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Regulating Possibly Sentient Human Cerebral Organoids

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Due to their contested ethical and legal status, human cerebral organoids (HCOs) have become the subject of one of the most rapidly expanding debates in the recent bioethics literature. There is no doubt that their potential scientific usefulness is immense. Human cerebral organoids constitute 3D biological cultures grown in a lab to work as a placeholder model for the human brain, and their similarity can allow us to engage in research that would otherwise not be possible. Yet, it is precisely this similarity that raises ethical issues. That is, if these organoids resemble human brains, might they deserve similar protections?

This dilemma was introduced by Greely (2021), who argued that as these surrogate systems are becoming more similar to the human brain there is also an increased chance that the same moral considerations apply as to work with human subjects; the same considerations that prompted a move to use of a surrogate system in the first place. With the rapid pace of progression in this field, the ethical issue is one that should be considered with urgency. Primarily, this is because cerebral organoids could develop consciousness, and thus could have moral status, especially if they are able to feel positively and negatively valenced states. In their recent target article, Zilio and Lavazza (2023) draw on work in consciousness studies, in addition to ethical theory, in order to evaluate the moral status of potentially conscious cerebral organoids.

In response to this ethical dilemma, Zilio and Lavazza advocate for the use of a precautionary principle, according to which we should act as if these systems are conscious, in order to prevent potentially avoidable harms. We are happy that the authors are defending a precautionary approach, as one of us has previously defended a similar position (Birch & Browning 2021); this paper argued that research on organoids should be regulated under a precautionary principle regarding the likelihood of sentience, where

this should be based on whether they possess the neurological architecture assumed to be sufficient for conscious experience under any credible theory of consciousness. In this commentary we wish to further defend this proposal against its dismissal by Zilio and Lavazza, and argue that their additional ontological criterion is unnecessary.

Zilio and Lavazza cite Birch and Browning's proposal for a precautionary principle for regulating research on human organoids, but go on to reject it, citing Żuradzki (2021) to claim that using this principle based only on consciousness "could lead to an overestimation of the moral status of HCOs." However, it is unclear precisely why this should be the case. The authors admit that consciousness is a sufficient criterion for moral status, but here seem concerned that some conscious organoids may be awarded *too much* moral status. The worry seems to be that conscious organoids could be given higher moral status than some other entities the authors think are worthy of protection, such as human beings that lack consciousness. We think such worries are unfounded, for two reasons.

First, the precautionary principle as first formulated included a caveat regarding taking *proportionate* measures to protect potentially conscious organoids. What counts as proportionate is clearly a matter of debate, but it is plausible that this would scale with the level of consciousness the entity is likely to have. That is, protection for subjects with a minimal level of consciousness would similarly be minimal, while for subjects with a higher level and richer conscious experience would correspondingly be awarded greater protections. Given this, it becomes less likely that HCOs would receive an overestimated moral status, as it is unlikely that they would have more than minimal conscious experience. Where future development makes it possible that they do have a richer form of consciousness, it no longer seems excessive to award

them a higher level of protection. Related to this, and as noted by the authors, protection and regulation would only be implemented in relation to the perceived interests of the subject. Minimally conscious organoids will probably have simple interests, primarily in not suffering, and this may still allow for a wide range of uses.

Second, using this principle to regulate use of HCOs does not need to say anything about the moral status of non-conscious human beings. The authors seem concerned that adopting a consciousness-based precautionary principle may lead to decreased protections for these beings, however we don't see this as a likely outcome. The contexts are different, and the principle is not intended to apply to regulations regarding the treatment of human beings. As the authors discuss, there may be additional reasons to favor a higher moral status, or different protections, for human beings such as those in a vegetative state. This could include the possibility of consciousness persisting in vegetative-state patients, the possibility of them emerging from this state, moral status based on their past possession of consciousness, or moral status in virtue of their relationships to family and friends who care about their fate. Similarly too for thinking about human embryos—their higher moral status could equally well be explained in virtue of the future development of its consciousness and the likelihood of becoming an individual with a richer conscious experience. None of these considerations are relevant to the case of HCOs, and none should bear on the principles used in determining appropriate regulation for their use.

For these reasons, we don't see a need to add an additional ontological criterion for determining the status of HCOs, where a consciousness-based principle can suffice. As we have shown, there is no reason to think that use of a consciousness-based principle will lead to an 'overestimation' of the moral status of organoids, or that it need threaten the moral status of non-conscious human beings. Precautionary reasoning based on sentience is an increasingly common principle used in protection of non-human animals (Birch 2017), where the consensus has shifted to include all vertebrates and octopuses (Low et al. 2012), with recent research even influencing UK legislation to include other cephalopod mollusks as well as decapod crustaceans (Birch et al. 2021; Crump et al. 2022a,b). Rather than overestimating the moral status of these animals, it seems to have appropriately awarded necessary protections. Use of the principle in this area has not had the types of effects the authors are

concerned about, and neither do we think it will in the case of cerebral organoids.

An ontological criterion stands on shaky ground, as it is very unclear what justifies its use, other than creating the preferred outcome regarding moral status in the cases they consider. A consciousness-based principle has a clear rationale: consciousness creates a capacity for suffering, and suffering is widely considered to be morally relevant. It is now extremely common to take mental properties to establish moral status (Jaworska & Tannenbaum 2023). The same is not true for ontological categories, where the moral significance of these is not well-established. There is no strong positive case made for why (controversial) Aristotelian metaphysical categorizations are the right kind of things to guide moral inquiry or how they are relevant for neuroscientists thinking about the ethical implications of their work.

The main reason Zilio and Lavazza give in favor of their ontological criterion is that it captures some intuitions regarding the differential moral status of human cerebral organoids when contrasted with organoids of other types or origins, or conscious entities of other kinds (non-human animals, artificial intelligences). While they stipulate that when considering different beings with an equivalent level of consciousness we intuitively would not award them equal moral status, this claim is questionable. First, it is unclear how widely spread this intuition really is—it is not one shared by the authors of this commentary, for instance. Second, while there is some role for intuitions in moral reasoning, they should not be used unquestioningly. Intuitions can be subject to bias of various kinds and should be investigated to determine if they are justified in the contexts in which they are being drawn on. The worry in particular is that such intuitions are vulnerable to anthropocentric biases, with an inflated sense of human importance.

Thus, we do not see any reason against using a consciousness-based approach to regulating the use of human cerebral organoids. We are concerned by the inherent danger in discriminating against the potential suffering of plausibly conscious systems, through adding further criteria related to human uniqueness. We thus advocate a closer integration of sentience research going on in different cases, such as non-human animals, artificial intelligence, human embryos, and neural organoids. Research in these fields would greatly benefit from developing uniform standards that could be guiding policy-makers to develop consistent legislation without the need to introduce new and potentially contentious criteria. It is almost

universally agreed that the capacity to suffer matters morally, and sentience research is making great strides toward assessing different levels or degrees of richness of this capacity. This is what should inform our ethical deliberations, and regulation of use.

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OPEN PEER COMMENTARIES



Macro-bio-ethical Versus Micro-bio-ethical Issues Concerning Human Brain Organoids

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BACKGROUND

Organoids, in general, have become an established theme in *bioethics*. However, brain organoids are almost unique due to the vital and symbolic nature of the organ they reproduce, albeit partially, *in vitro*: the brain. Not only is the brain the major component of the central nervous system, with essential motor and cognitive functions, it also houses the human

consciousness, and with it, the ability to personify the “moral agent” and to employ moral responsibilities with respect to other moral agents, “moral patients” and self, or those emanating from each moral agent. Consequently, if brain organoids are conscious, this would raise the question of the moral nature of these organoids and its implications (Sawai et al. 2022).

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