techniques for influencing the brain certainly raise interesting issues, but addressing them requires greater analytical refinement and more engagement with pertinent court opinions and legal literature.

COMPETING INTERESTS
The authors declare no competing interests.

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Illes *et al.* reply: Kuersten and Wexler[1] raise several important points in response to our 2017 paper[2]. Overall, we agree and recognize that the US patent system can promote the translation of science into invention. We applaud successes it has had in this regard. At the same time, we respect the position of other countries in declining pathways for medical method patents in light of concerns that they may interfere with the skill and judgment of physicians who would be forced to consider infringement when making treatment decisions or prevent scientists from advancing their fields (for example, ref. 3).

If the authors are troubled that we may be playing on both sides of the fence here, we clarify that we did not intend either to promote a new patent system or to argue that patent rights for techniques of modulating brain regions should not be permitted. Although Kuersten and Wexler[1] equated our argument to pharmacological agents for depression, what we commented on is more akin to claims of ownership over all possible pharmaceutical compounds that could affect one or more brain regions. That is a big catchment area. Similarly, we raised the analogy to patenting gene sequences not because patents on methods of modulating a brain region are equivalent, but because granting a large number of poorly defined and interlocking patents may have the same effect as patenting a brain region. This would be comparable to patenting a naturally occurring gene sequence without the corresponding benefit of developing novel therapeutic technologies based on the interlocking patents.

The authors take issue with our choice of only three cases in support of our arguments. We note that the three we selected provide balanced examples of egregious, moderate and relatively acceptable patents that involve the brain. We deliberately did not provide a quantitative analysis of patents other than to document their exponential growth in number, especially in view of the many nonmedical actors coming onto the landscape with relevant applications. As Kuersten and Wexler[1] point out, some may overreach. In our opinion, even one overreach in this context is too many.

Ultimately, the authors miss the critical point of our paper: patents that refer to a loosely interconnected and unfettered list of applications and brain regions undermine, rather than promote, the potential benefit of an invention to users and recipients. We firmly believe that patents that are not clearly explained and entail overly broad claims, where litigation would be required to determine the precise meaning, will create roadblocks to innovation rather than pathways to promote it. We reiterate that we are not opposed to the protection of intellectual property as allowed by law; we uphold our objection, however, to runaway uses of the patent instrument that imply neuroscientific certainty where it does not exist, that pathologize behaviors that are not pathological only to create new conditions for commercial potential, and that place the interests of financial gain over respect for persons and the interests of patients.

We suggest that, rather than dismissing the issues that our interdisciplinary effort raised, legal scholars, ethicists, members of the neuroscience specialties and representatives of industry partner to use their complementary expertise in a timely way to prevent any further downward slide on this slippery patent slope. Indeed, as we suggested, proactive guidance from within the professions is essential to achieving this goal. Jointly and collaboratively, we can, if not ought to, push for better evidence to support patent claims and for patent examiners who are better trained to deal with brain-related claims. We predict that if these goals are not achieved, external restrictions will be placed on patents for nervous system input–output technologies over internally self-regulated systems that can far more desirably and effectively advance ethically and legally sound science and innovation.

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The authors declare no competing interests.

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Ten ways in which He Jiankui violated ethics

To the Editor: In late November, the world learned that He Jiankui, an associate professor at the Southern University of Science and Technology in Shenzhen, China, had edited human embryos, at least two of which were brought to term through an *in vitro* fertilization (IVF) pregnancy. At the time of writing, the data describing these experiments had yet to be peer reviewed. Irrespective of the problematic nature of science by press announcement, the methods, timing and procedures used by He in his clinical trials violate several ethical norms, including international consensus guidelines, national regulations and well-established principles of bioethics. He is not a medical doctor, but rather received his doctorate in biophysics and did postdoctoral studies in gene sequencing; he lacks training in bioethics, responsible conduct of human research, or a background in evolutionary biology that might have informed him of some of the glaring deficiencies in his work.

Here I list ten ethical principles that He violated through his interviews, website, meeting presentation and the accompanying news reports in China and the United States that featured him.

A first problem is that He's work is a violation of an international consensus on if, whether, or when the editing of human embryos should be permitted. At the First International Summit on Human Gene Editing in 2015 in Washington, DC, the organizing committee released a statement[1] that it would be "irresponsible to proceed with any clinical use of germline editing unless and until (i) the relevant safety and efficacy issues have been resolved, based on appropriate understanding and balancing of risks, potential benefits, and alternatives, and (ii) there is a broad societal consensus about the appropriateness of the proposed application." Thus far, these conditions have not been met[2]. He has published his own ethical guidelines[3] on the justification for his clinical research (some of which he himself has broken).

Second, He has not reported prior studies of CRISPR edits on embryos of mice, primates and humans. There is a void in the scientific literature as to He's prior work on editing embryos. His English language publications (19 in PubMed) list only a single publication involving CRISPR editing.

Third, reporting of off-target effects and highlighting of the risks of gene-editing embryos was insufficient. Off-target and undesirable 'on-target' effects are commonplace with the use of CRISPR–Cas9 and represent the most prevalent risks to an organism. He acknowledged such risks in his public statements but falsely reports that he has determined how to eliminate them or interpret them as irrelevant to the functioning organism.

Fourth, He failed to gather sufficient information and follow scientific consensus on the minimal risks that would make gene-editing of embryos permissible. No references are given in He's writings, website or public statements on the consensus or lack thereof that there are minimal risks in undertaking gene editing of embryos at the current state of knowledge.

Fifth, He did not comply with the national ethical guidelines in China for embryo research. In 2003, China issued guidance to IVF clinics that prohibits the implantation of embryos used in research. He's clinical trial was removed from China's Clinical Trial Registry for not providing data on safety and validity of his work.

Sixth, He failed to work within the ethical framework of his own university. The Southern University of Science and Technology disassociated itself from He's clinical trials and did not give ethical approval for his embryo-editing experiments.

Seventh, enhancement—widely acknowledged as the most ethically problematic frontier of germline gene editing—took precedence in He's experiments over curing a life-threatening disease. All evaluations of human germline gene modification agree that, if there is ever to be a justification for such experiments on human beings, they should focus on curing a life-threatening or debilitating disease for which there is no alternative therapy[4]. He rationalized his experiments as potentially protective against HIV infection, which can be prevented in ways other than embryo gene editing.

Eighth, He engaged in undue inducement of parents. Ethical guidelines on recruiting people into clinical trials recognize the problem of extravagant inducements. He communicated to prospective parents that his trial would cover IVF payments, supportive care and a daily allowance. The amount adds up to about $40,000, which can be considered a sufficiently high inducement that it would cloud the parents judgment in making a reasoned decision about risks and benefits[5].

Ninth, He was at fault for not providing an acceptable informed consent document. The informed consent form that he submitted to his research subjects was a 23-page document. It contained many technical terms, had no discussion about the meaning and significance of off-target effects or undesirable on-target changes on the child, and protected his team from responsibility for unforeseen risks. It also failed to inform the parents of alternative methods of preventing HIV infection. There was no evidence that the university or a government ethics body reviewed and approved the informed consent form.

Finally, He did not inform parents in the trial of his conflicts of interest. He has roles in several companies in Guangdong Province and Beijing as an active board member or investor[6]. Such involvement requires disclosure for an individual participating as principal investigator in a clinical trial. There were no such disclosures in the informed consent form.

On the basis of the above, I contend that the ethical infractions in this work are among the most egregious that have been recorded in modern medical history since the Second World War. There is every reason for researchers across the world to be embarrassed and for the scientific community to speak of this work as "reckless."

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The author declares no competing interests.

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