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Abstract

Recent advances in the use of induced pluripotent stem cells and culture media that mimic the three-dimensional structure of the extracellular matrix have permitted the development of human brain organoids for *in vitro* disease modeling. However, organoids present a highly salient ethical risk, with significant concerns regarding potential consciousness, moral status, and legal personhood contingent upon sentience, as well as socioeconomic barriers to access. This article explores the challenges associated with the application of brain-based consciousness indices to organoids, which are currently incapable of communicating mental states and possess a unique functional organization. While recent philosophical shifts associated with the rise of artificial intelligence (AI) have led to expansive definitions of consciousness and agency, applying analogous paradigms to organoids overlooks ongoing harms to model organisms used in biomedical research and risks delaying neurological drug development, exposing human trial participants to side effects, and discarding promising therapeutics before they reach the clinical stage. Neuroethical frameworks surrounding organoids must avoid distraction by highly speculative apprehensions, and instead emphasize practical issues of informed consent in sample collection and unrestricted entry to minimize the potential harms for patients and researchers.

Keywords: human brain organoids, neuroethics, theories of consciousness, sentience, agency, personhood, moral status

1. Disease Modeling Without the Model Organism

After months of progressive weakness and cognitive decline, a battery of standard neurological tests brings no answers for a previously healthy patient, ruling out dementia, slow-moving infections, and rare autoimmune conditions. In a desperate attempt to uncover the diagnosis, geneticists turn to whole-exome sequencing, a technique that reveals multiple unexplored mutations affecting the prion protein.[1] The prognosis is terminal, yet the novel disease becomes a tool for unveiling the mechanisms of prion-related neurodegeneration. Drawing a cell line with the mutation of interest from the patient, researchers generate a three-dimensional culture that measures only millimeters in diameter. The approach incorporates regional differences in brain organization and interactions between neurons and glia, providing insights into prion disease through RNA sequencing and cellular imaging.[2]

While the routine use of personalized *in vitro* disease models for patients with undiagnosed

neurological conditions remains distant, human brain organoids that contain neurons in a three-dimensional framework mimicking the mechanical properties and protein composition of the extracellular matrix alongside other central nervous system cell types, such as astrocytes, oligodendrocytes, and microglia, have already been engineered to study a wide range of disorders, including Alzheimer's disease, amyotrophic lateral sclerosis (ALS), schizophrenia, and post-COVID-19 neuroinflammation.[2-4] Organoids offer a distinct advantage over two-dimensional human neuronal cell cultures and animal brains, allowing developmental signaling molecules to better establish spatial gradients while permitting direct translation of results to treat patients and mitigating the potential for failure when new drugs are advanced from preclinical animal models into human trials.[3,4] However, the process of generating organoids brings both compelling benefits and troubling ethical considerations. Organoids originate from human-derived stem cells, ensuring a genome identical to the patient whose disorder is being investigated, and reducing the need for animal models that may imperfectly approximate diseases.[4,5]

For neurological conditions that defy a precise, single-gene explanation, stem from mutations at functionally ambiguous sites, or involve unknown epigenetic changes, organoids can be invaluable for understanding the mechanisms that drive symptoms. Methods ordinarily infeasible in live human tissue could be applied to organoids, including electrophysiology, scRNA-seq, a technique to measure gene expression at the transcriptional level in individual cells, and ChIP-seq, which involves sequencing sites in the genome bound by a particular protein to identify abnormal interactions with DNA.[6] Nonetheless, the brain-like nature of organoids generated from human biological material raises significant and visceral fears, as the technology could represent a *functional analog* for the human brain. With sufficient complexity and synapse count, the ability of organoids to recapitulate the cellular composition and organization of neural tissue may enable the development of circuits and activity patterns resembling those found in the human brain. Consequently, the neuronal cell cultures could model a human range of cognitive characteristics and acquire the capacity to respond to the environment, vulnerability to moral harm, a sense of "self," or even consciousness.

Organoids represent effective and biologically similar models of human brain disorders, but fears that the neuronal cell cultures are conscious may give pause to widespread implementation in research. As its central argument, this paper aims to demonstrate that such concerns are fundamentally speculative in nature; organoid consciousness is difficult to verify empirically, and distant when weighed against the practical implications of improving human health through research and reducing the suffering of laboratory animals. Overstating the possibility for consciousness threatens to shift the focus away from the scientific benefits and more imminent ethical issues associated with neuroscience research in organoids while also creating regulatory hurdles.

2. The Anatomy of Consciousness

The perception that organoids are full-fledged microcosms of the human brain has become pervasive, largely due to the sensationalist headlines of popular science publications. "Minibrain" has turned into a widely-used buzzword for organoids, and while it effectively communicates their role as human brain models, the term creates an illusion of a functionally complete organ, fueling misconceptions and overestimations of the cultures' capacity for information processing and humanlike abilities.[7-10] Organoids are typically restricted to a single brain region; forebrain models have been generated to investigate Zika virus-induced

microcephaly and midbrain models to study Parkinson's.[11] In the philosophical sense, consciousness remains a topic of continuing debate, but is generally considered to involve first-person and subjective elements; in a conscious cognitive or perceptual experience, there is "something it is like" for the subject that is having a feeling.[12,13] Neuroscience, for its part, dodges the challenge of providing a mechanistic explanation or account for how consciousness arises, instead either correlating it with certain patterns of neural activity based on the observed and reported experiences of patients, or going a step further and establishing a direct identity relation with neuronal firing.[14] Neuroscientific theories of consciousness are primarily designed for use as diagnostic tools in unresponsive, brain-injured patients, not as complete explanatory paradigms. Thus, they may place varying levels of emphasis on certain aspects of brain activity. For subsequent discussion, the working interpretation of consciousness will draw on both philosophical and neuroscientific conceptions, where consciousness is a first-person subjective phenomenon associated with specific changes to physical states in the neurons of the experiencer, which are detectable but do not provide a causal account. However, even with such a composite definition, the notion of consciousness remains somewhat too broad and murky to address the central moral challenge of whether it is acceptable to subject organoids to experiences that might be painful or restrict their flourishing.

From an anatomical standpoint, consciousness requires the presence of a system that is able to parse and integrate large consciousness requires the presence of a system that is able to parse and integrate large amounts of information from multiple, functionally-distinct brain structures into an experience.[15] Such a condition for consciousness is consistent with biological intuitions. For example, while the number of neurons in the human spinal cord or gastrointestinal tract may rival that of an insect or small mammal brain, we tend not to situate consciousness in those divisions of the nervous system because they lack an identifiable center for the convergence and processing of the information contained within neuronal firing. It then follows that a single-region organoid lacks the basis for consciousness—recapitulating the properties of only one brain area, it has neither a subspecialized, information-integrating system, nor inputs from multiple functionally distinct regions. While attributing consciousness to a particular brain structure or characteristic may be counterproductive or excessively reductionist, the *thalamus* is known to facilitate the multisensory integration of information through reciprocal signaling loops with the cerebral cortex, and empirical evidence from intraoperative neurostimulation on human patients suggests that the *claustrum* or *left anterior insula* may be required for consciousness.[15,16] By definition, there cannot be a "thalamus-like" or "claustrum-like" specialization within a neuronal cell culture that is functionally homogeneous, which would appear to shut the door on consciousness for single-region organoids.

Whole-brain organoids contain multiple regions corresponding to the midbrain, forebrain, spinal cord, and other broad divisions of the central nervous system, and may present more compelling cases for potential consciousness due to greater heterogeneity in cell types and circuits.[17] However, all organoids currently remain limited to the millimeter scale, as inadequate vascular development starves cells of oxygen and leads to necrosis at the center of the structure, which experiences hypoxia due to a lack of direct contact with culture media.[3] While brain size is not directly correlated with capacity for consciousness, a critical quantity of cerebral cortex is likely required for the necessary information-integrating ability; even the largest organoids are smaller than mouse brains by an order of magnitude, and may fail to meet such a benchmark.[18]

3. Adjudicating the Status of Organoids Based on Sentience

The judgment about personhood, agency, and moral status in organoids is ultimately contingent upon *sentience*, with consciousness as the first prerequisite. It is instructive to turn towards the concept of sentience, defined here as the capacity for valenced experiences—those that feel good or bad, with the potential to provoke or avert suffering.[19] *Suffering* refers to any *negatively valenced experience* that a subject desires to avoid, regardless of whether its basis is physical, psychological, or both.[20] Sentience is therefore predicated upon consciousness, as it implies *having an experience*, although the two concepts should not be considered coextensive. Neural activity could generate "white noise" feelings that are *conscious experiences* in the sense of "being like something," but lack the motivational or valenced component of *sentience,* particularly in the earliest-diverging phylogenetic groups of animals with rudimentary nervous systems analogous to small and structurally simple organoids.[21] However, as organoids cannot communicate potential experiences of suffering and happiness to an experimenter, it is impossible to directly measure their *capacity for sentience*, making it necessary to draw on an evaluation of the conduciveness of their neural architecture to *consciousness*. Even if organoids can be shown to possess biological hardware consistent with consciousness, such an argument will have only accomplished the minimal condition to begin staking the claim of sentience. The consciousness-sentience chasm bears relevance to the later appraisal of speculativeness in the ethical calculus of organoids, and must be considered when analyzing the prospect of organoid consciousness.

4. Biological Theories of Consciousness

Several frameworks offer biological explanations for consciousness, supported by varying degrees of plausibility and empirical validation. The *Orchestrated Objective Reduction* theory situates consciousness in quantum coherence between neuronal microtubules, but fails to account for the role of neurotransmitters, receptors, and postsynaptic potentials, providing no clear avenue for experimental observation.[22] The *Global Workspace* theory posits that incoming data can generate a conscious experience when it enters the "global workspace" of distant brain regions connected by long-range projections, allowing the information to be simultaneously utilized by several specialized areas.[14,15] The *Integrated Information* theory assigns a φ *(phi)* value to measure the amount of information, or reduction of uncertainty, generated in an integrated matter by circuits and systems that cannot be separated into independently functioning submodules. While the mathematical definition of φ is complex, it can be approximated without data from individual neurons through measures of brain activity, such as electroencephalogram (EEG) or functional magnetic resonance imaging (fMRI).[14,15,23,24] Both the *Global Workspace* and *Integrated Information* theory suffer from a pivotal flaw—they do not provide a deep, causal explanation of how patterns of neural activity produce consciousness, and instead focus on characteristics of the entire system, while not accounting for small-scale brain processes. Neurostimulation studies face a similar issue, with the added concern of limited sample sizes that may fail to account for variability among individuals. Additionally, both theories overgeneralize the concept of consciousness to systems that are inconsistent with intuition. The *Global Workspace* theory posits that a computer system made up of multiple interconnected modules is conscious.[25] The *Integrated Information* theory goes even further, suggesting a single, independently functioning light sensor is conscious, simply because it generates information beyond what is contained in its components alone.[25]

5. Challenges With Measures of Consciousness

While neuroscientific theories may offer specific metrics of consciousness, they can at best provide a surface-level predictive account of select biological aspects of experience. Consciousness measures are inherently correlational and hindered by an "explanatory gap"; even if a particular theory perfectly predicts consciousness when some value *C* is greater than 100, it is not clear why or how C > 100 has anything to do with first-person subjective conscious experience.[14,26] The clinical application of the *Integrated Information* theory, for example, relies on a perturbational complexity index (PCI), an analog for φ that evaluates EEG responses to exogenous magnetic or electrical stimulation to measure consciousness.[27] However, it would be unreasonable to assume that a certain PCI value is identical or absolutely correlated with the experience of consciousness. Although the multiple realizability of consciousness is somewhat limited by the requirements of sensory systems and brain structures, conscious experiences could still arise through a vast but finite set of possible neural activity patterns, with many producing drastically different values of PCI or other indices.[28] In a speculative study predicting recovery among patients in vegetative states, PCI proved inaccurate in 1 of 8 cases, signifying that consciousness indices are often imperfect and unreliable.[27]

Humans represent the easiest model with respect to detecting consciousness, as they are capable of verbally reporting experiences, enabling researchers to clearly establish correlations between neural and mental events. The problem of identifying consciousness in organoids is infinitely more vexing. Without clearly observable behavior, theories and indices are necessary to determine whether an organoid is conscious, yet such measures were initially developed and validated using human studies. If a mental state can be produced by several patterns of activity even when considering the brain of a single individual, it stands to reason that the divergence of underlying neural firing could be far greater between a human and organoid undergoing the same experience. Direct observation of an organoid's neural activity using an electrode array is possible, but unlikely to be fruitful. Even if the precise state of every neuron is continuously measured—which would require a degree of spatial resolution that is currently unattainable—there is no way to definitively assign meaning or function to the firing since the neural code of each cell in the organoid is unknown.[29] Biological computing platforms integrate organoids with traditional hardware and harness activity for information processing, suggesting that meaning may be assigned to neural activity without human-interpretable communication on the part of the organoid. Such systems are based on closed-loop stimulation, where sensory inputs in electrical form are supplied by a researcher according to the organoid's outputs, enabling learning through changes in synaptic strength.[30] While the organoid is not entirely passive, correlations between neural signatures and organoid-generated behavioral events, like moving the paddle in a video game of Pong, are preset by the experimenter.[30] An organoid lacking sensory stimulation is a black box of spontaneous neural activity, without any human-determined, external frame of reference to attribute meaning. In practical terms, these limitations of identifying organoid consciousness suggest that quantitative metrics are predictors, not proxies, for consciousness in the pragmatic and phenomenological sense. Numerical measures of consciousness can at best represent theories for the evaluation of an ethical risk, rather than means to reaching definitive conclusions, with waning effectiveness when applied beyond the organisms in which they were originally developed.[30]

6. Scientific Benefits of Organoids

Organoid consciousness cannot be entirely excluded, despite anatomical characteristics and activity indices demonstrating its low probability,

precisely on account of the difficulties in translating metrics from humans to other systems. Nonetheless, it is essential to evaluate the potential for moral harm in relative terms; organoids carry only a remote possibility of suffering when terminated in comparison to animal models, which are routinely subjected to harmful protocols.[31] When the prospect of applying research to relieve human suffering is distant in comparison to the harm inflicted on animals, organoids can sidestep the additional question of whether the experimentation is *ethically excusable*.[32] In fact, the very existence of animal experimentation assumes that model organisms must be *fundamentally similar to Homo sapiens* for meaningful clinical application of the findings, signaling that humanlike suffering is occurring on a grand scale.[32] Even if there is some likelihood for consciousness in organoids, any claim of suffering would add a further layer of improbability through the requirement for *sentience*, and the corresponding assertion that their experiences not only exist but have valence. On the other hand, many forms of animal experimentation inherently assume that suffering is occurring in order to be valid; established paradigms in neuroscience and psychology, such as the forced-swim test for rodents, are explicitly designed to model and evaluate suffering from depression.[33] The existence and severity of animal suffering strikes at the central issue with precautionary arguments surrounding the use of organoids in research. While it may be an instructive exercise to "err on the liberal side" regarding the attribution of consciousness to organoids, doing so threatens to downplay the possibility that applying the neural cell culture technology in research can prevent ongoing, obvious harm to animals.[34] If science makes an effort to shift as much animal experimentation as possible into organoids, and they are later determined not to suffer, a great deal of harm would have been prevented. In the unlikely event that organoids do turn out to suffer, the outcome will be a "moral tie," for the suffering will have been shifted from one category of subject to another. While one might attempt to assert that suffering is ethically worse when experienced by an organoid compared to an animal, the claim would be tantamount to a speciesist argument that the human origins of the organoid's cells make it morally superior.[32]

Beyond the definitive relief of animal suffering, organoids have the unique potential to *reduce or prevent human suffering* in ways that animal models cannot. New drug candidates for neurological diseases can be screened with much higher throughput in organoids compared to model organisms, which reduces the time to find an effective hit and begin clinical trials, ultimately improving and saving more human lives.[35] Furthermore, brain organoids could be generated from a patient's own cells and auto-transplanted for reconstructive purposes to treat strokes and traumatic injuries.[35] For reasons that are often poorly understood, animals or other models may fail to accurately replicate uniquely human biology, leading to unexpected and severe side effects. The trial of TGN1412, a novel drug designed to suppress the immune system, is a prominent case in point; after successful testing in monkeys, human volunteers received the compound, only to experience the contradictory effect of extreme immune activation, leading to multi-organ failure and hospitalization.[36] While more easily overlooked, organoids also bring the unique advantage of minimizing the number of "missed" new pharmaceuticals, which may be safe and effective in humans or human-derived cells, but are abandoned before reaching clinical trials due to harm or lack of effect in animals.[36]

The applications of *Organoid Intelligence (OI)* to biological computing could bring further benefits to humans in the clinical sphere and beyond. Connecting organoids to conventional computer hardware could enable information processing in a manner analogous to AI and machine learning, only far more energy-efficient.[37] The resulting organoid intelligence systems could ultimately be used to

analyze large amounts of biological data for diagnostic and drug development purposes and may even take over the role of conventional computing hardware in the longer term, preventing human suffering from environmental contamination associated with excessive and irresponsible energy use.

7. Agency, Legal Personhood, and Moral Status

Aside from hindering the use of organoids, centering speculative ethical concerns can invite misunderstandings that may lead to counterproductive regulation. Terminological confusion regarding organoids extends to the concept of agency, driving fears that could unnecessarily hinder drug-development efforts for neurological diseases. Established theories of agency involve intentional action, making it difficult to classify organoids as agents without ascribing goal-oriented, motivated mental states, which would require the implausible classification of organoids as *sentient* when *consciousness* alone is already quite unlikely.[38] Under recent reconceptualizations within the philosophy of technology, an *agent* must merely be distinct from its environment with the capability for behaviors that occur without external causation and adaptive responses when inputs change.[39,40] While such frameworks are useful for highlighting the promises and pitfalls of AI by attributing agency to novel technology, they lead to frivolous and unhelpful categorizations elsewhere. If an organoid could be classified as an agent, so could a bacterium, or even a large macromolecule capable of self-assembly. Applying an excessively broad definition of agency risks confusion with the more restrictive and consequential notion in widespread use, leading to peculiar limitations on organoid research, which might become formalized through the concept of *legal personhood.* If animals that display outward signs of consciousness, such as an orangutan in Argentina and an elephant in Pakistan, have been accorded rights and protections under the subcategory of *natural persons,* which encompasses the non-corporate legal category of born, biological individuals, what prevents courts from granting the same status and protections to organoids on precautionary grounds?[41,42] Legal frameworks for personhood might be expanded to encompass organoids based on the assumption that the neuronal cell cultures have the capacity for complex responses or internal mental states comparable to species like hippopotamuses, dolphins, and dogs.

Assigning personhood to organoids would also lead to the attribution of *moral status* as a consequence, which requires that a subject has interests that matter for its own existence.[43] While the boundaries of legal personhood vary by jurisdiction, it has so far been limited to humans and animals that display evidence of complex, goal-directed actions, suggesting that the category necessarily implies moral status. By consequence, legal personhood for organoids would either imply that a subject can have rights without clear evidence of interests, which appears logically inconsistent, or that the neuronal cell cultures have *moral status*, and, thus, its prerequisite condition of *sentience.*[44]

Therefore, attributing legal personhood to organoids would not only create a regulatory hindrance, but also inadvertently hand down an ontological judgment on whether organoids are conscious by statute alone. If organoids are nonconscious entities devoid of interests and cares, it follows that they lack *moral status in themselves*, making their destruction after use in research seemingly inconsequential. However, the act can still bear ethical implications by way of emotional suffering for other subjects, including family members, despite not directly affecting patients, such as in the case of unauthorized collection of body parts from deceased individuals at the Alder Hey hospital in Britain.[45]

Granting organoids legal personhood could open up avenues to the sanction or criminal

prosecution of researchers for inflicting harm on organoids, posing a significant hindrance to studies with clinical applications. Currently, the use of animals in research in the United States is guided by the *Improved Standards for Laboratory Animals Act* of 1985, which requires the establishment of an Institutional Animal Care and Use Committee (IACUC) that provides internal oversight for animal research.[46] However, the IACUC is not mandated to report to the USDA for enforcement by inspections and investigations, leaving a legal loophole for unnecessary or harmful animal research to continue.[47] While the Act is explicitly limited to warm-blooded research species, does not grant personhood, and excludes *in vitro* models like organoids, increasing awareness of complex animal cognition could conceivably lead to changes that make classifications based on broader characteristics, such as the ability to intentionally respond to stimuli.[47] In that event, the legal structure for animals could potentially be applied to organoids, stifling researchers with investigations and fines in the absence of conclusive evidence for animal-level cognition in organoids.

A similar issue surrounding the legal classification of organoids could arise through regulations designed to safeguard patients in clinical trials. The 2018 revision of the Common Rule of the Code of Federal Regulations defines a *human research subject* as "a living individual about whom an investigator conducting research obtains information or biospecimens," making the inclusion of organoids under clinical trial protections dependent upon their categorization.[48] Considering the common tendency to situate the essence of a person in the brain and mind, organoids that develop sufficiently humanlike cognitive abilities might be categorized as "living individuals" in a regulatory context, prompting interpretations of the Common Rule that could prevent research institutions from receiving federal funding, or mandate that organoids be granted data confidentiality and provide informed consent for any procedures or compounds administered. The bipartisan FDA Modernization Act 2.0 of 2022 represents a positive step by doing away with requirements for preclinical animal models and explicitly permitting "cell-based assays" and "other nonhuman or human biology-based test methods," which would encompass organoids.[49] Nevertheless, it remains important for state and local regulations, as well as laws in other nations, to avoid restricting the use of organoids in research through overly-broad or ambiguous applications of terminology.

8. Prioritizing Utility and Balance

Beyond hindering or reducing the use of organoids altogether, ethical fears surrounding consciousness distract from more imminent disparities in access to the technology. Gene editing and RNA interference-based therapies are already in development for a range of heritable neurological conditions, including Huntington's disease and epilepsy. As a result, organoids are not only research tools, but practical platforms to study rare neurological conditions in order to develop custom treatments targeted to a patient's specific mutation.[50] However, the resources necessary to produce organoids are significant; reagents alone can cost up to $5,000 per organoid, in addition to lab equipment and labor.[51] While clinical trials typically provide free investigational drugs, individualized therapeutics requiring organoids for testing could limit access to patients with adequate financial resources and nations with universal healthcare systems that cover expensive rare disease treatments, exacerbating socioeconomic disparities once commercialized. For individuals with extremely rare diseases, testing a potential treatment in a typical randomized controlled trial may be infeasible due to a small affected population, making an evaluation in a preclinical model followed by a single-patient approval through the FDA's expanded access pathway the only possible option.[52] In an era of

personalized medicine, patients who lack the resources to have prospective treatments tested in organoids generated from their own cells for high-quality preclinical data might face greater uncertainty and an increased risk for side effects. Poorly conceived applications of organoids also threaten to siphon attention away from biomedical research. The case of the American composer Alvin Lucier, who donated blood to produce organoids that generate music through spontaneous activity after his death, raises a unique question of whether serving as the cell donor for an organoid can justify copyright over the creative results of its neural activity. Such experimentation may be considered wasteful in utilitarian terms, taking finite resources away from research and clinical studies.[53]

The practical consideration of informed consent in the harvesting of patient samples for research deserves special attention for organoids. While biosample collection is already tainted by the ethical issue that material can be obtained from an unconscious patient without their knowledge, analogous to HeLa cells harvested without consent, organoids invite further questions surrounding patients' decisional capacity. Since brain organoids are used to model neurological disorders that may produce a cognitive decline in the patients from which cells are derived, determining whether a subject truly comprehends the implications of participating in a study may extend beyond signatures on a form, requiring a multidisciplinary evaluation. While ethical scholarship surrounding neurological patients has understandably focused on issues of clinical care, it would be prudent to adopt similar measures of advance directive and power of attorney in relation to the contribution of cells and genetic material for research use.[54] Considering the broad success of organ donor registration with driver's license applications to improve accessibility to timely transplants, a similar measure of advance consent could be implemented to collect tissue samples that might be used to generate organoids.

9. Precautionary Arguments

The case of organoids also prompts broader examination of the scenarios under which precautionary arguments surrounding new technologies are more or less effectively applied. In scenarios such as germline genome editing, the harms posed by inaction compared to action are asymmetric; the severity of the "worst-case scenario" is both uncertain and extremely high. For example, not performing germline genome editing leads to known suffering in patients born with genetic disorders, while doing so comes with a low probability of highly detrimental outcomes, such as off-target effects leading to more disabling conditions, or creating novel forms of discrimination based on individuals' edited status. However, the reckoning is markedly different for organoids. The exclusion of organoids from research will cause suffering in animal models and humans with certainty, while the analogous consequence is more remote if organoids have their niche in research. Unlike with genome editing, the harms of action versus inaction are *symmetric* for organoids; in both cases, living subjects experience a similar manner and extent of suffering, for it would be challenging to claim that the negatively valenced experience of an organoid is worse than that of an animal. It therefore appears that asymmetry and high uncertainty in possible harms are key factors in determining whether precautionary arguments are sensible.

10. Conclusion

The approach to human brain organoids must strike a judicious equilibrium, aiming to maximize the benefit for patients with neurological conditions and prevent the most imminent ethical risks of informed consent and societal disparities. Moral concerns associated with remote possibilities of organoid consciousness and suffering must be appropriately weighed against the ongoing harms

inflicted upon animals and humans as a result of biomedical research. Unless proven to possess mental states, caution regarding consciousness and moral status must be exercised through neurobiological, philosophical, and legal optics with the terminologically clear assumption that *organoids are a technology without sentience or personhood*, and adequate attention must be directed towards commonplace ethical challenges rather than speculative concerns.

References

1. Stranneheim, H., Lagerstedt-Robinson, K., Magnusson, M., Kvarnung, M., Nilsson, D., Lesko, N., Engvall, M., Anderlid, B., Arnell, H., Johansson, C. B., Barbaro, M., Björck, E., Bruhn, H., Eisfeldt, J., Freyer, C., Grigelioniene, G., Gustavsson, P., Hammarsjö, A., Hellström-Pigg, M., . . . Wedell, A. (2021). Integration of whole genome sequencing into a healthcare setting: high diagnostic rates across multiple clinical entities in 3219 rare disease patients. *Genome Medicine, 13*(1), 40. https://doi.org/10.1186/s13073-021-00855-5
2. Quadrato, G., Brown, J., & Arlotta, P. (2016). The promises and challenges of human brain organoids as models of neuropsychiatric disease. *Nature Medicine, 22*(11), 1220–1228. https://doi.org/10.1038/nm.4214
3. Rubio, A. D., Hamilton, L., Bausch, M., Jin, M., Papetti, A., Jiang, P., & Yelamanchili, S. V. (2025). A Comprehensive Review on Utilizing Human Brain Organoids to Study Neuroinflammation in Neurological Disorders. *Journal of Neuroimmune Pharmacology, 20*(1), 23. https://doi.org/10.1007/s11481-025-10181-x
4. Chen, H. I., Song, H., & Ming, G. (2019). Applications of Human Brain Organoids to Clinical Problems. *Developmental Dynamics, 248*(1), 53–64. https://doi.org/10.1002/dvdy.24662
5. Zhang, W., Jiang, J., Xu, Z., Yan, H., Tang, B., Liu, C., Chen, C., & Meng, Q. (2023). Microglia-containing human brain organoids for the study of brain development and pathology. *Molecular Psychiatry, 28*(1), 96–107. https://doi.org/10.1038/s41380-022-01892-1
6. Mariani, J., Coppola, G., Zhang, P., Abyzov, A., Provini, L., Tomasini, L., Amenduni, M., Szekely, A., Palejev, D., Wilson, M., Gerstein, M., Grigorenko, E. L., Chawarska, K., Pelphrey, K. A., Howe, J. R., & Vaccarino, F. M. (2015). FOXG1-Dependent Dysregulation of GABA/Glutamate Neuron Differentiation in Autism Spectrum Disorders. *Cell, 162*(2), 375–390. https://doi.org/10.1016/j.cell.2015.06.034
7. Letzter, R. (2021, March 4). *Scientists grow human-Neanderthal hybrid 'minibrains' in petri dishes.* LiveScience. https://www.livescience.com/human-neanderthal-minibrains-created.html
8. Starr, M. (2023, January 1). *Scientists Grew Stem Cell 'Mini Brains' And Then The Brains Sort-of Developed Eyes.* ScienceAlert. https://www.sciencealert.com/scientists-grew-stem-cell-mini-brains-and-then-the-brains-sort-of-developed-eyes
9. Starr, M. (2024, December 18). *Human Minibrains Launched Into Space Thrived in an Unexpected Way.* ScienceAlert. https://www.sciencealert.com/human-minibrains-launched-into-space-thrived-in-an-unexpected-way
10. Thierry, G. (2019, October 25). *Lab-grown mini brains: we can't dismiss the possibility that they could one day outsmart us.* The Conversation. http://theconversation.com/lab-grown-mini-brains-we-cant-dismiss-the-possibility-that-they-could-one-day-outsmart-us-125842
11. Qian, X., Nguyen, H. N., Song, M. M., Hadiono, C., Ogden, S. C., Hammack, C., Yao, B., Hamersky, G. R., Jacob, F., Zhong, C., Yoon, K., Jeang, W., Lin, L., Li, Y., Thakor, J., Berg, D. A., Zhang, C., Kang, E., Chickering, M., . . . Ming, G. (2016). Brain-Region-Specific Organoids Using Mini-bioreactors for Modeling ZIKV Exposure. *Cell, 165*(5), 1238–1254. https://doi.org/10.1016/j.cell.2016.04.032

12. Gennaro, R. *Consciousness.* Internet Encyclopedia of Philosophy. https://iep.utm.edu/consciousness/#H4
13. Nagel, T. (1974). What Is It Like to Be a Bat? *The Philosophical Review, 83*(4), 435–450. https://doi.org/10.2307/2183914
14. Schurger, A., & Graziano, M. (2022). Consciousness explained or described? *Neuroscience of Consciousness, 2022*(1). https://doi.org/10.1093/nc/niac001
15. White, A. J., Kohman, R. E., Aach, J. D., Lopes, M., Lunshof, J. E., Paulsen, B., Pigoni, M., & Hyun, I. (2024). No Need to Worry About Consciousness in Brain Organoids. In I. Hyun, & J. E. Lunshof (Eds.), *Human Brain Organoids: Scientific and Ethical Considerations* (pp. 35–40). Springer Nature Switzerland. https://doi.org/10.1007/978-3-031-72371-1_3
16. Koubeissi, M. Z., Bartolomei, F., Beltagy, A., & Picard, F. (2014). Electrical stimulation of a small brain area reversibly disrupts consciousness. *Epilepsy & Behavior, 37*, 32–35. https://doi.org/10.1016/j.yebeh.2014.05.027
17. Quadrato, G., Nguyen, T., Macosko, E. Z., Sherwood, J. L., Min Yang, S., Berger, D. R., Maria, N., Scholvin, J., Goldman, M., Kinney, J. P., Boyden, E. S., Lichtman, J. W., Williams, Z. M., McCarroll, S. A., & Arlotta, P. (2017). Cell diversity and network dynamics in photosensitive human brain organoids. *Nature, 545*(7652), 48–53. https://doi.org/10.1038/nature22047
18. Wang, Q., Ding, S., Li, Y., Royall, J., Feng, D., Lesnar, P., Graddis, N., Naeemi, M., Facer, B., Ho, A., Dolbeare, T., Blanchard, B., Dee, N., Wakeman, W., Hirokawa, K. E., Szafer, A., Sunkin, S. M., Oh, S. W., Bernard, A., . . . Ng, L. (2020). The Allen Mouse Brain Common Coordinate Framework: A 3D Reference Atlas. *Cell, 181*(4), 936–953.e20. https://doi.org/10.1016/j.cell.2020.04.007
19. Birch, J. (2024). The Concept of Sentience. In J. Birch (Ed.), *The Edge of Sentience: Risk and Precaution in Humans, Other Animals, and AI* (pp. 23-42). Oxford University Press. https://doi.org/10.1093/9780191966729.003.0003
20. Brady, M. S. (2018). What Suffering Is. In M. S. Brady (Ed.), *Suffering and Virtue* (pp. 11-31). Oxford University Press. https://doi.org/10.1093/oso/9780198812807.003.0002
21. Ginsburg, S., & Jablonka, E. (2007). The Transition to Experiencing: I. Limited Learning and Limited Experiencing. *Biological Theory, 2*(3), 218–230. https://10.1162/biot.2007.2.3.218
22. Hameroff, S., & Penrose, R. (2014). Consciousness in the universe: A review of the 'Orch OR' theory. *Physics of Life Reviews, 11*(1), 39–78. https://doi.org/10.1016/j.plrev.2013.08.002
23. Tononi, G. (2004). An information integration theory of consciousness. *BMC Neuroscience, 5*(1), 42. https://doi.org/10.1186/1471-2202-5-42
24. Massimini, M., Boly, M., Casali, A., Rosanova, M., & Tononi, G. (2009). A perturbational approach for evaluating the brain's capacity for consciousness. *Progress in Brain Research*, 177, 201–214. https://doi.org/10.1016/S0079-6123(09)17714-2
25. Van Gulick, R. (2026, March). *Consciousness.* Stanford Encyclopedia of Philosophy. https://plato.stanford.edu/entries/consciousness/
26. Levine, J. (1983). Materialism and Qualia: The Explanatory Gap. *Pacific Philosophical Quarterly, 64* (October), 354–361. https://doi.org/10.1111/j.1468-0114.1983.tb00207.x
27. Rosanova, M., Casarotto, S., Derchi, C., Hassan, G., Russo, S., Sarasso, S., Viganò, A., Massimini, M., & Comanducci, A. (2023). The perturbational complexity index detects capacity for consciousness earlier than the recovery of behavioral responsiveness in subacute brain-injured patients. *Brain Stimulation: Basic, Translational, and Clinical Research in Neuromodulation, 16*(1), 371. http://dx.doi.org/10.1016/j.brs.2023.01.731
28. Mallatt, J., & Feinberg, T. E. (2021). Multiple Routes to Animal Consciousness: Constrained Multiple Realizability Rather Than Modest Identity

Theory. *Frontiers in Psychology,* https://doi.org/10.3389/fpsyg.2021.732336
29. Eggermont, J. J. (1998). Is There a Neural Code? *Neuroscience & Biobehavioral Reviews, 22*(2), 355–370. https://doi.org/10.1016/S0149-7634(97)00021-3
30. Kagan, B. J., Duc, D., Stevens, I., & Gilbert, F. (2022). Neurons Embodied in a Virtual World: Evidence for Organoid Ethics? *AJOB Neuroscience, 13*(2), 114–117. https://doi.org/10.1080/21507740.2022.2048731
31. Reardon, S. (2025). *New NIH office to reduce use of animals in research.* Science. https://www.science.org/content/article/new-nih-office-reduce-use-animals-research
32. Singer, P. (2011). *Practical Ethics* (3rd ed.). Cambridge University Press.
33. Can, A., Dao, D. T., Arad, M., Terrillion, C. E., Piantadosi, S. C., & Gould, T. D. (2012). The Mouse Forced Swim Test. *JoVE,* (59), e3638. https://doi.org/10.3791/3638
34. Lavazza, A., & Reichlin, M. (2023). Human Brain Organoids: Why There Can Be Moral Concerns If They Grow Up in the Lab and Are Transplanted or Destroyed. *Cambridge Quarterly of Healthcare Ethics, 32*(4), 582–596. https://doi.org/10.1017/s096318012300021x
35. Liu, X., Zhou, Z., Zhang, Y., Zhong, H., Cai, X., & Guan, R. (2025). Recent progress on the organoids: Techniques, advantages and applications. *Biomedicine & Pharmacotherapy, 185*, 117942. https://doi.org/10.1016/j.biopha.2025.117942
36. Akhtar, A. (2015). The Flaws and Human Harms of Animal Experimentation. *Cambridge Quarterly of Healthcare Ethics, 24*(4), 407–419. https://doi.org/10.1017/S0963180115000079
37. Smirnova, L., Caffo, B. S., Gracias, D. H., Huang, Q., Morales Pantoja, I. E., Tang, B., Zack, D. J., Berlinicke, C. A., Boyd, J. L., Harris, T. D., Johnson, E. C., Kagan, B. J., Kahn, J., Muotri, A. R., Paulhamus, B. L., Schwamborn, J. C., Plotkin, J., Szalay, A. S., Vogelstein, J. T., . . . Hartung, T. (2023). Organoid intelligence (OI): the new frontier in biocomputing and intelligence-in-a-dish. *Frontiers in Science, 1*, 1. https://doi.org/10.3389/fsci.2023.1017235
38. Schlosser, M. (2019). Agency. In E. N. Zalta (Ed.), *The Stanford Encyclopedia of Philosophy*. Metaphysics Research Lab, Stanford University. https://plato.stanford.edu/entries/agency/
39. Barandiaran, X. E., Di Paolo, E., & Rohde, M. (2009). Defining agency: Individuality, normativity, asymmetry, and spatio-temporality in action. *Adaptive Behavior, 17*(5), 367–386. https://doi.org/10.1177/1059712309343819
40. Floridi, L. (2025). AI as Agency without Intelligence: On Artificial Intelligence as a New Form of Artificial Agency and the Multiple Realisability of Agency Thesis. *Philosophy & Technology, 38*(1), 30. https://doi.org/10.1007/s13347-025-00858-9
41. Kurki, V. A. J. (2023). *Legal Personhood*. Cambridge University Press. https://doi.org/10.1017/9781009025614
42. Pallotta, N. (2023, Aug 3). *Argentine Court Declares Cougar a "Subject of Rights".* Animal Legal Defense Fund. https://aldf.org/article/argentine-court-declares-cougar-a-subject-of-rights/
43. Jaworska, A., & Tannenbaum, J. (2018, March). *The Grounds of Moral Status.* Stanford Encyclopedia of Philosophy. https://plato.stanford.edu/archives/spr2018/entries/grounds-moral-status
44. Lavazza, A. (2020). Human cerebral organoids and consciousness: a double-edged sword. *Monash Bioethics Review, 38*(2), 105–128. https://doi.org/10.1007/s40592-020-00116-y
45. Barratt, D. (2022). *Liverpool Children's Hospital Collects Body Parts Without Authorization.* EBSCO. https://www.ebsco.com/research-starters/law/liverpool-childrens-hospital-collects-body-parts-without-authorization
46. *US Public Law 99-198 (AWA 1985)*. Michigan State University Animal Legal & Historical Center.

https://www.animallaw.info/statute/us-awa-us-public-law-99-198-awa-1985
47. Agricultural Law Information Partnership. *Animal Welfare Act.* National Agricultural Library. https://www.nal.usda.gov/animal-health-and-welfare/animal-welfare-act
48. *45 CFR Part 46* (2026). Code of Federal Regulations. https://www.ecfr.gov/current/title-45/subtitle-A/subchapter-A/part-46
49. Adashi, E. Y., O'Mahony, D. P., & Cohen, I. G. (2023). The FDA Modernization Act 2.0: Drug Testing in Animals is Rendered Optional. *The American Journal of Medicine, 136*(9), 853–854. https://doi.org/10.1016/j.amjmed.2023.03.033
50. Hamzelou, J. (2023). *More than 200 people have been treated with experimental CRISPR therapies.* https://www.technologyreview.com/2023/03/10/1069619/more-than-200-people-treated-with-experimental-crispr-therapies/
51. Hopkins, H. K., Traverse, E. M., & Barr, K. L. (2021). Methodologies for Generating Brain Organoids to Model Viral Pathogenesis in the CNS. *Pathogens,* https://doi.org/10.3390/pathogens10111510
52. *Expanded Access* (2025). U.S. Food & Drug Administration. https://www.fda.gov/news-events/public-health-focus/expanded-access
53. Cook, R. (2025). *Revivification.* Art Gallery of Western Australia. https://artgallery.wa.gov.au/whats-on/exhibitions/revivification/
54. Vaishnav, N. H., & Chiong, W. (2018). Informed Consent for the Human Research Subject with a Neurologic Disorder. Seminars in Neurology, 38(5), 539–547. https://doi.org/10.1055/s-0038-1668077

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