Creating Brain Organoids Isn't a "No-Brainer"

In October of 2019, researchers gathered at the Society for Neuroscience in Chicago to discuss an ambitious project that, in addition to sounding straight out of a science fiction movie, faced an acute ethical dilemma: at what point does growing a brain stop becoming a scientific experiment, and instead breach the threshold of artificially created human sentience?

The extraordinary process of growing human brains hearkens back to the development of the infamous "Ear Mouse." This pithy epithet labeled a mouse with one jarring characteristic—a human ear attached to its back—that resulted from Harvard researchers Joseph and Charles Vacanti creating and studying human ears in a lab and showing that they could develop in a mouse—thus opening the door for creating artificial human organs. Ear Mouse was seen as an impressive, albeit unnerving, human feat. Above all, it set in motion the search for engineering human organs or organoids, tiny organs borne out of three dimensional stem cell cultures, to study human diseases.

It was not until decades later that scientists began making strides in the study of human brain organoids. Sculpted from cultured human pluripotent stem cells, they formed a platform to study a plethora of neurological processes. Most notably, scientists could use these brain organoids to study biochemical and cellular pathways involved in a variety of illnesses and disorders, including Alzheimer's disease, autism, and schizophrenia. Previously, scientists had a limited toolbox to examine such afflictions. A mouse brain provided inadequate insights into the complexity of human brain disorders and experimenting on human subjects indubitably carried its own host of ethical complications. Hence, the implementation of brain organoids quickly caught on. Stanford University's Associate Professor of Psychiatry and Behavioral Sciences, Sergiu Pasca, for instance, utilized these organoids to examine the cerebral cortex and further investigate Timothy syndrome, a rare but devastating brain development disorder. More recently, a team of neuroscientists at the University of California, San Diego, led by a professor of Pediatrics and Cellular & Molecular Medicine, Dr. Alysson Muotri, have run drug trials on organoids in an effort to understand how to protect the human brain from COVID-19.

Although organoids have enabled scientists to study the inner workings of the human brain in unprecedented ways, one glaring concern lurks in the background—the possibility of brain organoids acquiring human consciousness. Apprehension surrounding this issue immediately arose in April of 2017, after scientists belonging to Harvard University's Department of Stem Cell Research and Regenerative Biology detected that brain organoids responded to light. The organoids' electrical activity after light was shone on them prompted many to question the potential for organoids to develop complicated neural systems of their own, and possibly even become sentient. Moreover, Dr. Muotri's team found that premature infants and brain organoids demonstrated similar waves of neurological activity, posing the risk of what science editor for *The Guardian* Ian Sample called "crossing the ethical line."

At the aforementioned 2019 Society for Neuroscience meeting, researchers and neurologists coalesced in an effort to define the "ethical line." The National Academies of Sciences, Engineering, and Medicine proposed a more thorough protocol for how to regulate the use of brain organoids. At the crux of this ethical discourse lay the seemingly inextricable question of what consciousness even is, and what to do if brain organoids exhibit such a phenomenon.

As Martha J. Fara, a cognitive neuroscientist at the University of Pennsylvania, once explained, "...Our ethical concern is with conscious mental life, and conscious suffering in particular, rather than with unconscious information processing." Could brain organoids demonstrating electrical activity be equated with "conscious mental life"? And if so, would the next step in the development of these organoids be the ability to sense pain?

Some of the fears pertaining to organoid consciousness are subsiding. In the words of Dr. Han-Chiao Isaac Chen, also a neuroscientist at the University of Pennsylvania, brain organoids are "still very, very primitive and rudimentary compared to even the brain of a mouse, let alone the brain of a human," suggesting that the signs of consciousness and conscious suffering would be negligible.

However, there is no consensus yet among scientists and ethicists regarding the degree of consciousness within brain organoids and our ability to even assess consciousness and suffering if it were to arise in them. How would the detection of pain in organoids shift our views regarding the generation of brain organoids? Is the electrical activity found in sensory neurons activated by pain-inducing stimuli equivalent to the human conscious sensing of "pain"? Should we be only guided by concerns about possible pain and suffering in organoids or should we equally monitor the emergence of "thoughts"? Are the potential gains in alleviating human neurological diseases sufficient to wade into these ethically murky waters?

Perhaps the best way to tackle these questions is by looking to scientific technologies similarly rife with ethical dilemmas—genome editing and human cloning—and the approaches scientists are taking to address them. In both cases, panels of scientists, ethicists, and community members, such as patients or their family members, are coming together to establish clear guidelines on how further investigations should proceed. The layered voices of each member of this multidisciplinary panel serve as an exemplary model for tackling bioethical challenges.

A similar panel must be established for brain organoid research. Despite being relatively young, this research is already posing ethical concerns that will become increasingly difficult to resolve as this research progresses. A cohesive framework, agreed upon by scientists, ethical experts and community members needs to be developed as soon as possible. The inclusion of the voices of patients suffering from neurological diseases and their family members, who are all major public stakeholders in this research, is especially important to ensure broad representation. Charting an ethically responsible course in the exciting era of organoid research will allow us to maximally reap the benefits of this revolutionary science without compromising our core values.