Situating brain regions among patent rights and moral risks

Dylan Roskams-Edris, Stacey Anderson-Redick, Zelma H Kiss & Judy Illes

What is the ethical value of awarding patent rights that implicate regions of the brain?

There has been a sea change in the position of neurotechnologies in daily life. Even before 2012 with the introduction of the US National Institutes of Health's Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, indeed as far back as the 1990s Decade of the Brain[1], substantial investments of global capital have been placed in neuroscience[2–4]. This has led to industry-funded patent analysis of pervasive neurotechnologies[5] and patents explicitly directed at delivering neurotechnologies to consumers[6]—trends that imply both the resources and the interest required to catapult neurotechnologies into a position where establishing strong intellectual property (IP) claims will take on unprecedented importance.

There has yet to be a true legal reckoning about the place of neurotechnologies within the IP landscape. While biotechnologies like PCR[7], stem cell lines[8], genetic diagnostics[9], and, more recently, CRISPR–Cas9 (ref. 10) have been subject to academic discourse and legal scrutiny, the same is not true of neurotechnological innovations, such as deep brain stimulation and transcranial magnetic stimulation (TMS), to name a few. The lack of such deliberation may be attributed to the fact that most neurotechnologies have yet to actually make it into the direct-to-consumer marketplace, although there is sporadic activity today around TMS, for example, that purports to enhance concentration and attention, and electroencephalography for the detection of mild brain injury.

A useful comparison can be made with the early days of genetic testing before it became a widespread and lucrative practice. This analogy is also suitable to thinking about commercial strategies and subsequent legal reactions. For example, in the case of *Association for Molecular Pathology v. Myriad Genetics*[11], the challenge to the patentability of genetic material was not initially motivated by concerns about the nature of genes as patentable material, but by frustration on the part of physicians, patient groups, researchers, and industry actors with the aggressive IP protection strategies that Myriad Genetics imposed on its *BRCA1/2* screen[9]. The legal challenge then capitalized on principled arguments about what is and is not patentable subject matter.

Neurotechnologies have yet to reach usage widespread enough to cause such fervor, yet scientific–legal hybrid patents that mention brain regions in their claims are emerging. To understand the evolving domain, we performed a patent landscape analysis to identify the rights that are being awarded in this context, and to examine their potential legal, commercial, and ethical ramifications. We applied a search algorithm through *The Lens* patent database (http://lens.org/), specifically designed for mapping innovation trends. We customized an algorithm to retrieve patents with claims containing references to brain regions, spatially directed therapies, and a method or a process. Then through manual curation, we restricted the analysis to claims in granted, non-pharmaceutical medical methods and commercial and consumer patents within the United States. By doing so, we concentrated the analysis on a narrowly defined but representative set of patents in one of the largest global medical and consumer markets, and avoided errors due to double counting of the same patents filed in multiple jurisdictions[12]. **Figure 1** shows the results of the analysis: a rise in the number of brain-region-related patents between 1976 and 2015 and, of particular note, a 14-fold increase in granted patents between 1995 and 2015.

Ethical and legal considerations

The first practical challenge to patents that relate to brain regions is well known to patent law: the danger of overbroad, vague, or obvious claims[13]. These related features of a patent can alone or collectively lead to uncertainty about the boundaries of infringement. Consider, for example, US patent 9,327,069 (ref. 14; **Table 1**). An intervention that uses any one of the broadly defined techniques and brain areas identified could lead to a claim of infringement. Patent 9,050,463 (ref. 15) articulates the well-defined target of Parkinson disease. However, unlike the third example in **Table 1**, patent 9,283,389 (ref. 16) that is clear with respect to neuroanatomy, technology, and circumscribed disease targets, patent 9,050,463 (ref. 15) refers to a wide variety of brain regions, including structures within the limbic system, the pituitary gland, and a cerebral ventricle. These are only tenuously related to the equally broad range of targeted conditions that are mentioned—autism, psychological disorders, and even bad habits—while protecting a technology described as an electrical stimulus with a claim to the large frequency range greater than 100 Hz.

Interlocking patents further compound the complexity of the problem with the possibility of leading to a full, though time-limited, monopoly over interventions on a particular brain region by controlling all practical methods of introducing stimulation to, or detecting

Dylan Roskams-Edris and Judy Illes are at the National Core for Neuroethics, Division of Neurology, Faculty of Medicine, The University of British Columbia, Vancouver, British Columbia, Canada; Stacey Anderson-Redick is at Article One Partners, New York, New York, USA; and Zelma H. Kiss is in the Department of Clinical Neurosciences, Hotchkiss Brain Institute, University of Calgary, Calgary, Alberta, Canada.
e-mail: jilles@mail.ubc.ca or zkiss@ucalgary.ca

Table 1 Three case examples of 2016 patents with claims of varying clarity and specificity related to brain regions, technologies, and purposes

Patent number and title	Brain regions mentioned	Technology	Purpose	Notes
US 9,327,069 Methods and systems for treating a medical condition by promoting neural remodeling within the brain	Temporal lobe, cerebral ventricle, structure within a limbic system, pituitary gland, brainstem, cerebral cortex (claim 4)	Input: electrical (claim 1) Output: electrical activity of said brain, a chemical level of said brain, a neurotransmitter level, a hormone level, and a medication level (claim 3)	To treat autism, a psychological disorder, a neurodegenerative disease, a chromosomal abnormality, a bad habit, or an injury to said brain (claim 5)	Covers a large and poorly defined set of brain regions, output technologies, and disease targets. Also invokes a wide range of stimulation above 100 Hz (claim 7)
US 9,050,463 Systems and methods for stimulating cellular function in tissue	27 widely dispersed and functionally unrelated brain regions as well as Brodmann areas 1–48 (claims 15 and 31)	Input: both electrical and non-electrical (claims 4–7)	To treat Parkinson disease (claim 1)	Has a well-defined disease target. References a large number of regions for which there is no evidence of benefit in treating PD
US 9,283,389 Method of treating movement disorders of a living being	Subthalamic nucleus (STN), substantia nigra pars reticulate (SNr) (claim 1)	Input: deep brain stimulation (claim 1) Output: detecting activity states (active versus rest) (claim 3)	To treat movement disorders, Parkinson disease, and gait disturbances. (claims 1, 10, & 11)	Patent is clear with respect to neuroanatomy, technology, and circumscribed disease targets

Source: Lens patent database (http://lens.org/)

activity from, that area. Consider, for example, the subthalamic nucleus, a common target for treating Parkinson disease[17]. If the patents in a collection of overly broad or non-novel patents overlap, and all practical methods of interacting with this nucleus were protected, and the owners of those rights resisted cooperative approaches to licensing, then the claim that the brain region itself is not patented would seem to be only an illusory technical-legal one. We could expect both proximal clinical effects that would make the landscape of available treatments uncertain or inaccessible, and unpredictable long-term effects depending on what new research reveals about novel functions and regional interconnectedness.

As a practical matter, overly broad or obvious claims can stifle innovation when blurry conceptual lines prohibit accessibility and generate uncertainty, rather than encourage scientific and technical creativity[18]. Given the ever-increasing disease burden of psychiatric and neurological disorders[19], neither the suppression of innovation nor a 20-year patent hold would benefit society or promote the goals of a wellness-centered approach to health care.

Myriad illuminates how practical challenges can motivate principled ones. The first principled challenge is that brain regions are natural phenomena and that, like genes, must be excluded from patentability[20]. While the patents we identified do not attribute rights over brain regions *per se*, it is reasonable to be concerned that intransigence on the part of rights holders and restricted access to brain regions could lead to a novel development in the natural phenomenon exception.

A second principled challenge resides with the special position of the brain in the architectural framework of cognitive and mental processes[21]. Unlike static phenomena within the world such as a scalpel or a genetic sequence, mental processes are dynamic, as are the functions of the regions that underlie them. A patent, or group of patents over interventions related, for example, to the prefrontal cortex and executive functioning or to the claustrum and human consciousness, would be tantamount to fettering individual rights to self-determination, autonomy, and free and rational choice. Functionally defined brain regions represent a set of dynamic, interconnected phenomena to which no legal rights, use rights or otherwise, should attach.

Finally, there are ideological issues. What is the purpose of a patent regime in science and medicine? Is it to encourage innovation or to support the welfare of people? While the substantial investment in neuroscience research has undoubtedly led to products that result in improvements to human health, it has been argued that profit is a misguided driver of health benefits[22]. Taking the view that health care is a moral endeavor, an IP regime that better indexes compensation to actual health outcomes rather than to global demand and market share is more palatable. If regulation privileges freedom and choice in human health as the ideal then, again, there seems to be little room for claims on the brain.

An anticipatory neuroethics stance

The patent landscape is now in the calm before the storm of marketable and pervasive neurotechnologies. Contrary to the current 'patent first, ask questions later' approach in the United States that is underpinned by economic justification, this anticipatory analysis of practical, principled, and ideological considerations would suggest that a 'questions first' approach is more suitable to the context of the human brain and brain regions. At stake is both the ethical and social value of biomedical materials, and relationships and trust in health care. Indeed, the most basic bioethics principles of beneficence and justice apply. Judges and lawmakers in the future may look to international law[23] and precautionary

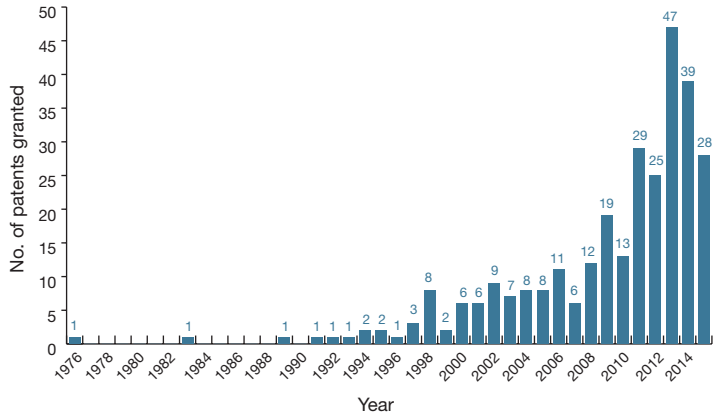

Figure 1 Number of patents implicating brain regions (1976–2015).

principles[24] to shape legal provisions, but bear in mind the Collingridge dilemma: once an approach is rolled out, it quickly becomes difficult to roll back[25].

We conclude that the increasing trend toward brain-related patent rights likely introduces more risk than benefit to individuals and society. Neither industry nor entrepreneurs ought to be discouraged by this conclusion, however. It merely emphasizes and upholds the important focus of health-related patents on the development of devices or pharmaceuticals, new mechanisms of action and delivery, and other innovation that is independent of the cells or systems that they may target. Simply stated, brain biomaterial and brain processes cannot be invented and, like genes, they similarly ought not to be owned.

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COMPETING FINANCIAL INTERESTS

The authors declare no competing financial interests.

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