Letter to Editor

# Organoids are Natural Simulators

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## Dear Editor

Today, with the help of advanced technologies in the field of using powerful and differentiable human stem cells, organoids of the cerebral cortex have been prepared, which can help restore the cerebral cortex's structural and functional characteristics on a limited scale. By providing new disease simulation models, bioengineering provides practical models for using personalized medicine and selecting the most efficient drugs. It can design transplantable prostheses in cases of analysis or damage to a specific area of the brain (1, 2). Researchers have found that cortical organoids are similar in structure and function to the electroencephalographic network of the human brain after birth and provide a suitable model of the growth and development of brain networks in newborns (3, 4). Examining the dishes containing cell cultures has shown that the mentioned organoids have simulated the complexity of the neural structures in the brain's cortical areas and cell diversity. In this respect, they have a significant advantage over the two-dimensional cultures of nerve cells (5-7). Also, human genetic content is not considered in the use of animal models; therefore, organoids in this field can be more successful than animal models (8). The results obtained from the recent investigations on mouse cerebral cortex organoids have shown that these organoids, after being transplanted to the target site, go through the stages of vascularization to transport nutrients and oxygen, thus preventing the death of necrotic cells. In the organoid, it causes the increase of axonal branches to the surrounding tissues (9). In these studies, the activities of a small number of cells were investigated, and the investigations were mainly carried out locally. So far, no study has investigated the long-term functional response of transplanted organoids to external stimuli of the host. Therefore, conducting long-term and focused studies on the electrophysiological activity of organoids and improving their structure is very important. This is even though the current technologies do not provide the conditions to carry out such valuable multi-dimensional experiments.

The high sensitivity of the brain tissue to stopping the blood flow and causing cerebral ischemia has caused a wide effort to investigate effective pharmaceutical agents in reducing this vulnerability. Cerebral ischemia can disrupt the normal process of anesthesia and surgery. Over the past years, using anesthetics has been considered a potential and effective treatment option due to their ability to increase inhibitory synaptic transmission, prevent toxicity and excitability caused by glutamate, and suppress brain metabolism. For this reason, various studies have been conducted on using different anesthetic compounds effective in reducing nerve damage caused by ischemia. Many studies have been conducted on using anesthetics to prevent brain nerve damage in animal models and the pathophysiology of brain ischemia. These studies have come with different results. Researchers have found that some anesthetic compounds such as propofol, barbiturates, and other volatile compounds can improve nerve damage caused by ischemia in a short period.

On the other hand, based on the results of other studies, this protective effect does not have favorable stability and cannot remain long after ischemia. Therefore, the mentioned anesthetic drugs do not provide lasting protection (10). It seems that carrying out these investigations with the help of experimental models based on organoid structures made based on cerebral cortex tissue and optical imaging can be associated with more convincing results. In addition, the use of organoids provides the possibility of examining the neural activity that propagates between the organoid and the brain tissue and determines the brain's response to the stimuli produced by the transplanted organoid. On the other hand, post-mortem histological examination can investigate the relationship between the morphological characteristics and synapses of human organoids with the mouse brain cortex. It also provides the possibility to evaluate the responses of the transplanted organoid and cerebral cortex to anesthetic agents.

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## Conflicts of Interest

The authors declare that there are no conflicts of interest.

## References

1. Corrò C, Novellasdemunt L, Li VSW. A brief history of organoids. Am J Physiol Cell Physiol. 2020;319(1):C151-c65.
2. Eiraku M, Watanabe K, Matsuo-Takasaki M, Kawada M, Yonemura S, Matsumura M, et al. Self-organized formation of polarized cortical tissues from ESCs and its active manipulation by extrinsic signals. Cell Stem Cell. 2008;3(5):519-32.
3. Sato T, Vries RG, Snippert HJ, van de Wetering M, Barker N, Stange DE, et al. Single Lgr5 stem cells build crypt-villus structures in vitro without a mesenchymal niche. Nature. 2009;459(7244):262-5.
4. Heydari Z, Moeinvaziri F, Agarwal T, Pooyan P, Shpichka A, Maiti TK, et al. Organoids: a novel modality in disease modeling. Biodes Manuf. 2021;4(4):689-716.
5. Bock C, Boutros M, Camp JG, Clarke L, Clevers H, Knoblich JA, et al. The Organoid Cell Atlas. Nat Biotechnol. 2021;39(1):13-7.
6. van den Brink SC, van Oudenaarden A. 3D gastruloids: a novel frontier in stem cell-based in vitro modeling of mammalian gastrulation. Trends Cell Biol. 2021;31(9):747-59.
7. Lee KH, Kim TH. Recent Advances in Multicellular Tumor Spheroid Generation for Drug Screening. Biosensors (Basel). 2021;11(11).
8. Montes-Olivas S, Marucci L, Homer M. Mathematical Models of Organoid Cultures. Front Genet. 2019;10:873.
9. Yan H, Konstorum A, Lowengrub JS. Three-Dimensional Spatiotemporal Modeling of Colon Cancer Organoids Reveals that Multimodal Control of Stem Cell Self-Renewal is a Critical Determinant of Size and Shape in Early Stages of Tumor Growth. Bull Math Biol. 2018;80(5):1404-33.
10. Thalheim T, Quaas M, Herberg M, Braumann UD, Kerner C, Loeffler M, et al. Linking stem cell function and growth pattern of intestinal organoids. Dev Biol. 2018;433(2):254-61.