The importance of accurate representation of human brain organoid research

AUTHOR(S):

Kataoka, Masanori; Gyngell, Christopher; Savulescu, Julian; Sawai, Tsutomu

CITATION:

Kataoka, Masanori ...[et al]. The importance of accurate representation of human brain organoid research. Trends in Biotechnology 2023, 41(8): 985-987

ISSUE DATE:

2023-08

URL:

http://hdl.handle.net/2433/284136

Trends in Biotechnology

CellPress OPEN ACCESS

Science & Society

The importance of accurate representation of human brain organoid research

Masanori Kataoka [1], Christopher Gyngell [2,3], Julian Savulescu [4,5] and Tsutomu Sawai [1,6,*]

Representations of brain organoids in the media are often negatively or positively exaggerated without appropriate discussion. Here, we examine two topics (the possibility of consciousness and medical applications) and call on scientists, ethicists, and the media to represent brain organoid research and its ethical issues more accurately.

Increased interest in brain organoid research

Human brain organoids are self-organizing 3D neural tissues that are generated from human pluripotent stem cells, such as embryonic stem cells and induced pluripotent stem cells. Research into human brain organoids has advanced rapidly over recent years; at the same time, the ethical concerns that it raises have attracted increased scholarly[i] [1] and media attention, arousing public interest.

A recent study identified a fourfold increase in the number of news reports that were published on brain organoids, increasing from 30 in 2017 to 120 in 2019 [2]. Such public interest encourages public participation in discussions about the ethical issues related to human brain organoids, which is of great importance. However, another study revealed that media discussions of human brain organoids tend to drift away from the research itself [3]. This concern has been raised briefly in the past [4].

Inaccurate representations of brain organoid research do not come from the media alone: scientists frequently exaggerate their research, and ethicists can similarly overemphasize the accompanying risks and fail to have a nuanced discussion. In this article, we examine two of the topics that have received the most media interest: the possibility of brain organoids developing consciousness, and the potential of brain organoid research to have medical applications [3]. Although we acknowledge that providing value-neutral and accurate information alone is insufficient for effective public engagement with human brain organoid research [5], we contend that it is nonetheless crucial for scientists, ethicists, and the media to ensure accurate representation of the research in the public domain.

The possibility of consciousness

One of the common concerns regarding brain organoids is the possibility that they are conscious. This concern is important and needs to be addressed appropriately in line with advances in brain organoid research. To this end, it is vital to precisely assess the feasibility at each point in time. However, the possibility of brain organoids having consciousness appears to have been unduly exaggerated by the two types of discourse.

The first and most common is the discourse that portrays brain organoids as 'mini brains'. One study, which showed that long-term cultured brain organoids have the potential to acquire developmental features corresponding to the postnatal stage of the human brain, has been reported in the media under the headline "Mini brain" organoids grown in lab mature much like infant brains'[ii]. Another recent study, which created brain organoids containing gene variants derived from Neanderthals, was presented under the headline 'Neanderthal-like "mini-brains" created in lab with CRISPR' [6]. These headlines suggest that miniature versions of full infant or Neanderthal brains have been created.

However, for the foreseeable future, brain organoids will not be 'mini brains'. As well as being dissimilar to full human brains in many ways, human brain organoids are currently only able to replicate, imperfectly, a small portion of human cerebral tissue, from the early stages of its development. Scientists and ethicists understand this, but the public might believe that brain organoids are just miniature versions of the full human brain if the term 'mini brains' is overused without any further details. Such intuitive terms are partly inevitable to explain complicated scientific findings and to excite readers, and we do not intend to suggest that 'mini brains' should never be used. However, the term should be used more cautiously where there is not enough space to give both an adequate explanation and, ideally, a full explanation of its potential and limits. Importantly, there are currently calls from the scientific community to rethink the terminology used in brain organoid research [7].

Second, some discourses portray brain organoids more directly as if they already experience some kind of mental state. One study that sought to produce organoids with optical cups that are sensitive to light stimulus was reported under the headline 'Tiny human brain grown in lab has eye-like structures that "see" light'-[iii]. Although the meaning of the word 'see' is qualified by the use of quotation marks, such a headline nonetheless gives the impression that brain organoids can acquire the capacity for sight.

The word 'see' of course could have several meanings in this context. It could mean react to light in terms of neuronal firing or it could mean perceive visual objects, which presupposes a conscious entity to perceive. However, this second

possibility is contrary to the view held by most scientists working in this field, that something as simple as current organoids could not support consciousness as evidenced by the 2021 guidelines of the International Society for Stem Cell Research.

Even if brain organoids were to become conscious, it would be another exaggeration to describe such a development as having 'crossed an "ethical rubicon"'[iv]. The sciences have long used conscious animals for research purposes, and the breeding of laboratory animals is also a frequent occurrence. Therefore, conciliatory regulations are in place, allowing research to proceed with due regard to animal consciousness, even though the status quo may not be ideal. Ethicists have accordingly proposed flexible frameworks for the creation and use of future conscious brain organoids [8], but such nuanced views are rarely to be found outside professional ethics papers.

Both types of discourse portray brain organoids as being much closer to the full human brain than they in fact are, a trend that can cause society to perceive brain organoids as being far more threatening and having greater moral significance than they in fact do. This could result in public distrust in research, detracting from its beneficial applications or generating antipathy toward them, or even the strict regulation of research. Recent interview studies suggest that citizens have moral concerns about brain organoids, especially in terms of consciousness, personality, and cloning [9,10]. Cognitive psychology research has also shown that attempting to provide value-neutral information about technologies with little known risk can polarize risk perceptions between people with contrasting worldviews [11]. Therefore, brain organoid research that is related to the abovementioned concerns will require more careful reporting to encourage constructive public engagement.

Medical applications

In contrast to reporting on the potential of brain organoids to be conscious, media representations of the potential applications of human brain organoids have been subdued, focusing on the treatment of neurological diseases and disorders [3]. For instance, very few media articles acknowledge the potential transplantation of brain organoids into human brains [12].

Nevertheless, even in regard to medical applications, there is danger of miscommunication. Medical applications of human brain organoids will be limited to certain classes of neurological disorder for the foreseeable future, because brain organoids can currently only model some brain tissues in their early stages of development. For diseases the etiology of which lies in this stage, such as microcephaly (caused by the Zika virus), brain organoid research has contributed to pathophysiological understanding and drug discovery. However, using brain organoids to model diseases with late onset or diseases that do not involve the structural malformation of neurons, categories that cover several mental illnesses, is challenging. Thus, the headline 'Gene-edited brain organoids are unlocking the secrets of autism'[v] clearly exaggerates the role of brain organoids in autism spectrum disorder (ASD) research. For such diseases, brain organoids currently have important, but only limited, utility [13].

As brain organoid technology improves, there is a possibility they will resemble the full human brain and have wide utility in the study of neurological disease. However, this development poses ethical dilemmas regarding consciousness. Disregarding these intricacies and proposing that human brain organoids could have medical potential for various diseases comes with a risk: if these ambitious projections are not fulfilled, it could lead to a loss of public trust.

Accurate scientific information may also be disrespectful to patients. One study has shown how several scientific papers, through their wording as well as their diagrams (which oppose white 'healthy organoids' against dark 'autistic organoids'), represent ASD as being pathological. This conflicts with the view of the neurodiversity community that the neurological characteristics of people with ASD are part of human diversity [14]. Such a conflict could be mitigated, if not avoided, by more careful use of language and accompanying graphics.

Concluding remarks

Research into human brain organoids is enhancing our understanding of the human brain. However, the public attention that it is currently attracting risks generating unnecessary misunderstanding in society. To avoid this, scientists, ethicists, and the media need to promote more accurate representation and discussion. In addition, it has been noted that public concerns about human brain organoids may differ from ones now reported [15]. Further empirical research on citizens' concerns and communication reflecting them is required.

In stem cell research and therapy, disconnections between the actual research and its public reception have resulted in serious problems, from various instances of research misconduct to increases in global medical tourism, that is, receipt of (often unapproved) stem cell therapies that are not yet regulated. Fortunately, research into human brain organoids is still at an early stage, meaning that now is a crucial time for learning from such previous mistakes.

Acknowledgments

T.S. was funded in whole, or in part, by Japan Agency for Medical Research and Development (AMED) (grant number JP21wm0425021), JST-Research Institute of Science and Technology for Society (RISTEX) (grant number JPMJRS22J4), Japan Society for the Promotion of Science (JSPS) KAKENHI (grant number

21K12908), Mitsubishi Foundation, and Uehiro Foundation on Ethics and Education (grant number UEHIRO2022-0101). C.G. and J.S., through their involvement with the Murdoch Children's Research Institute, received funding through from the Victorian State Government through the Operational Infrastructure Support (OIS) Program. This research was funded in whole, or in part, by the Wellcome Trust (grant number WT203132/Z/16/Z). For the purpose of open access, the authors have applied a CC BY public copyright license to any Author Accepted Manuscript version arising from this submission.

Declaration of interests

J.S. is a partner investigator on an Australian Research Council grant LP190100841, which involves industry partnership from Illumina. He does not personally receive any funds from Illumina. J.S. is a Bioethics Committee consultant for Bayer. The other authors have no interests to declare.

Resources

[i]www.isscr.org/policy/guidelines-for-stem-cell-research-and-clinical-translation/

[ii]https://neurosciencenews.com/mini-brain-human-brain-development-17846/

[iii]www.newscientist.com/article/2287207

[iv]www.theguardian.com/science/2019/oct/21/scientists-may-have-crossed-ethical-line-in-growing-human-brains

[v]www.wired.com/story/gene-edited-brain-organoids-are-unlocking-the-secrets-of-autism/

[1]Graduate School of Humanities and Social Sciences, Hiroshima University, Hiroshima, Japan
[2]Murdoch Children's Research Institute, Melbourne, VIC, Australia
[3]Department of Paediatrics, University of Melbourne, Melbourne, VIC, Australia
[4]Centre for Biomedical Ethics, National University of Singapore, Singapore, Singapore
[5]Wellcome Centre for Ethics and Humanities, University of Oxford, Oxford, UK
[6]Institute for the Advanced Study of Human Biology (ASHBi), Kyoto University, Kyoto, Japan

*Correspondence:
tstmsw@hiroshima-u.ac.jp (T. Sawai).

https://doi.org/10.1016/j.tibtech.2023.02.010

References

1. Sawai, T. *et al.* (2021) Mapping the ethical issues of brain organoid research and application. *AJOB Neurosci.* 13, 81–94
2. Ide, K. *et al.* (2021) Ethical aspects of brain organoid research in news reports: an exploratory descriptive analysis. *Medicina* 57, 532
3. Presley, A. *et al.* (2022) Media portrayal of ethical and social issues in brain organoid research. *Philos. Ethics Humanit. Med.* 17, 8
4. Munsie, M. *et al.* (2017) Ethical issues in human organoid and gastruloid research. *Development* 144, 942–945
5. Boyd, J.L. and Sugarman, J. (2022) Toward responsible public engagement in neuroethics. *AJOB Neurosci.* 13, 103–106
6. Remmel, A. (2021) Neanderthal-like 'mini-brains' created in lab with CRISPR. *Nature* 590, 376–377
7. Pasca, S.P. *et al.* (2022) A nomenclature consensus for nervous system organoids and assembloids. *Nature* 609, 907–910
8. Koplin, J.J. and Savulescu, J. (2019) Moral limits of brain organoid research. *J. Law Med. Ethics* 47, 760–767
9. Bollinger, J. *et al.* (2021) Patients' perspectives on the derivation and use of organoids. *Stem Cell Rep.* 16, 1874–1883
10. Haselager, D.R. *et al.* (2020) Breeding brains? patients' and laymen's perspectives on cerebral organoids. *Regen. Med.* 15, 2351–2360
11. Kahan, D.M. *et al.* (2009) Cultural cognition of the risks and benefits of nanotechnology. *Nat. Nanotechnol.* 4, 87–90
12. Chen, H.I. *et al.* (2019) Applications of human brain organoids to clinical problems. *Dev. Dyn.* 248, 53–64
13. Chan, W.K. *et al.* (2020) Cerebral organoids as tools to identify the developmental roots of autism. *Mol. Autism* 11, 58
14. Barnhart, A.J. and Dierickx, K. (2021) Cultures and cures: neurodiversity and brain organoids. *BMC Med. Ethics* 22, 61
15. Evans, J.H. (2022) The public's ethical issues with brain organoid research and application. *AJOB Neurosci.* 13, 101–103