in classifying the relative intensity of an animal's reaction to different stimuli. For example, in NHPs, one could observe the reactions to various environmental enrichment objects (e.g., toys, swings, puzzles) and rank them based on engagement levels. Another concrete example could be analysing different vocalisation patterns of NHPs in response to varying environmental stimuli. By categorising and ranking these vocalisations, researchers can derive preferences or emotional states such as contentment or distress. This ranking can provide a basic understanding of preferences, though it does not provide quantitative differences between rankings.

Interval scales offer a more detailed measurement by allowing us to quantify the differences between rankings with a consistent scale. However, the zero point is arbitrary. To illustrate this, one could measure the stress levels of NHPs through hormonal assays, such as cortisol levels. Here, differences in cortisol concentrations can indicate varying degrees of stress responses to different environments, but the scale does not imply an absolute absence of stress at zero.

Ratio scales take it a step further by having a non-arbitrary fixed zero

point, which allows for the analysis of ratios. For instance, one could examine the time spent engaging in certain behaviours with a fixed nonarbitrary zero point representing no engagement. For instance, measuring the time an NHP spends in self-grooming or playing with conspecifics in relation to the overall time available for these activities, can provide insights into the positive valence associated with these behaviours. A higher ratio might indicate a higher positive valence attributed to that activity.

It is important to stress that effectively characterising individual sentience profiles through the employment of the three scales - ordinal, interval, and ratio - necessitates the grounding of these scales in empirically observed data, as opposed to relying on abstract measurement procedures, which is the approach taken by Birch et al. (2020).

The main challenge faced by measurement techniques is interpersonal comparison. Existing solutions, proposed for the human case (Binmore, 2009; Harsanyi, 1955; Narens and Skyrms, 2020) are unlikely to be useable for interspecies comparison, and even less for inter-individuals' comparison. This is because proposals aimed at levelling welfare rely on supposedly robust similarities in the psychology and the behaviour of individuals belonging to the same species (and on the ability that humans are supposed to have to reliably introspect and access the mental states of each other). Arguably, we can measure sentience in individuals and assign them individual sentience profiles. Using several scales for measurement we can measure individual sentience. Problems may arise when we want to compare scales measuring the subjective experiences of different individuals. As said, individual sentience profiles are individual because different animals could value experiencing the same event or environment very differently.

Individual sentience measurement techniques should not aim at mapping comparison between individuals but at profiling sentience in individuals in order to, where applicable, adjust experimental procedures and living conditions to favour their well-being. It is important to notice that researchers may encounter a potential conflict between accommodating inter-individual variations in sentience and maintaining control within an experimental protocol. Within an experimental or observational protocol, introducing different reinforcements based on individual preferences could inadvertently introduce confounding variables. One solution could be the implementation of a preliminary assessment phase. In this phase, researchers could determine the range of stimuli or reinforcements that are generally preferred and positively perceived by the majority of the subjects. Following this, the experiment could employ a set of standardised stimuli or reinforcements that fall within this range. This ensures that individual preferences are broadly respected while maintaining the consistency necessary for controlled experimental conditions. Additionally, integrating mixed-effects models in statistical analyses could be used to account for individual variations, where the individual subject can be included as a random effect. This approach helps in accounting for inherent individual variations while drawing conclusions from the experiment, ensuring that the integrity of the scientific investigation is preserved without compromising on the welfare of the subjects involved.

3.2. A balance in behavioural management

Individual sentience profiles should be embedded with the concept of behavioural management, which focuses on making refinements to the captive environment with the aim of influencing and enhancing animal welfare.

For example, Matsuzawa (2006) emphasised the importance of maximising the welfare of captive chimpanzees by establishing laboratory practices that prioritise environmental enrichment. This approach enables chimpanzees to engage in a wide range of behaviours that closely align with their natural behavioural repertoires while adhering to time budgets that resemble those observed in wild chimpanzees. Consequently, it is crucial to consider the distinctions between

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behaviours that are common in captivity but uncommon in the wild when developing environmental enrichment strategies (for a comprehensive review of behavioural measures of primate welfare, refer to Lutz and Baker, 2023).

Utilising behavioural management in tandem with scales for measuring individual sentience profiles would enable not only the classification of specific behaviours exhibited by NHPs as atypical for a species but also as atypical for a particular individual. This is vital for evaluating individual welfare and can be achieved through two methodologies as suggested by Erwin and Deni (1979), and Novak et al. (2017). The first method involves identifying behaviours observed in captive NHPs that are not exhibited by their wild counterparts as atypical. For instance, repetitive motions such as pacing and self-inflicted harm are behaviours rarely observed in the wild. The second methodology entails recognizing behaviours that occur with significantly different frequencies in captivity compared to in the wild. A quintessential example is excessive self-grooming. Although self-grooming is common among primates in the wild, extreme cases leading to baldness are rare. Monitoring variations in self-grooming through an individual sentience profile of a specific NHP could be indicative of fluctuations in well-being.

In relation to this, we can now consider reasons why measuring individual sentience profiles can contribute to optimal experimental research and reduce research costs.

Techniques such as socialisation, environmental enrichment, and positive reinforcement training have been observed to substantially affect both the behavioural and physiological aspects of animal welfare (Schapiro et al., 1993). These approaches not only mould the aptness of individual NHPs as research subjects but also influence the dependent variables typically measured in research studies involving captive NHPs (Schapiro, 2002).

For instance, in research centred around immunodeficiency viruses, where immunological variables like lymphocyte subsets, cytokines, and proliferation assays are crucial, customised behavioural management strategies (like single, pair, or group housing; Schapiro et al., 2000) can affect changes in immunological parameters, independent of experimental manipulations. Therefore, the provision of adept and compassionate care, coupled with a commitment to improving primate welfare, is essential to produce scientifically rigorous data.

Moreover, in recent years, considerable efforts have been invested in researching the temperament or personality of animals, especially NHPs (Capitanio et al., 2011; Coleman, 2012; Freeman et al., 2013; Coleman and Pierre, 2014). While earlier research was mainly theoretical (Freeman et al., 2013; Latzman et al., 2017), newer studies have been emphasising the practical applications of understanding NHP temperament (Robinson et al., 2016; Capitanio, 2017; Coleman, 2017; as reviewed by Robinson and Weiss, 2023). One application involves subject selection by identifying animals optimally suited for specific research protocols. For example, animals with high scores on exploratory temperament dimensions may be better suited for certain studies than those with lower scores (Capitanio, 2017). This strategy aims to improve welfare by avoiding the selection of individuals who may have difficulties with specific projects or procedures. For instance, individuals with a nervous temperament may not be ideal for infectious disease studies as they exhibit evidence of glucocorticoid desensitisation and possess physiological attributes that might affect their inflammatory responses to infection. Additionally, assessing temperament in subject selection can help minimise interindividual variation by aligning temperaments across control and experimental subjects. This research underscores that evaluating temperament can improve both the welfare of NHP subjects and the value of the data they generate (Capitanio, 2017; Coleman, 2017).

In summary, understanding how individual NHPs subjectively evaluate their welfare as experimental subjects and as captive animals, is advisable for generating trustworthy and vigorous research data, particularly when NHPs serve as models in biomedical research. The implementation of behavioural management strategies that encompass socialisation, environmental enrichment, and positive reinforcement training typically leads to an increase in individual-appropriate behaviours and a decrease in abnormal behaviours. Furthermore, these strategies can produce physiological and immunological response patterns that signify the appropriateness of NHP subjects for usage in biomedical and other research endeavours.

4. Discussion

The challenges of setting standards for measuring individual sentience involve balancing the pursuit of animal welfare and the need for optimal experimental results. Developing reliable measures for individual sentience is integral to achieving ethical treatment of animals and obtaining high-quality data in scientific research. This necessitates a composite approach incorporating behavioural management, environmental enrichment, and an understanding of individual preferences and temperaments.

The ethical debate over the regulations on nonhuman animal research, in particular, NHP neuroscience research, is divided. On the one hand, the scientific community is increasingly applying more stringent ethical standards of regulations in order to guarantee the welfare of NHPs involved in neuroscientific translational research. On the other hand, the technicity of scientific reports represents a barrier to public opinion, which is fueled with mixed information on what these standards imply. To bridge this divide neuroscientists are providing detailed and valuable reports to explain the need for NHP neuroscience research (Mitchell et al., 2018; Mendez et al., 2022) But there are also internal barriers to the scientific community, due to the lack of unified ethical standards across research facilities and across countries. For example, there is a lack of consensus about how to assign sentience to NHPs. Over the years, a growing number of scientists have joined forces to formulate the basis for an Animal Research Declaration (Petkov et al., 2022). Here it has been suggested to include in the principles of the declaration the recognition of individual sentience profiles. This is a viable tool, and it holds the potential to contribute to the assessment of the subjective experiences of NHPs in neuroscience research and of their life in captivity, improving both the evaluation of research efficacy and animal welfare. The triad of ethical uniformity, the implementation of consolidated animal welfare standards, and the enhancement of scientific data quality represent the core challenges confronting NHP neuroscience researchers. In this light, it is important to accentuate the necessity for an international consensus on ethical standards for NHP research. These standards should encapsulate an appreciation for sentience in NHPs as individually-valenced experiences. This entails acknowledging the heterogeneity in subjective experiences and well-being assessments among members of the same species and within the parameters of research protocols.

This paper has focused on the rationale behind the measurement of individual sentience in NHPs, taking into account the nuanced differences in sentience among individuals. Two pivotal aspects have been discussed: firstly, the juxtaposition of singular metric intensities against the multifaceted patterns of multiple metrics in sentience evaluation, and secondly, the demarcation between ordinal, interval, and ratio scales, and the advocacy for their judicious application contingent on the specific circumstances.

5. Conclusion

The task of establishing standards for measuring individual sentience in NHPs necessitates an intricate balance between enhancing animal welfare and ensuring the rigour of scientific research. This paper has elucidated the importance of recognizing and measuring individual valenced experiences of NHPs in the context of neuroscience research. Through an analysis of measurement techniques and the challenges associated with them, it has been suggested that a multifaceted

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approach is necessary.

The establishment of individual sentience profiles represents a step forward in understanding the subjective experiences of NHPs, which is foundational for ethical considerations and effective behavioural management. The synthesis of ethical coherence, comprehensive animal welfare standards, and scientific data integrity are critical in surmounting the challenges faced in NHP research.

As the scientific community ventures forward, the need for collaborative efforts in establishing international standards cannot be overstated. These standards must encompass a granular understanding of sentience as a spectrum of individually-valenced experiences among NHPs. This, coupled with an agile and context-sensitive application of measurement scales, will prove pivotal in safeguarding the welfare of NHPs and fortifying the scientific contributions derived from such research.

Author contributions

The author confirms being the sole contributor to this work and has approved it for publication.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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Appendix A. Supplementary data

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