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Evaluating neuroprivacy concerns in human brain organoid research

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Neuroprivacy, or the privacy of neural data, has attracted considerable interest. Here, we explore the implications of neuroprivacy in human brain organoid research, detailing different interpretations of this right. Findings suggest a limited connection between neuroprivacy and brain organoid research, underscoring the importance of further examination of this critical issue.

With the recent rapid progress in neurotechnology, there has been an increasing emphasis among stakeholders on the need for normative principles to protect the brain and neural activities. This concern has led to the introduction of the new notion of 'neurorights', which comprise several human rights related to the brain and mind (see Council of Europe Round Table[i]) (Box 1). Neurorights are being actively explored around the world, with some jurisdictions, such as Chile and the US state of Colorado, making attempts at legislation.

One essential aspect is neuroprivacy, or the privacy of neural data. Neurorights were initially established for neurotechnologies, such as brain–computer interfaces, but they can extend to more basic neuroscience, including research with functional magnetic resonance imaging (fMRI) or electroencephalography (EEG). They may apply further to research involving human brain organoids (Box 2). Human brain organoid research depends on cell donation. Indeed, some have stressed the importance of de-identifying materials donated for brain organoid research in terms of neuroprivacy [1].

However, it remains unclear how well donor data associated with human brain organoids should be protected under the new guise of neuroprivacy. To examine this point, it is important to recognize that discussions on neuroprivacy often focus, in effect, on mental privacy. The primary concern here is the protection of mental information that could be read or inferred from neural data. There is apprehension that neuroimaging data could reveal a person's memories, intentions, or preferences. Importantly, not all neural data are related to mental states. For instance, data on the physiological characteristics of neural tissue might not provide insights into a person's mental state, but could still contain information on sensitive brain diseases, which warrants protection. Therefore, in some cases, neuroprivacy refers to the privacy of neural data itself, regardless of whether it reveals mental states. Thus, neuroprivacy is an umbrella term that encompasses different subjects and legal interests, each with distinct implications for brain organoid research.

First, we considered whether the protection of mental privacy is an issue in human brain organoid research. If brain organoids can disclose the mental state of the cell donor, this could raise concerns about violating the mental privacy of the donor. However, this is not possible for fundamental reasons. Since brain organoids are developed from scratch using stem cells, they cannot replicate neural circuits of the donor that support memories, intentions, preferences, and other mental states. Even when using induced pluripotent stem cells (iPSCs) with the same genetic information as the donor, the developmental process differs from that of the donor brain. Certainly, the ethics of brain surrogates, including brain organoids, have raised concerns about whether donor memories can be revealed; however, this applies only to *ex vivo* human brains and not to brain organoids [2].

In the context of scientific communication, we believe that it is important to emphasize that the mental states of a donor cannot be revealed by brain organoids. Some empirical studies suggest that people often misunderstand this point, leading to concerns about the transference of donor's thoughts or personality to brain organoids [3,4]. The misconception that regards human brain organoids as mental duplicates of the donor could jeopardize human brain organoid research, making it appear ethically questionable. This could result in limited public acceptance of this research or unnecessarily strict regulations that hinder its long-term beneficial applications [5]. Therefore, eliminating this misconception is crucial for encouraging constructive ethical and regulatory debates regarding human brain organoid research. Also note that while ethical concerns have been raised regarding the minds of individuals born through human reproductive cloning being identical to those of their donors, this argument is no longer considered credible.

Second, neuroprivacy can mean the privacy of neural data *per se*. In this sense, neuroprivacy is relevant to human brain organoid research. Although it is unclear whether all physiological data of the donor's neural tissue recapitulated in brain organoids warrant protection, some studies have raised particular concerns. Brain organoids generated from patient-derived iPSCs have served as models for various brain disorders, including Miller–Dieker syndrome, microcephaly, autism spectrum disorder, Timothy syndrome, and Alzheimer's disease [6]. As long as these

Box 1. Neurorights

Neurorights are a proposed set of human rights aimed at safeguarding the brain and neural activities. These rights have been called for to address new ethical and legal concerns in recently advanced neurotechnologies [10]. The right to mental privacy is a key component of neurorights, as it protects against unauthorized access to, and misuse of, neural data that could reveal personal thoughts, memories, and preferences. Cognitive freedom ensures that individuals have the right to control their own mental processes and resist coercive or involuntary manipulation through neurotechnologies. Psychological continuity protects a person's identity, which could be affected by cognitive interventions or alterations in neural function. Furthermore, neurorights advocate for equitable access to cognitive enhancement technologies to prevent exacerbation of social inequalities.

Re-interpreting neurorights through human rights instruments may be a vital step toward establishing a global standard for the use of neurotechnologies[iii]. However, defining the scope and limits of neurorights in a rapidly evolving technological landscape remains a significant challenge. Moreover, raising public awareness of neurorights is essential to ensure informed discussions and decisions regarding the use of neurotechnology.

organoids successfully model such disease, they can exhibit certain disease-related features of the donor's neural tissue. In fact, brain organoids are adept at mimicking neural malformations during early development, making them useful for drug screening in diseases that have an etiology related to this phase, such as Zika virus-induced microcephaly [7]. However, organoid-based disease modeling raises privacy concerns, particularly when brain organoids are derived from the cells of patients with conditions vulnerable to stigmatization. In such cases, measures should be taken to ensure donor anonymity [8]. A similar privacy issue can arise in the handling of incidental findings during the creation of brain organoids [8].

However, it appears unnecessary to introduce a new concept of neuroprivacy, separate from existing privacy discussions, to address the protection of sensitive disease information in brain organoid research. The needs to protect personal information about a disease is not specifically related to the brain. Indeed, there are patient-derived organoids other than brain organoids, for which privacy protection is very important. An oft-cited example is intestinal organoids produced from iPSCs derived from patients with cystic fibrosis [8]. It is unlikely that such case and disease studies using brain organoids require different rationales for privacy protection. Introducing the concept of neuroprivacy in the latter would be similar to introducing the concept of 'bowel privacy' in the former, which has no more meaning than merely identifying the organ in which the cause of the disease resides. However, as the bowl-privacy example might suggest, the neologism 'neuroprivacy' could serve the purpose of drawing renewed attention to existing issues rather than introducing new ones. If confined to this heuristic meaning, we might consider the protection of sensitive information in human brain organoid research as a 'neuroprivacy issue'.

Box 2. Neurotechnologies and human brain organoids

Neurotechnologies encompass tools and devices interfacing with the nervous system to record, modulate, or enhance neural activity. Brain–computer interfaces (BCIs) allow direct communication between the brain and external devices. Neuroimaging technologies, such as fMRI and EEG, provide insights into brain activity and structure, aiding clinical research on neurological and psychiatric disorders [11]. Neuromodulation devices, including deep brain stimulation (DBS) and transcranial magnetic stimulation (TMS), modulate brain activity and have shown efficacy in alleviating symptoms of conditions such as Parkinson's disease, seizures, and depression [12]. Emerging applications aim to enhance cognitive functions through neurofeedback and other BCI technologies [13].

Human brain organoids are 3D neural structures derived from human stem cells that exhibit certain aspects of human brain structure and function. The generation of brain organoids involves the differentiation of pluripotent stem cells, such as induced pluripotent stem cells, embryonic stem cells, and tissue stem cells, into neural progenitor cells [14,15], which then self-organize into complex structures that resemble the early development stages of the brain. Brain organoids are invaluable for modeling disorders such as Alzheimer's disease, autism spectrum disorders, and microcephaly, providing insights into disease mechanisms and potential therapeutic targets. They also offer platforms for drug screening and studying human brain development.

Other privacy concerns have been raised in human brain organoid research [8,9], which are indeed significant ethical issues in this area. However, none of these concerns are particularly relevant to neural data. In fact, despite the extensive literature on privacy in organoid research, there are no specific references to brain organoid research except for the aforementioned issues related to brain diseases. For example, iPSC-derived human brain organoids share genetic information with their donors; therefore, protecting the genetic privacy of the donors is a challenge. However, this challenge is common to all studies using iPSCs. Furthermore, separating organoids from more comprehensive donor information could diminish the scientific and clinical value of the research [8]. Without access to donor information, brain organoids cannot be studied in terms of a wider range of characteristics, and neither can they be used in precision medicine. Thus, it is preferable to retain as much the donor information as necessary while protecting it more stringently. In particular, biobanks involving multiple research institutions require proper governance in terms of collaboration with various partners, data management, and data sharing, and possible donors should be informed of such governance during the consent process [9]. Again, these issues are all common in research using human biological materials, stem cells, or organoids research in general. Therefore, there is no need for additional neuroprivacy protection in human brain organoid research.

The International Society for Stem Cell Research has already established guidelines on privacy issues in stem cell research,

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including human brain organoid research[ii], which recognize the importance and difficulties of maintaining the confidentiality of genetic data and recommend keeping donors' relevant information and sharing data on a firm basis to safeguard donor privacy. While current practices in stem cell or organoid research regarding privacy protection may not be ethically perfect, it is reasonable that human brain organoid research has not been singled out for special consideration.

Finally, we wish to clarify what we are not claiming. First, our skepticism regarding neuroprivacy is not intended to diminish the importance of privacy protection. Rather, we argue that privacy protection in this domain has been a longstanding issue that does not necessarily require a new concept to be identified and analyzed. Additionally, we do not deny that neuroprivacy is significant in other contexts, particularly in regulating neurotechnologies targeting the entire human brain. Furthermore, our discussion primarily concerns *in vitro* human brain organoid research. Studies where human brain organoids are fused with, or transplanted into, other human tissues may indeed raise different kinds of privacy concern, which warrant further investigation. Last, we do not imply that further regulations are not necessary for human brain organoid research beyond those pertaining to privacy. The moral and legal status of human brain organoids, the ethical and legal implications of their transplantation into animals, their connection to machines, and the appropriate form of consent for cell donation are under active debate. It is crucial to exercise caution and prudence when assessing the relevance of various rights to the research or development in question, to carry out that research responsibly.

Author contributions

Conceptualization: M.K., S.I., C.K., T-L.L., T.S.; investigation: M.K.; funding acquisition: T.S.; supervision: T.S.; writing – original draft: M.K.; writing – review and editing: M.K., S.I., C.K., T-L.L., T.S.

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Declaration of interests

The authors declare no competing interests.

Resources

[i]www.coe.int/en/web/bioethics/round-table-on-the-human-rights-issues-raised-by-the-applications-of-neurotechnologies

[ii]www.isscr.org/guidelines

[iii]https://unesdoc.unesco.org/ark:/48223/pf0000389768.locale=en

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References

1. Hoppe, M. *et al.* (2023) Human brain organoid code of conduct. *Front. Mol. Med.* 3, 1143298
2. Farahany, N.A. *et al.* (2018) The ethics of experimenting with human brain tissue. *Nature* 556, 429–432
3. Haselager, D.R. *et al.* (2020) Breeding brains? Patients' and laymen's perspectives on cerebral organoids. *Regen. Med.* 15, 2351–2360
4. Evans, J.H. (2024) *Disembodied Brains: Understanding our Intuitions on Human-Animal Neuro-Chimeras and Human Brain Organoids*, Oxford University Press
5. Kataoka, M. *et al.* (2023) The importance of accurate representation of human brain organoid research. *Trends Biotechnol.* 41, 985–987
6. Amin, N.D. and Paşca, S.P. (2018) Building models of brain disorders with three-dimensional organoids. *Neuron* 100, 389–405
7. Watanabe, M. *et al.* (2017) Self-organized cerebral organoids with human-specific features predict effective drugs to combat zika virus infection. *Cell Rep.* 21, 517–532
8. Boers, S.N. *et al.* (2019) Organoids as hybrids: ethical implications for the exchange of human tissues. *J. Med. Ethics* 45, 131–139
9. Bredenoord, A.L. *et al.* (2017) Human tissues in a dish: the research and ethical implications of organoid technology. *Science* 355, eaaf9414
10. Ienca, M. (2021) On neurorights. *Front. Hum. Neurosci.* 15, 701258
11. Perez, D.L. *et al.* (2021) Neuroimaging in functional neurological disorder: state of the field and research agenda. *NeuroImage* 30, 102623
12. Denison, T. and Morrell, M.J. (2022) Neuromodulation in 2035: The Neurology Future Forecasting Series. *Neurology* 98, 65–72
13. Gruzelier, J.H. (2014) EEG-neurofeedback for optimising performance. I: a review of cognitive and affective outcome in healthy participants. *Neurosci. Biobehav. Rev.* 44, 124–141
14. Lancaster, M.A. *et al.* (2013) Cerebral organoids model human brain development and microcephaly. *Nature* 501, 373–379
15. Hendriks, D. *et al.* (2024) Human fetal brain self-organizes into long-term expanding organoids. *Cell* 187, 712–732