GLOBAL NEUROETHICS SUMMIT 2020-2021

A Neuroethics Integration Landscape Report

This report was prepared by Anna Zimmer, a graduate student at Emory University Center for Ethics as part of her bioethics practicum. Anna worked in collaboration with the Global Neuroethics Working Group (mentored by co-chair Dr. Karen Rommelfanger) and the NIH BRAIN Neuroethics Program (mentored by director Dr. Khara Ramos) to landscape the neuroethics and neuroscience integration literature with the aim of advancing the integration efforts.

Introduction

History of neuroscience & neuroethics

While neuroscience as field is young relative to other scientific fields, the study of the brain and mentation dates back thousands of years[1]. Neuroscience includes a wide range of subjects including cognitive neuroscience, neuroimaging, psychiatry, and neurolinguistics[2]. It follows, then, that neuroscientists ask questions as detailed as the function of a particular enzyme and as broad as the role of the brain in consciousness and identity formation. The exploration of and answers to these neuroscience questions have implications beyond therapeutics, for example – they have implications that reach as far as altering our understanding of what it means to be human[3, 4]. These unique questions, in degree or kind, asked by neuroscience have contributed to the rise of neuroethics in the past two decades[5], though neuroethical issues have existed as long as neuroscience has[6]. The study of consciousness, for example, has implications for obtaining informed consent and utilizing new diagnostics, therapeutics, and interventions for improved quality of life[7-9]. Advances in the understanding of neural function is changing the fundamental understanding of free will[10]. Neuroethics also applies at the intersection of neuroscience and the law (hereafter *neurolaw*). For example, advances in fMRI have led to neuroethics questions of the role of neuroscientific evidence in the courtroom[11]. Additionally, research in decision-making has implications for how jurors make decisions about guilt[12]. These studies exemplify the neuroethical questions asked in response to neuroscientific discovery.

Definitions of Neuroethics

Neuroethics, broadly speaking, "studies implications of neuroscience for human self-understanding, ethics, and policy"[15]. Unsurprisingly, though, consensus on the definition and the execution of its mission is lacking[16]. Racine and Sample characterize the blurry boundaries

of neuroethics by describing the views from which neuroethics is conducted, the objects of interest, and the overarching goals of neuroethics[17]. First, neuroethics can be viewed through different lenses, such as a scientific and humanistic lenses[16]. Even these lenses, though, can point toward different objects. Some consider the brain to be the object of interest, others the mind[16, 17]. Third, the goals and subsequent execution of neuroethics are diverse, as well, with varying opinions about how neuroethics should be involved (or not) in education, training, research practices, and policy formation[17]. This report will take a macro-scale view of neuroethics and neuroscience integration, arguing that integration ought to be prioritized because it helps translation, and as a result this paper will not be granular in its assessment of what integration should look like.

Importantly, many argue that neuroethics has a mission distinct from its sister bioethics; many of the ethical issues raised by neuroscience are fundamentally different than the ethical issues raised by biology and medicine, given that findings in neuroscience reveal characteristics of personhood, consciousness, and the mind[3, 14, 18, 19]. In other words, the distinction between neuroethics and bioethics is warranted.

Calls for Neuroethics in Neuroscience Endeavors

Local: the NIH BRAIN Initiative

There has been recent increased energy dedicated to integrating neuroscience and neuroethics[14, 20, 21]. The movement to integrate neuroscience and neuroethics is facilitated by the evidence that integration leads to "responsible…rigorous, reproducible, and representative"[22] research and facilitates the ethical application of research findings[14, 20]. We hope that understanding the current landscape of neuroethics and neuroscience integration will provide necessary context strengthen the case that neuroscience and neuroethics integration ought to be prioritized.

Unsurprisingly, there is no consensus on what integration of neuroscience and neuroethics should look like[18, 20, 23-26]. Some proposed ideas include longitudinal ethics education, institutional infrastructure, and Ethical, Legal, and Social Implications (ELSI) research, ethics consultants, inclusion of ethics team members, and/or stakeholder involvement[27]. Many of these efforts are already underway[23, 24, 28]. Indeed, integration has been promoted by the BRAIN Initiative since its inception, specifically beginning with the publication of the report Gray Matters in 2014 written by the Presidential Commission for the Study of Bioethical Issues[27, 29].

As part of a midpoint evaluation of the progress of the NIH BRAIN Initiative, the NIH Director created the Advisory Committee to the NIH Director (ACD) Working Group on BRAIN 2.0 Neuroethics Subgroup (BNS), which was made up of neuroethics experts, many of whom also serve on the NEWG[14]. The BNS was tasked with reviewing the goals of the BRAIN Initiative (as set out in the BRAIN 2025 report[30]) and reporting their findings to the NIH Director for consideration[14]. This Neuroethics Roadmap titled "The BRAIN Initiative and Neuroethics: Enabling and Enhancing Neuroscience Advances for Society" (hereafter Neuroethics Roadmap) presents suggestions for the NIH Director regarding the BRAIN Initiative, ethical issues that may be raised by BRAIN Initiative-funded research, and considerations for neuroethics and neuroscience integration[14]. The Neuroethics Roadmap also outlines possible goals for neuroscience and neuroethics integration, including the needs to support institutions and trainees, clarify neuroethics concerns of BRAIN Initiative researchers, and "identify…successful strategies and models for effective neuroethics engagement"[14].

In response to the Neuroethics Roadmap, the American Journal of Bioethics Neuroscience (AJOBN), the flagship journal of the International Neuroethics Society, published a special issue with critical reflections of the roadmap[14, 31]. The main ideas in this special issue can be summarized in three themes. First, broad, creative conceptions of neuroethics and neuroscience integration are needed[18, 23, 24, 26, 32-36]. There is a call for further understanding of what exactly integration looks like [24, 32], especially in light of the tension that persists between the fields of neuroscience and neuroethics[26]. For instance, neuroethicists and neuroscientists could be collaborators, as opposed to other formulations of their relationship[35]. This collaboration could include the creation and implementation of standard research protocols [23, 36]. It could also include a system whereby philosophers define neuroscience terms, ethicists determine if the features of those terms have moral weight, and neuroscientists decide how these terms apply to their research[34].

There is also increasing acknowledgement that expanding the conventional collaboration between neuroscience and neuroethics is needed [18, 23, 34]. Some have argued for increased work in philosophy to bolster the understanding of concepts routinely used in neuroscience, such as consciousness[34]. (While these arguments for expansive collaboration with fields such as philosophy are well-taken[18, 32, 33], the scope of this paper will remain narrowly on the integration of neuroscience and neuroethics.)

The second theme highlighted by the AJOBN special issue on neuroethics and neuroscience integration is investment[23, 37]. Rommelfanger expresses the importance of "creat[ing] opportunities for meaningful training and engagement" for neuroethicists and neuroscientists, a type of investment requiring both time and financial support[37]. Goering and

Klein also call for investment in neuroethics integration in neuroscience, particularly in the form of infrastructure[23].

Investing in neuroethics and neuroscience poses significant challenges. Planning and prioritizing integration investment must persuade budget-makers that funding integration should be prioritized amongst other competing priorities. Determining the amount of funding required for effective and sustainable integration support also presents another challenge. Perhaps the most daunting challenge, though, is the development and prioritization of aims for integration, as, again, there is no consensus on what integration looks like or ought to look like for neuroethics and neuroscience[18, 23].

The third theme highlighted in the AJOBN special issue is that of representation, especially in conversations about neuroethics integration with neuroscience[29, 37], research subject selection[38, 39], and data reporting[23]. Each of these three themes highlights the ongoing formulation of neuroethics and neuroscience integration and the challenges faced by those working toward this goal. As we will see, these challenges are not limited to the BRAIN Initiative in the United States.

Global: the International Brain Initiative

In response to the growing field of neuroscience accompanied by increasingly complex ethical questions, the Global Neuroethics Working Group (GNWG) of the International Brain Initiative (IBI) was founded[40]. The IBI is a consortium of national brain projects from across the globe, and the initiative aims to expedite understanding of the human brain[40]. Given the recognized need for culturally-informed conceptualizations of and approaches to neuroethics, the GNWG created a list of Neuroethics Questions for Neuroscientists (NeQNs) at the inaugural Global Neuroethics Summit (GNS) in 2017, the "annual product"[41] of the GNWG[21, 42]. The GNWG also hosted a workshop in February 2021 that was attended by experts in neuroscience, engineering, ethics, medicine, and philosophy[43]. Prior to the workshop, these experts were asked, via an informal survey, their opinions on definitions of neuroethics, desired outputs of neuroethics, and hurdles for neuroethics integration[44]. Respondents tended to prioritize a definition of neuroethics that centered on the "application of ethical theory and reasoning to neuroscientific research" rather than a definition that focused on how neuroscience research can inform theory and practical ethics or can inform our understandings of identity and moral judgment[43]. The respondents indicated that the most valuable outputs for neuroethics are policy insights or recommendations for neuroscience research (other choices included clarifying philosophy of consciousness, improving the impact of neuroscience research, cost savings from anticipating study implications, and maintaining/increasing public trust)[43]. The survey also revealed that most respondents saw the under-funded, -resourced, and

-incentivized nature of neuroethics as hindrances to neuroethics integration[43]. Other concerns included the "poor communication between neuroscientists and neuroethicists" and a perceived lack of benefit in adding neuroethics to neuroscience[43]. These international colleagues' responses, while a small sample, exemplify the heterogenous conceptions of neuroethics. Of note, the respondents did not name improving the impact of neuroscience research as the most valuable output for neuroethics, but rather prioritized recommendations.

With the complex current landscape of integration in mind, highlighted by the Neuroethics Roadmap and the GNS survey results, the following section will outline our central argument – that integration begets translation, so integration ought to be prioritized.

Integration Begets Translation

Integrating neuroethics and neuroscience maximizes the research translation, thereby reducing human suffering[36]. One immediate criticism of this statement is that not all research aims to reduce human suffering. For (an especially comical) example, a study from 2016 aimed to investigate disgust of cheese using fMRI[45]. While it seems unlikely that applying the findings of this work, or even just explaining the findings to the public, would reduce human suffering, the lack of obvious applicability to human suffering does not rule out the possibility. In other words, just because a study does not seem to have relevance to improving the human condition does not mean the results will be forever irrelevant and unhelpful.

An additional criticism is that even if the research aims to reduce human suffering the translation may not necessarily have that aim. Consider a project that is aiming to find a cure for diabetic neuropathy by numbing injured nerves and enhancing healthy nerve function. The researchers find out that there is not much interest in their discovery for patients with diabetic neuropathy, but rather significant interest among professional climbers, as the nerve numbing and enhancement was found to improve climbers' abilities to grasp holds. Again, just because a study has an outcome that is perhaps viewed as frivolous (commercial use nerve agent for professional climbers), does not rule out the possibility of the findings being applicable to human pathology in the future. Considering research translation generally as something aimed to reduce human suffering applies to more studies than it may seem at face value. Thus, for this piece, I will assume that research translation aims to reduce human suffering.

There are a few proposed mechanisms in support of the assertion that integrating neuroethics and neuroscience maximizes research translation. We propose a mechanism for three stages of the research process (Figure 1). **First, neuroethics helps advance scientific questioning during proposal formation and therefore more pertinent research outcomes**[14]. Consider a collaborative discussion between a neuroethicist and neuroscientist about

approaches to research with human subjects. A neuroethicist could bolster understanding of values that influence the questions being asked by the neuroscientist. The neuroethicist could also confirm, perhaps through empirical research, that these values align with the values prioritized in the community of human subjects. This is particularly important work, given that science research aims that consider the values of the target community are more likely to have active participants in clinical trials[46], and, by extension, to have successfully translated research.

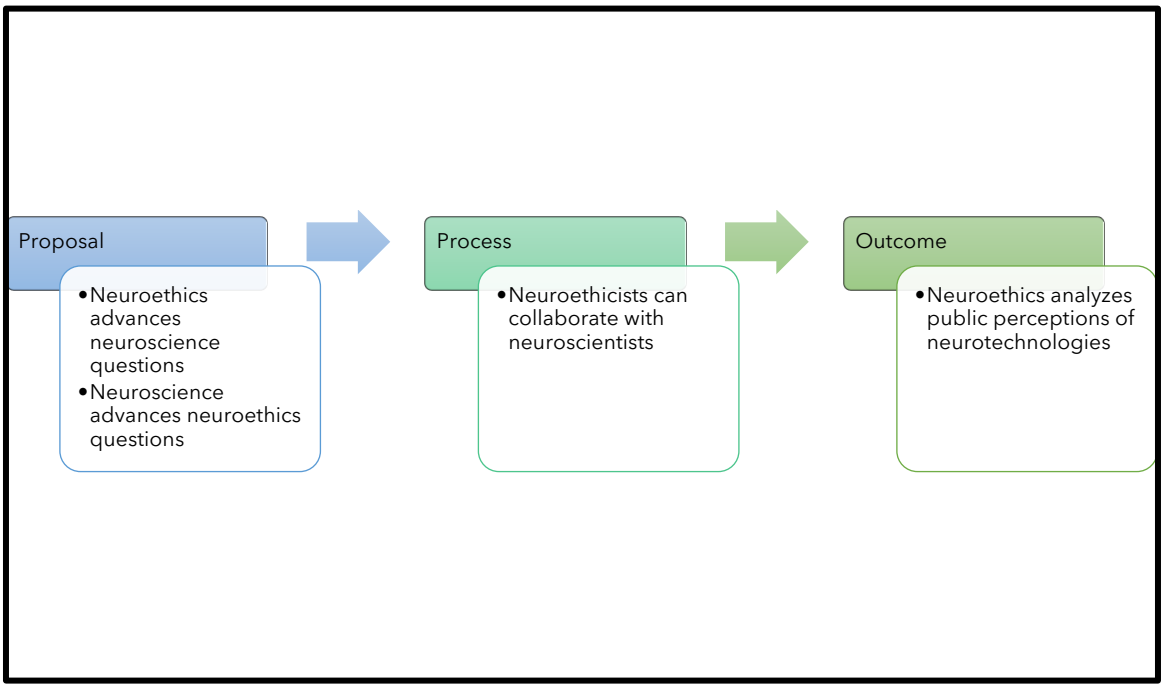

Figure 1

Neuroscientists may argue that scientific questioning is best performed by scientists and that neuroethicists do not have the training necessary to participate in fruitful considerations of what scientific questions should or should not be asked. Indeed, the concern about the limited scientific knowledge of ethicists, and even the expertise of ethicists at all [47], is a longstanding concern [48, 49]. Vukov et al. [25] argue, though, that scientists, neuroethicists, and philosophers can play distinct roles in the scientific process; scientists are indeed well-suited for scientific questioning, and philosophers and neuroethicists can play roles that add value to this questioning by the identification of features and the identification of morally relevant features, respectively [25]. Thus, scientific questioning can include neuroethicists in a way that does not interfere with the scientific expertise of neuroscientists.

While neuroethics help advance scientific questioning, the reverse is also true – **neuroscience can help advance neuroethics questioning through the neuroscience of ethics** (Figure 1)[5, 16]. Racine et al. describe potential contributions of neuroscience to neuroethics, including development of theories, brain-based morality, and identification of mechanisms of morality[16]. While these aims are admittedly aspirational, they are worth considering, especially given the contributions science has made to the quality of ethics research in other disciplines, namely genetics and genethics[50]. (Of course, genetics and genethics have notable differences from neuroscience and neuroethics, but the overlap is sufficient for the point here [51].) The NIH's National Human Genome Research Institute (NHGRI) pointed out in a 2014 report that ELSI research has improved in quality because of increased understanding of genetics[50]. Though geneticists may not have uncovered ethical theories or discovered gene-based morality (though a recent paper suggests virtuous behavior is heritable [52]), genetics research has strengthened the accompanying ELSI research[50]. So, broadly speaking, science research has the potential to strengthen ethics research questioning.

The second way integrating neuroethics and neuroscience maximizes the desired outcomes of research is through real-time collaborations during the research process (Figure 1). These collaborations beget translation by increasing research efficiency through 1) expediting inter-researcher and cross-disciplinary critique 2) and troubleshooting. One example of real-time conversations aiding neuroscience research is outlined in Goering and Klein's piece explaining how the Center for Neurotechnology at the University of Washington has facilitated collaborations among members of the center, avoiding the often years-long process of communicating with other scientists and ethicists through journal publications[23]. Neuroethicists are also useful in troubleshooting when unanticipated ethical concerns arise mid-project. Both expediting dialogue among researchers and troubleshooting ethical dilemmas impeding research advance neuroscience research timelines, thereby moving research closer to translation.

Some might suggest that these roadblocks can be easily anticipated by neuroscientists themselves, that neuroscientists recognize ethical challenges with human subject research, with informed consent, with privacy of neural data. This may be true. However, we argue that neuroethics integration with neuroscience *aids* in the anticipation of potentially devastating roadblocks, not that neuroethics is *required* for neuroscience. Neuroethics always applies to neuroscience, explicitly or implicitly, but of course neuroscience can be conducted without explicit mention of ethical considerations.

Another strong objection may come from basic scientists who are not necessarily aiming for translation in their work. Why should a scientist working to find the structure of a neuron-based

protein that is seemingly unrelated to any known human pathology (or suffering) be interested in involving a neuroethicist? One response is to consider neuroethicist involvement on a continuum rather than a lever; there are reasons to have varying degrees of neuroethicist involvement in neuroscience research. Perhaps a neuroscientist studying consciousness using an implantable device in unconscious individuals would have more involvement of a neuroethicist than a researcher aiming to understand the folding of a particular neuronal protein that was not known to be involved in any human pathology (or suffering). Just because a research group has seemingly few, if any, ethical dilemmas does not mean that a neuroethicist is irrelevant. Recall that neuroethicists are skilled in identifying values of stakeholders and that the practice of science is value-laden, no matter how seemingly removed from concrete applicability to human suffering[53, 54]. Each scientific endeavor occurs at the expense of another – there are finite resources for science funding. Thus, a neuroethicist could be key in identifying stakeholders for science research projects and the values of those stakeholders.

The last and perhaps most obvious way neuroethics can bolster neuroscience research translatability is by remaining involved in the translation of scientific outcomes (Figure 1). Public engagement is an important and increasingly prioritized aspect of science research, including neuroscience specifically[14]. Neuroethicists can participate in the process of translating science for public use and understanding through recursive analysis of public acceptance (or not) of neurotechnologies, independent empirical research about perceptions of new neurotechnologies or neuro-related medicines, and/or collaboration with neuroscientists to troubleshoot ethical dilemmas in translation.

One criticism of this approach to neuroethics and neuroscience integration may be that neuroethicists cannot remain impartial participants in neuroscience research application. For instance, imagine a neuroethicist and neuroscientist working together to understand the public's opinion about a new smartphone application (app) that analyzes text messages for signs of mental illness, alerting the user with resources as needed. This app has the potential to be valuable for both the neuroethicist and neuroscientist, both financially and personally (think career advancement). Would the neuroethicist be able to be an impartial team member? No, likely not. But not for the expected reasons. Any integrated approach to neuroscience and neuroethics likely means that neuroethicists are working alongside neuroscientists, building relationships, completing projects, and engaging the public, and this would likely lead to a compromise in objectivity on the part of the neuroethicist. Indeed, the concern about ethicists becoming "insiders", thereby compromising their mission, is a longstanding concern[18]. While this concern is certainly an important one, the response need not be that neuroethicists should not be involved in translating neuroscience, or that neuroethicists should not work alongside

neuroscientists generally – we have seen that neuroethicists can play important roles in advancing neuroscientific discovery. Rather, this concern can be taken seriously while also involving neuroethicists in the translation process. One approach to address this concern could be having neuroethicists as external reviewers or consultants *and* as team members.

Exemplary Applications of Integration & Conclusion

While there are not many programs aiming explicitly to integrate neuroethics and neuroscience, there are many examples of efforts to integrate ethics in STEM in general. A few notable programs include ethics integration at the NHGRI, the University of Washington's Center for Neurotechnology, and the NIH's Common Fund Bridge2AI. Each effort operationalizes (or will operationalize, in the case of Bridge2AI) integration differently, demonstrating the complexity of, and possibilities for, integrating ethics and STEM. Importantly, integrating neuroscience and neuroethics could mirror similar efforts in other fields, such as genetics and ethics integration[50].

The NHGRI of the NIH created Centers of Excellence in ELSI Research (CEER) to integrate Ethical, Legal, and Social Implications (ELSI) into institutional settings to make this research readily available for policymakers, to improve agility of response to the rapidly changing field of genomics, and to train a diverse cohort of researchers[55]. The aforementioned 2014 report outlined some of the impact that ELSI research has had for genomic research practice, including improvement in informed consent practices, instituting of policies regarding participant privacy, and enactment of a law forbidding insurance companies from discriminating based on genetics[50]. The NHGRI Human Genome Project has a mandated 5% of their budget to spend on ELSI research[50]. Perhaps this is part of why the Neuroethics Roadmap mentioned the need for a BRAIN Initiative funding mandate for 5% of their research (similar to the Human Brain Project in Europe)[14] and why investment in integration was a theme in the AJOBN special issue.

One example of a neuroethics/neuroscience-specific integration strategy comes from the University of Washington. In their recent piece in AJOBN, Sara Goering and Eran Klein describe the integration of neuroethics in the University of Washington's Center for Neurotechnology[23]. At this center, neuroscience and neuroethics integration occurs through informal collaboration, facilitated by shared workspace and relationship-building at events such as whole-Center retreats[23]. They suggest that these informal collaborations improve efficiency in the research process because, rather than spending years communicating via time-intensive publications, these interdisciplinary experts can meet over lunch, for example[23].

Lastly, the rise of artificial intelligence (AI) has led to pushes to integrate AI and ethics[56, 57]. Bridge2AI at the NIH Common Fund will, in the coming months, make calls for new proposals for bridging AI technologies with medicine[57]. Aims include funding Integration, Dissemination, and Evaluation (BRIDGE) Center cores, experts from different fields who will work together to integrate technology, medicine, and social goals, and funding projects that generate data that uphold the FAIR principles[58] and "critically integrate ethical considerations" [57, 59, 60].

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