Neuroethical Responsibilities

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ABSTRACT: Neuroscience represents a dynamic area of biomedical research where neuroethical responsibilities for researchers are emerging. This paper is the companion piece to the French-language one also published in this issue of the Canadian Journal of Neurological Sciences. It serves as a review of recent advances in neuroethics through the lens of three cases: (1) incidental finding of anomalies in neuroimaging research; (2) creation of neurotechnologies that can lead to cognitive enhancement, and (3) responsible communication of research results. We propose and discuss a multidimensional framework of neuroethical responsibilities to help tackle these issues. The framework reiterates the fundamental role of scientific integrity, puts in the foreground social responsibilities pertaining to the eventual use of neuroscience knowledge, and highlights self-reflection in research and training of researchers.

RÉSUMÉ: Les neurosciences représentent un secteur dynamique de la recherche biomédicale où des responsabilités neuroéthiques pour les chercheurs émergent. Cet article accompagne la version anglaise publiée dans ce numéro du Canadian Journal of Neurological Sciences. Nous présentons des avancées récentes en neuroéthique à l'aide de trois cas: (1) la découverte fortuite d'anomalies en neuroimagerie; (2) la création de neurotechnologies pouvant conduire à l'amélioration de la cognition humaine et (3) la communication responsable des résultats de recherche. Nous présentons et discutons ensuite d'un cadre multidimensionnel de responsabilités neuroéthiques pouvant aider à aborder de front ces enjeux. Ce cadre réitère le caractère fondamental de l'intégrité scientifique, met de l'avant les responsabilités sociales à l'égard de l'usage éventuel des connaissances scientifiques et met à l'avant-plan la réflexion autocritique dans la recherche et la formation des chercheurs.

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Like genetics research, neuroscience moves at a fast pace. Unlike genetics, however, the brain sciences have enjoyed little systematic and interdisciplinary ethical reflection until recently.[1] However, new applications of frontier neurotechnology bring ethical issues such as consent from vulnerable patients[2] and allocation of resource to the foreground.[3] Non-medical applications of neuroimaging in the criminal justice system[4] and in the field of education[5] have captured the attention of the public and sparked debates in the neuroscience and bioethics communities. There is also growing discussion about the ethics of neuroimaging in widely read magazines[6] and major scientific journals.[7,8] A number of issues are currently discussed and call upon proactive ethical responses (Table 1). Taking into account such recent advances, neuroscience represents an area of biomedical research where responsibilities for researchers are emerging.

This paper presents the context in which ethical issues emerge in neuroscience and the ensuing challenges for researcher responsibility. Three cases illustrate this context: (1) discovery of incidental finding of anomalies in neuroimaging research; (2) creation of neurotechnologies which can lead to cognitive enhancement and (3) communication of research results by researchers to the public. After analyzing these cases, we propose a multidimensional framework of neuroethical responsibilities that reiterates the fundamental role of scientific integrity, underscores social responsibilities pertaining to the eventual use of neuroscience knowledge, and the obligation of self-reflection in research and training of researchers. Recognizing that our analysis is non-exhaustive nor our recommendations final, we hope to stimulate discussion about the ethical issues of neuroscience. Our emphasis on emerging issues draws upon the tradition of ethical thought in neurology and psychiatry and the critical importance of formal research ethics.

Case 1
Incidental Finding of Anomalies in Neuroimaging Research

The powerful properties of neuroimaging techniques create specific challenges for researchers regarding the responsible

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Table 1: Emerging ethical challenges of neuroimaging for the research community

Issues	Challenges	Possible responses
Standardization and sharing of practices	Numerous obstacles impede the standardization of research practices that would facilitate the replication of studies and the introduction of functional neuroimaging into medical practice.[9]	Optimize expected benefits of neuroimaging by sharing methods and replicating studies. [10]
Incidental findings	Early studies suggest that unexpected clinically significant findings occur in about 2% of the adult and pediatric research subjects.[11-14] The discovery of clinical findings in research raises important issues related to researcher responsibility.[15]	Explicitly address the potential for incidental findings in research protocols and informed consent. Develop model IRB and research practices.
Privacy, confidentiality and cognitive privacy	Recent discussion reveals concerns about the protection of personal privacy and cognitive privacy (privacy of thought) in databanks containing large numbers of scans.[16-19]	Ensure that appropriate measures necessary to protect privacy and confidentiality are implemented.
Predictive and diagnostic uses	The diagnostic and predictive use of neuroimaging, similarly to genetic testing in the absence of symptoms, notably in cases of Alzheimer's disease, schizophrenia and depression may one day become reality.[20-22]	Gain an understanding of patient views. Maintain an awareness of discrimination and stigma that may arise from imaging results and respond as needed.
Commercialization and conflicts of interest	Neuroimaging services are sometimes sold directly to consumers, without medical consultation. This practice occurs most often in the United States[23,24] but is developing in Canada. Certain practices are considered quackery.[25,26] Conflicts of interest are arising in the medical community.[27]	Avoid and mitigate conflicts of interest in for-profit imaging through transparent communication and consent.
Access, fairness and allocation of resources	The shortcomings in access to imaging services has led to the flourishing of diagnostic imaging services offered by the private sector in Canada.[28] Those who can pay for these services can pass ahead of other patients and thus access specialized services more rapidly.	Reflect on social justice and the role of the private sector in the Canadian health care system.
Balanced presentation and hasty use of results	The public and media over-invest the power of neuroimages, which can lead to hasty interpretation and application of results.[29-31]	Provide and reiterate a balanced presentation of research results to the public. Identify precautions to take in the generalization of results.

conduct of research when anomalies in healthy subjects are exposed. These discoveries are called "incidental findings" (or IFs) and can be defined as anomalies of potential clinical significance not suspected prior to the brain scan.[32] Real life cases of IFs can serve to illustrate some of the challenges raised. A young medical student from Stanford University has related her own experience (see: http//neuroethics.stanford.edu: The Case of SH) of an incidentally found arterio-venous malformation.[33] Her compelling story ended with successful surgeries. She continues her studies in medicine, transformed by this experience as a patient and a student. An anonymous correspondent recently described in Nature how an incidental finding of a cerebral tumor found during research completely modified his life trajectory. After he divulged the incidental finding to an insurer, he was refused private employment insurance.[34]

The management of incidental findings raises important questions regarding the responsibility of researchers, and the responsibility of institutions where neuroimaging studies are undertaken. Preliminary studies suggest that such incidental findings occur in about 2% of the adult and pediatric population.[11-13] These data exceed those of some population studies such as those of the Central Brain Tumor Registry of the United States.[14] Even if the majority of IFs are found to be benign, their presence in the research environment raises important issues related to researcher responsibility.[15] The sources of the variability and incidence of anomalies need to be further examined. Moreover, there is little data on the cost and benefits of false positives. However, these anomalies cannot be simply ignored as some American scholars and courts[35-37] and emerging consensus suggest.[38] This topic of IFs underscores the value of researcher attitudes based on responsiveness to the volunteer as a person.

Case 2
Enhancing Human Cognition

The expected benefits of neuroscience are intimately associated with the alleviation of neurological and psychiatric illness. However, a more controversial kind of application is on the horizon, i.e., the use of diverse types of neurotechnology for the purposes of enhancing cognition, attention and emotion. About 15 years ago, the growing use of Prozac provoked a lively debate about the possibility of feeling "better than well".[39] Today, the possibilities of pharmacological enhancement and lifestyle-related use are multiplied in conjunction with the intensification of marketing by pharmaceutical companies.[40,41] In addition, the use of neuropharmaceuticals is increasing, and represents a growing health expenditure in Canada.[42-44]

The case of cognitive enhancement, where science and speculation are entangled, helps illustrate the value of prospective discussion in the neuroscience community about the broadened social responsibilities of researchers and the future consequences of cognitive enhancement applications. Table 2 (see page 4) presents the results of recent studies in neuroscience that could lead to neuropharmacological enhancements (e.g., concentration, memory, sleep). Also identified are some ethical issues associated with these possibilities, such as the clarification of the limits of enhancing neurotechnologies and the consequences of such uses.

Source of immense hopes for treatment, advances in neuropharmacology could also lead to a cosmetic neurology.[40] Related ethical issues are impressive. Enhancement could jeopardize distributive justice and cloud the meaning of medical intervention in modern societies.[56] Coercion represents another considerable issue given both the precedents in the use of enhancing products such as amphetamines in the context of the American military, as well as the high rate of Ritalin use among schoolchildren, and especially among boys.[41] It remains to be seen, however, if any enhancement of a cognitive function is truly possible and what are its medical and social risks.

Even though neuropharmacology may very well be the key sector in matters of enhancement, it is worth noting that other areas of research in neuroscience are resulting in neurotechnology with enhancement potential. For example, the hope of developing a functional brain-machine interface has been a driving force behind neuroengineering research for decades.[57] Recent advances suggest that the dream of a functional interface is coming closer to reality,[58-60] even though many significant challenges remain. The treatment of Parkinson's disease constitutes one of the most important medical successes attributed to these interfaces.[61] The applications of cerebral implants could now be extended.[2] For example, a Torontonian group recently published results suggesting the efficacy of deep-brain stimulation in the treatment of major depression.[62] Nicolelis, a prominent researcher in the field of neuroengineering, has suggested that such technology could provoke "a revolution in the way future generations interact with computers, virtual objects and remote environments, by allowing never-before-experienced augmentation of perceptual, motor and cognitive capabilities."[57] Some have asked if it will one day be possible to add sensory modalities or to accelerate the processing of information and cognitive processes in healthy individuals.[63] Presently, the invasive nature of interfaces limits such enhancement uses, but what would the outcome be if interfaces became even safer, less invasive and more socially acceptable?

Some are already seriously looking into such enhancement uses. Representatives from the Defense Advanced Research Projects Agency, an agency that funds many major brain-machine interface projects in the United States, has confirmed that their intentions are to enhance the performance of military personnel, for example, by allowing the surveillance of cerebral activity of personnel.[64,65] One study suggests that Transcranial Magnetic Stimulation, already used for the treatment of depression in Canada, could possibly serve to enhance cognitive performances temporarily and reversibly.[66]

Irrespective of enhancement, public perceptions reveal concerns about the rapid approval of the new uses of neurostimulators and the influence of conflicting interests, especially since the U.S. Food and Drug Administration standards for the approval of medical devices differ from those in place for the approval of drugs.[67] Device companies could be interested in broadening the use and sale of their approved products, sometimes using controversial strategies. For example, one of the main companies in this field was accused in 2003 of paying kickbacks to neurosurgeons who carried out spinal fusion surgeries.[3] This example illustrates that the process of developing neurotechnologies and the requirements associated

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Table 2: Examples of potential neuropharmacological enhancers

Enhancement opportunities and related challenges

Enhancement of concentration

The public is generally worried about the ethical use of methylphenidate (Ritalin) for the treatment of attention deficit/hyperactivity disorder (ADHD).[45] Research suggests that Ritalin can improve normal performance in the accomplishment of various tasks and in the functioning of short-term memory.[46,47] One study indicates that the recreational use of methylphenidate amounts to 17% among 283 respondents in an American liberal arts college.[48]

Enhancement of memory

Phamaceuticals that can compensate for cognitive deficits and memory mainly those caused by neurodegenerative illnesses such as Alzheimer's disease could possibly become enhancers of cognitive performance.[49,50] One study reports that Donepezil, an acytylcholinesterase inhibitor currently used in the treatment of Alzheimer's disease, improves the performance of commercial airline pilots in the context of simulation flights.[51]

Elimination of memories

A pilot study suggests that a β-adrenergic receptor blocking agent (Propranolol) can prevent or weaken the consolidation of undesirable memories associated with post-traumatic stress.[52]

Improvement of arousal

90% of prescriptions for *Provigil* are off-label, and some reported uses involve performance enhancement in sports, and remedying jet-lag.[53]

Possible responses

- Clarify the medical and ethical limits of enhancing neurotechnology.
- Determine if enhancements such as combating sleep or painful memories and sleep should be part of medicine.
- In the case of Ritalin in particular, take into account the vulnerability of children and adolescents, especially regarding coercion, social pressures, and resource allocation issues.
- Identify the causes of enhancement and the expectations and needs that are met by their use.
- Clarify the acceptable uses of enhancing neurotechnologies in order to prevent abuses and to ensure the best ethical uses possible.
- Predict the biological, psychological and social risks of arousal enhancement such as augmentation of waking hours[54] and other forms of enhancement.[55]

with their marketing are sometimes in conflict with the objectives of medicine, particularly where a public health system pays a portion of the costs of treatment.[68] Similar issues can be expected to surface if a market-driven approach to enhancement neurotechnology becomes more widely accepted. Indeed, precedents suggest that the interaction of enhancement practices with lifestyle uses, could greatly complicate the ethical analysis of enhancement neurotechnology.[41,69,70]

The participation of researchers in current and future discussions of cognitive enhancement seems essential to an enlightened public debate. In addition, current claims of enhancement may prove to be a utopia with unsuspected harmful consequences for its proponents. Indeed, if such illusions are not dispelled, society risks facing ill-informed uses.[50] Thus, in a context where the use of certain neurotechnologies with an explicit goal of enhancement is gaining ground, it is of utmost importance that the neuroscience community participates in proactive discussions regarding the uses of technology and its broader social consequences.

Case 3
Communicating Research Results Responsibly

Researchers must share their results and participate in knowledge transfer if the public is to be informed of neuroscience research and make good use of its products. When the funding of research comes partially from public sources, an ensuing obligation to share results of research is reinforced, if only to ensure the free dissemination of knowledge. In communicating the fruits of their work, researchers risk, however, misunderstandings of information or erroneous interpretations that lead to unwise uses.

Ancient and recent history in neuroscience reveals situations where certain troubling interpretations have been conveyed with sometimes dramatic consequences. For example, the popularization of psychosurgery[71] originated partially from optimistic reports found in the media.[72] Even if they have always been contested by cautious scientists, phrenologic theories and their applications in the fields of education, religion, law and health captivated some scientists as well as the public that frequented highly marketed phrenological "cabinets".[73] It must be recalled that Gall, the father of phrenology, wanted to introduce the analysis of cranial lumps to evaluate the risk of committing subsequent offences in accused criminals.[74] Another example reminiscent of our current neuroethics debates: at the beginning of the last century in Germany, pseudo-scientific techniques for the detection of electrical activity in the brain, such as diagnoscopy, fascinated the lay public. Theories of cerebral harmony and cerebral characterology disseminated by neuroscientists as influential as Cecile and Karl Vogt, promised to transform such techniques into tools of social management and vocational screening. When the German economy was in a dramatic state of collapse following the First World War, there was a political need for effective means of managing human resources and identifying good job candidates.[75] Thus, as these examples illustrate, hopes for neurotechnology transfer that today seem simplistic were founded on dubious interpretations of neuroscience and brain function.

The beliefs of the public and the interpretations of neuroscience by researchers interact with the broad political and social context, as history has shown. Today, the drive to find cures for human diseases reinforces expectations for medical technologies. Consequently, attempts to hastily apply neuroscience knowledge still abound. For example, in the 1990s, the media popularized results from a study that suggested that intellectual capabilities of very young children could be improved by simply listening to recordings of classical music.[76] This study was conducted on adults, in fact, and has been reproduced with difficulty. Nevertheless it led to the free distribution of recordings to all newborns in certain American states even though as a public health intervention it was based on debatable interpretations of cerebral development and synaptogenesis.[31] Another example: today the public can read in the media that the results of neuroimaging studies provide new bases for social practices as diverse as marketing, education, and ethics. These studies are often conducted on a small number of subjects and use discrete experimental designs. They have limits but few are reported in print media.[29] Adding to the challenge of responsible communication, a survey on public neuroscience literacy found that neuroimaging modalities are among the most misunderstood neuroscience concepts.[77] Thus, responsible interpretation is clearly not only an ancient but also a contemporary challenge. Benefits expected must be balanced against risks associated with communication and knowledge transfer. These trade-offs underscore the scope of the civic and democratic responsibility of researchers as well as the value of self-reflection on the limits of current neuroscience based on historical events.

Discussion

A Multidimensional Framework of Neuroethical Responsibilities

Our analysis of three cases stemming from contemporary neuroscience suggests that there are renewed challenges regarding the responsibility of researchers. We now propose and discuss a general framework of neuroethical responsibilities to respond to emerging challenges (Table 3, inspired by Racine,[78] and Illes, Racine and Kirschen[10]). We hope this framework will stimulate discussion about the different responsibilities of neuroscientists, their involvement in public debate, as well as the meaning of being an ethically-attuned researcher in today's research environment.

Scientific responsibility and integrity
Reiterate the fundamental importance of scientific rigor

Current pressures push researchers in all fields to heights of scientific productivity, but this trend can also negatively impact research.[79,80] A study published recently in Science suggests that serious professional misconduct occurs in an appreciable proportion of both junior and senior scientists.[81] The causes of this phenomenon are profound, and touch in one way or another all researchers. We recall the phrase of the former president of the Comité Consultatif National d'Éthique in France and distinguished scientist and physician, Jean Bernard, "that which is not scientific, is not ethical". The responsibility for rigor and commitment to integrity, inscribed in the guidelines of the Council for the International Organization of Medical Sciences, is fundamental.

Scientific integrity also fosters successful collaboration between researchers and promotes reproducible and sound knowledge.[82] Within a collaborative approach, benefits can also be achieved more rapidly than if research is poorly or not coordinated. Numerous obstacles such as limited funding for replication studies, for databanks allowing the consolidation of knowledge,[83] and for the sharing of analytical software and other tools used to generate or to analyze data[9] may hinder collaboration. They further form the basis for a call for active scientific responsibility.

Responsibility-responsiveness
Consider the interests of human subjects in an increasingly complex research environment

Research that is conducted on human subjects relies on the good will of research subjects. There is a tension between the subject as an instrument of research and the subject as a human being in the context, for example, of incidental findings and data

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confidentiality. Altruistic management of such issues appears desirable. An attitude that recognizes the interest of volunteers will serve the public and science best.

Civic and democratic responsibility

Adopt a broad outlook on the social consequences and implications of neuroscience

The public can rightfully expect the recognition of its contribution to research. Positive experiences with multi-directional communication that have enabled neuroscientists to exchange ideas with the public have occurred in Canada and elsewhere.[84,85] However, transfer of knowledge is not always an easy task, and numerous difficulties can arise for researchers wanting to share their results and exercise civic and democratic responsibility. As we discussed above, the public does not always have a thorough understanding of the science presented. The use of neuroimaging as proof in criminal law to obtain clemency from the jury[86,87] as well as the use of neuroimaging to survey the preferences of consumers,[8] are two other examples of limited public understanding that could lead to premature technology transfer. Historically, pitfalls were created when premature applications and interpretations became widespread. Adopting a broad outlook relative to the social consequences and implications of neuroscience can give clarity to the limits of knowledge and a balanced account of its expected benefits.

Table 3: Framework of neuroethical responsibilities

Responsibilities	Challenges	Possible Responses
Scientific responsibility and integrity	Reiterate the fundamental importance of scientific rigor.	Validate methods and support coordinated multi-site collaboration for the use of new neurotechnology.
Responsibility-responsiveness	Consider the interests of human subjects in an increasingly complex research environment.	Identify the interest of volunteers in the management of incidental findings.
Civic and democratic responsibility	Adopt a broad outlook on the social consequences and implications of neuroscience.	Provide a balanced presentation of the merits and limits of neurotechnology when interacting with media.
Prospective responsibility	Participate in discussions on the future of neuroscience and its applications.	Participate in ethical reflection on the possibilities of cognitive enhancement with neurotechnology.
Self-reflection	Reflect on precedent.	Analyze the history of neuroscience to better understand the current challenges and possible solutions.

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Prospective responsibility

Participate in discussions on the future of neuroscience and its applications

There are situations in which science and science fiction intermingle. Cognitive enhancement with neurotechnology is one example. Researchers may sometimes have reservations about certain predicted applications, but they must remain open to more distant scenarios, exercise proactive responsibility, and consider the remote consequences of their actions. The debate about enhancement is currently taking place. Scientists can leverage it to build a more ethically-informed neuroscience for the future.

Self-reflection

Reflect on precedent

In conclusion, we will emphasize a dimension of scientific responsibility that can be considered the backbone for the others: the necessity of self-reflection on one's own research practice. Historical precedent illustrates how researchers in neuroscience have supported infamous acts such as those leading to the extermination of the most vulnerable in the German Third Reich.[88] Contrary to this dismal cruelty, is the illustrious history of neuroscience. Great neuroscientists have marked history and humanity, their work positively changing lives by promoting a deepened understanding of the nervous system and the development of therapies and compassionate attitudes to neurological and psychiatric illness. For example, while many neuroscientists of the early twentieth century criticized dualism and supported monism, the great British neurophysiologist Charles Sherrington refused to promote the latter attitude. A cautious and reflective individual, he believed that monism would threaten culture and human values given the state of knowledge.[89] There are challenges in personal reflection in all fields of research. However, certain events such as the introduction of the humanities into the medical curriculum (medical humanities) may broaden the education of researchers and physicians and help to disseminate skills in critical and constructive self-reflection.

Conclusion

A Call to the Disquieted Moral Conscience

In exploring the diverse facets of normal and pathological functioning of the nervous system, neuroscientists participate in the development of healthcare. They thus contribute to the improvement in the quality of life of patients suffering from illness for which there is often still too few treatment options. In addition, as medico-scientific explanations of mental illness arise from advances in neuroscience, they dispel prejudices or stigma, and deepen the understanding of those who suffer from them.

However, responsible conduct in research yields multiple challenges for researchers and clinicians. The examples of incidental findings in neuroimaging, enhancement use of neurotechnology, and public communication of results demonstrate the necessity of a broad outlook on researcher responsibility. Hopefully, the proposed multidimensional framework of neuroethical responsibilities will nourish personal reflection concerning the ethical issues inherent in neuroscience, and a discussion of the role of neuroscience researchers as a community. If formal ethics guidelines assist researchers in conducting their research ethically; researchers remain the pillars of ethical research. As the bioethicist Hubert Doucet[90] has argued in ethical reflections about genetics, beyond codes and guidelines, a disquieted moral conscience is an asset possibly as valuable as the rules that can suppress self-reflection and awareness of individual responsibility.

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