

Brain organoids as models: neuroethics and epistemology

Human brain organoids are in vitro 3D models of the human brain generated from stem cells. They have raised several ethically-relevant questions, including those on sentience and moral status [1], following protection in research [2], ownership [3], and informed consent [4], among others [5]. The ethical discussion, however, has developed independently from any epistemological reflection on organoids as models of the human brain. This is not surprising, given that ethics and epistemology have long been kept separate. Recently, however, some authors have argued that advancements in the field of biotechnology call for an integrated approach [6].

In this paper, I propose a tentative analysis of brain organoids that may start filling the gap between the ethical and the epistemological discussion of their nature and use. I proceed as follows.

Firstly, the ethical issues will be briefly presented. Considerations on sentience, public engagement, informed consent, and the use of brain organoids instead of - or in combination with - animal models will be briefly overviewed. Second, I will focus on how the epistemological analysis could help guide the neuroethical discussion. Since no analysis of organoids as models is presently available, I hypothesize that brain organoids' role in biomedical science is similar to that of animal models. I will consider the distinction LaFollette and Shanks make between hypothetical and causal analogical models [7]. To see whether their framework also fits brain organoid research, I propose a case-study overview of the literature.

Understanding the nature and role of brain organoids as models is crucial to understand what kinds of inferences are licensed by such models and if they are valid. In turn, this can have important implications for the ethical discussion at the foundational and application levels. Given the fast pace of research, the ethical discourse would only benefit from this kind of multidisciplinary integration.

[1] Lavazza, A. (2021). 'Consciousnessoids': clues and insights from human cerebral organoids for the study of consciousness. *Neuroscience of Consciousness*, 2021(2), niab029.

[2] Koplin, J., & Savulescu, J. (2019). Moral Limits of Brain Organoid Research. *Journal of Law, Medicine & Ethics*, 47(4), 760-767. doi:10.1177/1073110519897789

[3] Mollaki, V. (2021). Ethical challenges in organoid use. *BioTech*, 10(3), 12. doi: <https://doi.org/10.3390/biotech10030012>

[4] Bollinger, J., May, E., Mathews, D., Donowitz, M., Sugarman, J. (2021). Patients' perspectives on the derivation and use of organoids. *Stem Cell Reports*, 16(8):1874-1883. doi: 10.1016/j.stemcr.2021.07.004.

[5] Barnhart, A.J., Dierickx, K. (2022). The Many Moral Matters of Organoid Models: A systematic review of reasons. *Med Health Care Philos*, 25(3):545-560. doi: 10.1007/s11019-022-10082-3.

[6] Loshe, S., Wasmer, M.S. & Reydon, T.A.C. (2020). Integrating Philosophy of Science into Research on Ethical, Legal and Social Issues in the Life Sciences. *Perspectives on Science* 2020; 28 (6): 700–736. doi: https://doi.org/10.1162/posc_a_00357

[7] LaFollette, H., & Shanks, N. (1995). Two Models of Models in Biomedical Research. *The Philosophical Quarterly* (1950-), 45(179), 141–160. <https://doi.org/10.2307/2220412>