A Tale of Two Chimeras: Applying the Six Principles to Human Brain Organoid Xenotransplantation

Cerebral organoid models in-of-themselves are considered as an alternative to research animal models. But their developmental and biological limitations currently inhibit the probability of fully replacing animal models.(1,2) Furthermore, these organoid limitations have, somewhat ironically, brought researchers back to the animal model via xenotransplantation – thus creating hybrids and chimeras. Traditional animal ethics frameworks, such as the well-known 3Rs (reduce, refine, and replace), have previously addressed chimeras and xenotransplantation of tissue.(3) But these frameworks have yet to completely assess the neural-chimeric possibilities.(3) And while the 3Rs framework was a historical landmark in animal ethics, there are identifiable gaps in the framework.(4) The authors propose to utilize an expanded 3Rs framework known as the Six Principles (6Ps).(4,5) This framework aims to expand upon the 3Rs, fill in the gaps, and be a practical means for assessing animal ethical issues like that of neural-chimeras and cerebral organoid xenotransplantation. The scope of this 6Ps application will focus on two separate but recent studies which were published in 2019 and 2020. First, they consider a study wherein cerebral organoids were grown from donors with Down syndrome and from neurotypical donors.(6) After these organoids were grown and studied, they were surgically implanted into mouse models to observe the physiological effects as well as any behavioral change in the chimera.(6) Second, they consider a separate study wherein neurotypical human embryonic stem cell derived cerebral organoids were grown and transplanted into mouse and macaque models.(7) The aim was to observe if such a transplantation method would contribute to therapies for brain injury or stroke.(7) The authors place both studies under the lens of the 6Ps framework, assess the relevant contexts of each case, and provide relevant normative conclusions. In this way, they demonstrate how the 6Ps could be applied in future cases of neural-chimeras and cerebral organoid xenotransplantation.

References

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