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Review Article

An XYZ-axis Matrix Approach for the Integration of Neuroscience and Neuroethics

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The recent, unprecedented advancement in neuroscience has led to new discoveries about the human brain and its function. Yet at the same time, it has spurred novel ethical and regulatory issues, and the field of neuroethics has emerged as an interdisciplinary endeavor to address these issues. Across the globe, extensive efforts have been underway to achieve the integration of neuroscience and Neuroethics, with active engagement not only from academia but also from the government, the public, and industry. However, in some countries, integrating neuroscience and neuroethics has proved to be a particularly challenging task. For example, in South Korea, the government has primarily driven the integration effort, and only a small group of researchers is properly trained for conducting an interdisciplinary evaluation of ethical, legal, social, and cultural implications (ELSCI) of neurotechnology. On the basis of the last few years of experience pursuing a government-funded neuroethics project in South Korea, we developed a new operational framework to provide practical guidance on ELSCI research. This framework consists of the X, Y, and Z axes; the X-axis represents a target neurotechnology, the Y-axis represents different developmental stages of the technology, and the Z-axis represents ELSCI issues that may arise from the development and use of the neurotechnology. Here we also present a step-by-step workflow to apply this matrix framework, from organizing a panel for a target neurotechnology to facilitating stakeholder discussion through public hearings. This framework will enable meaningful integration of neuroscience and neuroethics to promote responsible innovation in neuroscience and neurotechnology.

Key words: Neuroscience, Ethics, Three-dimensional, Social integration

THE BEGINNING OF A NEW ERA OF NEUROETHICS

Although neuroethics as an independent discipline has a relatively short history, ethical issues arising out of a clinical and scientific investigation of the human brain and its function have been studied for a long time from human rights and biomedical ethics point of view. In the 1930s, substantial efforts were made to examine and address ethical issues concerning practices in the fields of clinical psychiatry and neurosurgery, such as frontal lobotomy or forced hospitalization of patients with mental disorders, which were highly publicized abuses in the United States and Europe [1-3]. These efforts greatly improved the protection of patients' rights and led to the development of core ethical principles in human subject research and clinical care.

Neuroscience has also had its unique place and meaning in ethics and philosophy. For example, in Western philosophy, the ability to make an independent and rational decision lies at the core of what makes us human [4]. Free will, a modern concept of individual independence and autonomy, is the capacity to decide and act upon one's motives, values, and desires through careful deliberation. It also forms the basis of introspective thinking, a process that examines and reflects on one's own thoughts and feelings. The fact that

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these human cognitive characteristics fundamentally stem from the function of our brain makes the study of their neurobiological substrates particularly relevant in examining ethical thought and behavior [5].

However, when the conference the Dana Foundation hosted was held in San Francisco in 2002, neuroethics entered a new phase that went beyond the traditional framework and research in biomedical ethics [6, 7]. This conference drew considerable attention not only from human rights activists and ethicists but also from sociologists, lawyers, journalists, government officials, and marketing and advertising experts who came together to discuss and share diverse perspectives on recent developments in neuroscience and neurotechnology. The success of this conference indicates the interest in neuroscience as a rapidly growing discipline that encompasses various subfields and its potentially widespread implications in our society. This modern "gold rush" to unravel the mystery of the human brain has transformed the study of neuroethics to be largely driven by scientific and technological advancement, departing from traditional approaches in biomedical ethics and humanities. This landmark shift called for the integration of neuroscience and neuroethics, and some scholars have come to define neuroethics anew to reflect this change [6-9]. Furthermore, it has become essential to engage with various public and private stakeholders in the discussion of ethical issues in neuroscience and neurotechnology [10,11].

EFFORTS TO INTEGRATE ETHICS INTO NEUROSCIENCE AND NEUROTECHNOLOGY

Across the globe, we have been witnessing extensive efforts to achieve the integration of neuroscience and neuroethics. For example, in 2013, the Obama administration launched the Brain Research Through Advancing Innovative Neurotechnologies (BRAIN) Initiative, which aims to revolutionize our understanding of the human brain [12]. Then-President Obama charged the Presidential Commission for the Study of Bioethical Issues to "identify proactively a set of core ethical standards – both to guide neuroscience research and to address some of the ethical dilemmas that may be raised by the application of neuroscience research findings," emphasizing the need for integrating ethical and social issues in a major federal science initiative similar to what is seen in the Human Genome Project [13]. In response to this request, the commission gathered expert opinions and comments from the public through a series of meetings and hearings and published a two-part report. In this report, the committee underlined the importance of integrating ethics and neuroscience early and throughout the research endeavor. It further proposed various approaches to achieve the integration through (a) education at all levels, (b) institutional infrastructure, (c) research about the ethical, legal, and social implications of scientific research, (d) research ethics consultation, (e) stakeholder engagement, and (f) inclusion of an ethical perspective on a research team [13, 14]. The BRAIN Initiative also established the Neuroethics Working Group comprising both neuroethicists and neuroscientists to explore the neuroethical implications of BRAIN-funded research [15-18]. In an effort to fully integrate neuroethical considerations into the initiative, the Working Group developed a set of Neuroethics Guiding Principles to frame and navigate the neuroethical questions that BRAIN-funded research will likely prompt [19].

The EU's Human Brain Project (HBP), also established in 2013, is a large-scale flagship research initiative to investigate the complex structure and function of the human brain through an interdisciplinary approach at the interface of neuroscience and technology [20]. From the beginning of this project, the HBP has been committed to responsible research and innovation (RRI) and thus created the Ethics and Society subproject to broaden and enhance RRI within all HBP research. This subproject is structured around a number of activities, such as making certain HBP research is conducted in accordance with ethical and legal regulations and principles, identifying ethical and social concerns raised by the HBP research development, and providing opportunities for researchers to engage with diverse stakeholders to refine the objective and process of HBP research [21, 22]. The social, ethical, and reflective work in the subproject has produced more than 100 publications and several relevant reports [23].

Additionally, a number of professional societies and international research initiatives and organizations have made dedicated efforts to facilitate the integration of neuroscience and neuroethics. For example, the International Neuroethics Society, a leading professional society in the field, has offered various influential forums and opportunities, including annual meetings and webinars, to encourage and inspire research and dialogue among neuroethicists and neuroscientists on the responsible use of advances in neuroscience [24]. The International Brain Initiative (IBI), established by representatives from seven countries/regions – Japan, Korea, Europe, the US, Australia, China, and Canada – to advance neuroscience research through international collaboration and knowledge sharing, created the Neuroethics Working Group, emphasizing that neuroethics is an integral part of the global neuroscience enterprise [25]. One of the main activities of this working group is to hold the Global Neuroethics Summit to bring together the brain research projects in the member countries for more a culturally informed neuroethical analysis [26]. The Dana Foundation, which has had immense influence on the birth and growth of neuroethics as an academic discipline, recently announced its new focus on neuroscience and society and launched new activities and grant programs to ensure that new neuroscience discoveries and technologies are advanced in consideration of societal goals and human values [27].

CHALLENGES FOR THE INTEGRATION – LESSONS LEARNED FROM SOUTH KOREA

In some countries, however, the integration of neuroscience and neuroethics has been a particularly challenging task. For example, in South Korea, there have been attempts to promote the integration, but it had to, and still contends with, various challenges. In 2003, neuroscience was selected as one of the target technology areas of the 21st Century Frontier R&D program, a Korean national long-term, large-scale research project. Under the support of this program, the Neurohumanities Research Group was created in 2009 to examine the ethical, legal, and social implications of neuroscience. This group was a precursor of an institutionalized effort to integrate neuroethics and neuroscience but disbanded after the program ended in 2013 [28].

In 2014, the first notable attempt to achieve the integration was undertaken by a national initiative to establish a Brain Bank for the collection of human brain samples for neuroscience research. Korea has experienced longstanding societal reluctance to engage in postmortem autopsies and in the donation of human organs and tissues due to the legacy of Confucian culture that gives special respect to the body. This reluctance has made it difficult to collect human brain samples for scientific research [28]. Thus, in the process of creating the Brain Bank, substantial efforts were made to increase public awareness of the importance of brain donation and to examine associated ethical concerns. A regulatory framework to facilitate donation and research of the human brain was also introduced, amending the Brain Research Promotion Act, major legislation to foster brain research and facilitate commercialization of neurotechnology for the public's welfare [28].

Meanwhile, a plan for developing the Korean Brain Initiative (KBI), which aims to emulate the U.S. BRIAN Initiative, was first announced in 2016 but has failed several times to pass the preliminary feasibility analysis by the Ministry of Economy and Finance. The plan finally passed the analysis last May and will go into effect in 2023. Under this plan, KBI will announce its first funding opportunity in fall 2022 and invest 450 billion Korean won for the research and development of neurotechnology from 2023 for the next 10 years. However, during the prolonged dormancy in implementing the KBI, research on neuroscience and neurotechnology has needed to rely on short-term, sporadic government funding efforts. The lack of an overarching long-term plan for advancing neuroscience research and technology further led to uncertainties around which areas should be targeted and given priority for ethical integration.

Yet some continued efforts have been made to achieve the integration. In 2017, the Korean Brain Research Institute, one of the three leading entities of the KBI, organized the multidisciplinary Neuroethics Research Group (NRG). The NRG consists of experts from multiple fields – neuroscience, psychiatry, philosophy, ethics, psychology, sociology, and law – to address the ethical, social, and legal issues in the development of neuroscience and to provide relevant consultations. In this regard, the NRG is intended to serve as an institutional governance agency that provides guidelines for the ethical conduct of neuroscience research. In 2019, the Ministry of Science and Information Communication Technology also began to provide funding for neuroethics research through the National Research Foundation (NRF). That same year, South Korea joined the International Brain Initiative (IBI) to keep pace with the global efforts to integrate the two fields and has taken a leading role in the Initiative [25].

FACTORS IMPEDING THE INTEGRATION

However, despite this limited but meaningful advance in institutional efforts, integrating ethics into neuroscience research and technology has been hampered by several issues that made it difficult to even begin the conversation among relevant stakeholders [29]. First, a scant number of researchers have training and experience in the interdisciplinary investigation of ethical, legal, and social implications of neuroscience and neurotechnology. In fact, the number of bioethicists in South Korea is relatively small compared with that in the United States, and there are only a few academic societies with whom it is possible to share and discuss bioethical issues. Considering the absence of neuroethics expertise in Korea, one of the priorities in the process of integrating ethics in neuroscience was to establish an education and training program for neuroethics research. Yet it takes time to educate and train researchers, and until now, it has primarily been bioethics-related scholars in the humanities and doctors of psychiatry and neurology with a degree in ethics who have formed neuroethics expert groups.

In addition, the broad definition and scope of neuroscience or brain research makes it difficult for researchers to grasp the definition and scope of neuroscience as a subject area of neuroethics study. Neuroscience has evolved as a broad multidisciplinary science spanning a number of fields. According to the definition under the Brain Research Promotion Act in Korea, "brain research"

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consists of four fields – brain science, medical and pharmacological brain science, brain engineering, and all other related fields. On the basis of this definition, the NRF of Korea classified 311 out of a total of 4,241 areas of study to be included in brain research [29]. Some of these 311 subfields of brain research are newly emerging fields or were created by combining existing fields.

Moreover, although obtaining an in-depth understanding of neuroscience research and technologies is critical to anticipating and analyzing their potential ethical, legal, and social implications, this fact further discouraged scholars in humanities from actively engaging in neuroethics research. Bioethicists in Korea have considerable experience in ethical, legal, and social implication (ELSI) research in germ cell-related ethical issues, human cloning, and genome projects. Genetics was undoubtedly a difficult field of science for bioethicists to understand, but its rather specific scope enabled researchers to conduct ELSI research with only certain core knowledge on genes, germ cells, the human cloning process, stem cells, and so forth. However, the unprecedented advancement in neuroscience and the continuing expansion of the field made it difficult even for scientists and engineers to grasp new findings and cutting-edge technologies in the field; this has posed a barrier to integrating ethics into neuroscience [29].

For researchers who study neuroethics with approaches and methods that have long been established in ethics and philosophy, understanding cutting-edge neurotechnology and examining its potential implications is an uncharted area they have not previously explored, which often collides with the approaches and methods these researchers have used. Researchers' adherence to traditional ethical and philosophical studies on neuroscience has impeded embracing a new undertaking of neuroethics to investigate the real-world impacts of neuroscience and neurotechnology. There has also been a lack of effort to identify and understand the ethical concerns neuroscientists and engineers have regarding their own research and technology, which thus resulted in a failure to build a common understanding between neuroscientists and neuroethicists on how to achieve the integration of these two fields [29].

Finally, a backlash against neuroethics research mainly driven by the government was another factor that hampered the process of integration. The debate over ethical misconduct of embryo stem cell research in early 2000 followed by a national scandal in Korea revealed, and intensified, conflicts between pro-government scholars and scholars who want to maintain academic independence [30]. As a result, government-directed brain research initiatives and plans have faced some criticism, which kept some researchers from participating in these initiatives and plans.

NEED FOR A CLEAR FRAMEWORK FOR THE INTEGRATION OF NEUROSCIENCE AND NEUROETHICS

The trials and errors that occurred in Korea demonstrated that in countries where neuroethics is emerging as a new field, the lack of experience and expertise, compounded by the rapid scientific and technological development in neuroscience, can impede achieving the integration of neuroscience and neuroethics. Other socio-cultural issues unique to a country may also hamper the integration process. Having a well-defined framework to guide researchers without experience on how to approach and evaluate the wide-ranging societal impacts of neuroscience and neurotechnology is critical to avoiding such trials and errors. This framework would also make public investment be used more efficiently by preventing duplicative efforts and overlaps in analysis given that the integration is largely driven by government-funded research program in these countries.

More importantly, this framework would enable more meaningful integration of neuroscience and neuroethics. Without any guidance and effort, it would be difficult to expect constructive interaction between neuroscience and neuroethics (Fig. 1A). Focusing on either one of these two fields in the process of integration would also result in undesirable outcomes. For example, neuroethics that failed to incorporate technical advancements in neuroscience will not be able to provide practical guidance on the implications of this advancements (Fig. 1B), and neuroscience that failed to incorporate ethical considerations would be left without proper checks and balances to ensure responsible innovation (Fig. 1C). A clear operational framework would help neuroscientists and neuroethicists develop a new and balanced way to communicate with each other for the integration of the two fields, without one field's perspective overshadowing the other's (Fig. 1D).

Previously, several domestic and international research groups presented guidance to promote the integration [19, 22, 31-37]. In line with these efforts have also been attempts to provide a more concrete framework for neuroethical analysis. Here we will review the IEEE Neuroethics Framework as one representative example of these attempts and propose a new XYZ axis approach as an operational framework to provide practical guidance on ELSCI research in neuroscience and neurotechnology.

IEEE NEUROETHICS FRAMEWORK

The Institute of Electrical and Electronics Engineers (IEEE) formed the IEEE Brain initiative in 2015 to create a technical community that facilitates interdisciplinary collaboration to advance research and development of engineering and technology to im-

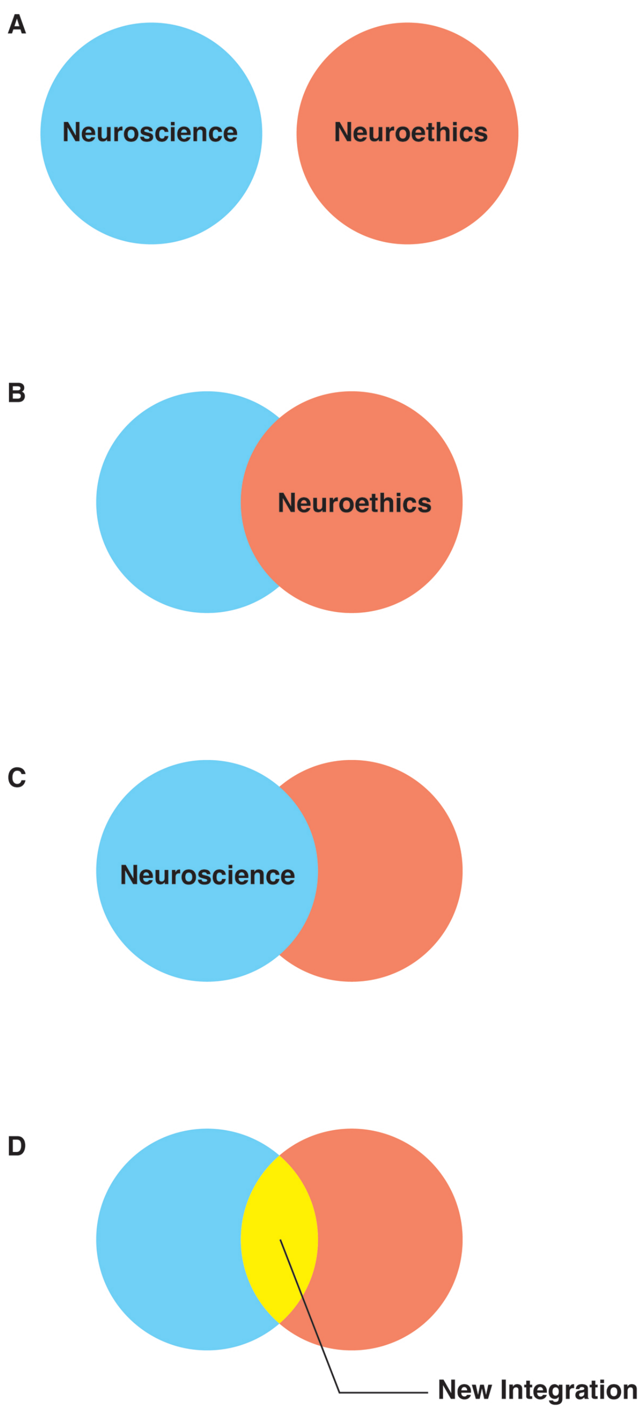

Fig. 1. Different forms of relationship between neuroscience and neuroethics. (A) The state of no meaningful interaction between neuroscience and neuroethics, (B) Neuroethics failed to incorporate technical advancements in neuroscience, (C) Neuroscience failed to incorporate ethical considerations, (D) Meaningful integration achieved between the two fields.

prove our understanding of the brain. As a part of the IEEE Brain initiative, the Neuroethics Subcommittee is developing a neuroethical framework for evaluating the ethical, legal, social, and cultural issues that may arise with the deployment of such neurotechnologies [38]. The long-term goal of this framework is to provide the basis for the development of a set of guidelines for engineers, researchers, applied scientists, practitioners, and neurotechnology companies that will help ensure the responsible development and use of new neurotechnologies. With this framework, it would be possible to learn about the ethical, legal, social, and cultural implications of neurotechnology without needing to survey all relevant neuroethics literature.

The IEEE Brain's Neuroethics Framework is organized as a matrix of specific types of contemporary neurotechnologies and their current and potential applications [38]. The columns represent different types of neurotechnology and currently consist of four technologies, namely, (a) technology for recording/sensing, (b) stimulating/actuating, (c) closed-loop, and (d) direct physical and biological modification [39]. The core areas identified for potential implementation of neurotechnology in the rows include (a) medicine, (b) wellness, (c) education, (d) work and employment, (e) military and national security, (f) sports and competitions, (g) entertainment, (h) the legal system, and (i) marketing and advertising. On the basis of this matrix, an international team of engineers, scientists, clinicians, ethicists, sociologists, lawyers, and other stakeholders explores and documents the ethical, legal, social, and cultural issues generated by the four particular neurotechnologies when applied in the specific areas identified above [38].

The ethical issues discussed under this Framework are categorized into five themes – (a) safety, well-being, and risk, (b) privacy and surveillance, (c) authority and power, (d) justice and fairness, and (e) agency and identity [39]. The legal issues include (a) safety, (b) security and privacy, and (c) liability and responsibility. Social issues involve (a) social benefits and disruptions and (b) peer and social pressure. Finally, cultural issues include (a) cultural differences in acceptance and use of technology and (b) the potential of the technology to foster or threaten intra-group culture.

The resulting documents are expected to promote further discussion by inviting input and new perspectives from a wide array of individuals with an interest in neurotechnology. Given the fast pace of technological development, the compilation of these documents is intended to serve as a living one, such that the themes and principles are to be revised as neuroscience and neurotechnology evolve [39]. After a few years of extensive discussion, the working groups within the Framework have drafted the documents for each core area and presented them at various international workshops, including the IBI and the OpenMind Consortium [40], for feedback. Recently, one of the working groups published a case study to demonstrate how the framework can be applied [41].

However, some critical factors are not addressed in the IEEE framework. First, this framework does not take into account which developmental stage a target technology is currently in. In other words, the axis in the existing matrix does not indicate, for example, whether the technology is in the stage of idea in the laboratory, in the stage of human subject research, or in the stage of commercial product marketed for the general public, although the focus and direction of ELSCI analysis can vary depending on the level of maturity of a neurotechnology. Second, the framework applies the same themes identified for ethical, legal, social, and cultural issues across all the four types of neurotechnology and their nine application areas and, thus, may miss unique problems relevant to a certain technology or its use in a specific application area. Third, as noted earlier, the goal of the IEEE framework is to develop guidelines for engineers, scientists, and neurotech companies, and it further argues that the guidelines will be of interest to a wide range of audiences and stakeholders as well. Yet, the framework does not include discussions on how to promote participation and engagement of the public, one of the most important stakeholders.

A NEW XYZ MATRIX APPROACH

Having reflected on the experience of pursuing a government-funded neuroethics research program in South Korea, we propose a new XYZ matrix approach, a detailed operational framework to provide practical guidance on ELSCI research of neurotechnology. This matrix consists of the X, Y, and Z axes (Fig. 2). The X axis represents a specific target neurotechnology, such as deep brain stimulation (DBS), transcranial magnetic stimulation (TMS), transcranial electrical stimulation (tDCS), or brain wave monitoring. If a sufficient pool of researchers exists to organize more than one interdisciplinary panel, it may be possible to target multiple technologies simultaneously. On the Y axis, unlike the IEEE's Framework, this new matrix approach explicitly accounts for the maturity of a target technology, which is classified under nine stages, namely, (a) in-vitro laboratory stage, (b) animal experiment stage, (c) non-human primate experiment stage, (d) exploratory human subject stage, (e) therapeutic human subject research stage, (f) non-therapeutic human subject research stage, (g) pre-market entry stage, (h) market entry (with restriction) stage, and (i) market entry (without restriction) stage. Here the term "market" refers to the direct-to-consumer market, which means a market for "products that can be purchased directly by a consumer, without any involvement of a researcher or treating clinician [42]."

This axis will allow us to determine the urgency and timeliness of examining the implications of a target technology. The Z axis represents the four major areas of neuroethical investigation – ethical, legal, social, and cultural implications (ELSCI) of a target technology. ELSI, which stands for ethical, legal, and social implications, refers to a multidisciplinary analysis of societal implications of novel and emerging biomedical research and associated or resulting technological advancement [43]. More recently, researchers began to acknowledge that societal implications of emerging biotechnology can differ across cultures and thus added culture as another distinct prong (ELSCI), as in the IEEE Neuroethics Framework. The sequence of the major areas of neuroethical investigation listed on the Z-axis follows this common notation in the field. However, this does not mean that a neuroethical analysis should be conducted in this precise order or should cover all four of these areas.

The colored lines in Fig. 2 illustrate two example cases that show how this matrix can be applied. The yellow line represents the first example – neuroethics research on legal issues regarding the use of tDCS, which is a type of non-invasive brain stimulation technique currently marketed to the public as one that can modulate cognitive functioning or ameliorate symptoms of certain mental disorders (e.g., depression) [44, 45]. The legal issues may include whether tDCS should be regulated as a medical device or how to prohibit unfair or deceptive marketing of tDCS devices. The red line denotes another example – neuroethics research on ethical issues regarding the use of DBS, an electrical stimulation technique using electrodes implanted into certain brain regions, which is at the stage of human subject research for therapeutic application. DBS has been commonly used to treat certain neurological disorders, such as Parkinson's disease, essential tremor, and epilepsy [46, 47]. Yet it is also being actively studied for its clinical applications in other types of disorders (e.g., post-traumatic stress disorder [48] and Alzheimer's disease [49]) and for potential dual use to alleviate the symptoms of the disorders (e.g., memory decline in patients with epilepsy or Alzheimer's Disease [50]). Some relevant ethical questions would include what the potential psycho-social impacts of DBS are and whether DBS can cause changes in a patient's perception of personal identity. Fig. 3 shows another illustration of the XYZ matrix approach to aid a better understanding of how the matrix works.

To implement this new matrix approach, we designed a step-by-step workflow, particularly for government-directed top-down research projects (Fig. 4). The first step is the selection of a target technology. In determining which technology to target, three factors should be considered – public interest in technology, maturity of a technology (including rigor and credibility of its scientific evidence), and urgency of the need to address ELSCI of a technology

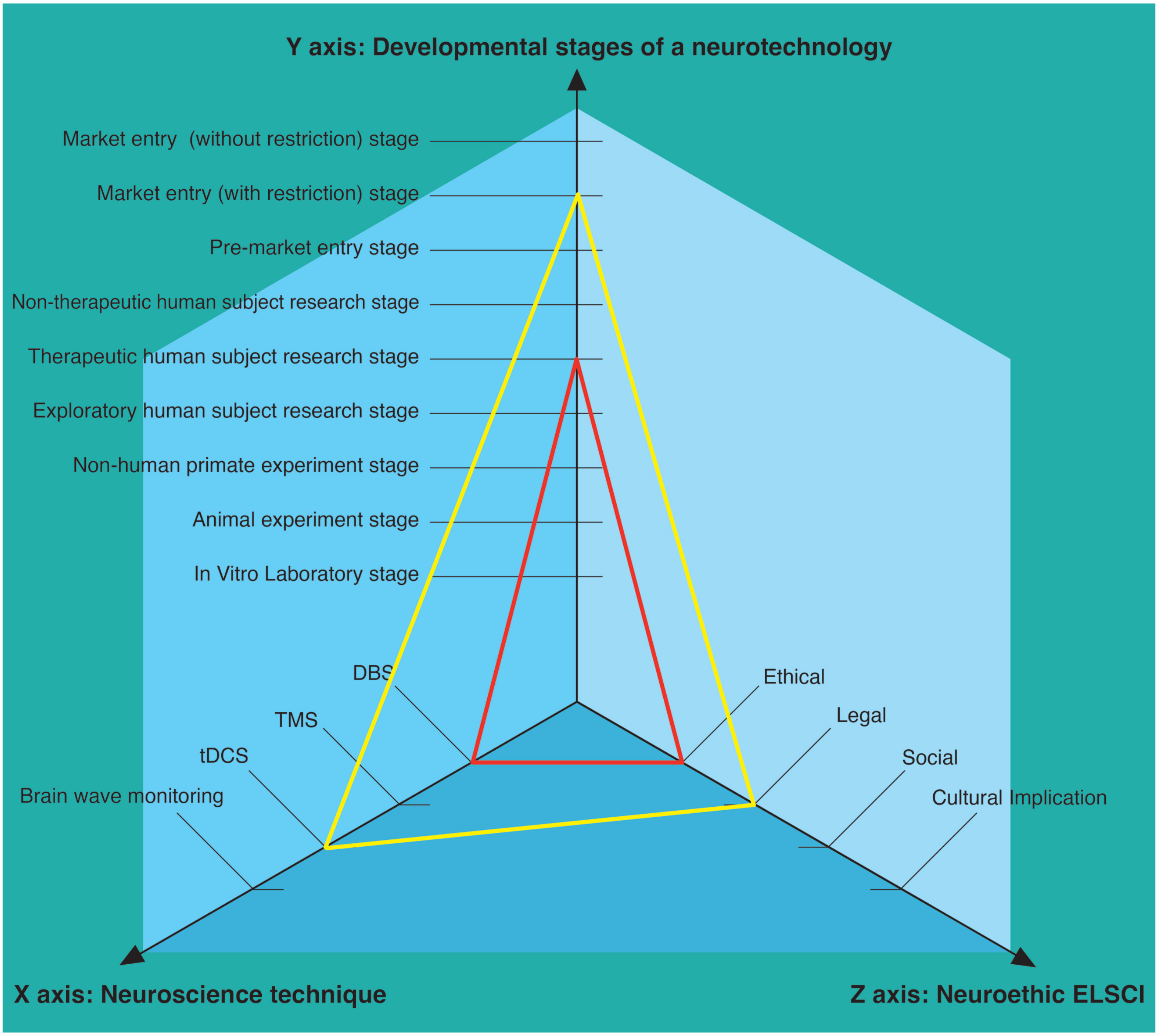

Fig. 2. An Illustration of the New XYZ Matrix Approach. The X axis represents a specific target neurotechnology. The list of technologies shown in the X-axis is provided solely for the purpose of illustration. The Y axis indicates the maturity of a target technology that is classified under nine developmental stages. The Z axis represents the four major areas of investigation, including ethical, legal, social, and cultural implications of a target technology. The yellow line shows neuroethics research on legal issues regarding the use of tDCS. The red line shows neuroethics research on ethical issues regarding the use of DBS.

(Step 1). Next, researchers from various fields including neuroscience, ethics, philosophy, sociology, and law will be invited to create a panel designated for a target technology (Step 2).

Once a panel is organized, neuroscientists and engineers will conduct an initial technical analysis, including a rigorous safety assessment of a target technology. On the basis of this analysis, introductory technical explanations of the mechanism and function of a target technology will be developed for members of the panel who are non-scientists (Step 3). Then the first whole-panel meeting will be convened to share the outcome of the initial technical analysis, and roles for each panel member will be assigned across different areas of ELSCI. To facilitate the allocation of roles within the panel, we developed six major areas/topics of ELSCI based on the Nuffield Council on Bioethics' report on novel neurotechnologies [51] and the neuroethics guiding principles from the U.S. BRAIN Initiative Neuroethics Working Group [19] – (a) safety, (b) autonomy, (c) personal data protection (data privacy), (d) fairness, (e) misuse of technology, and (f) analysis of violation of current

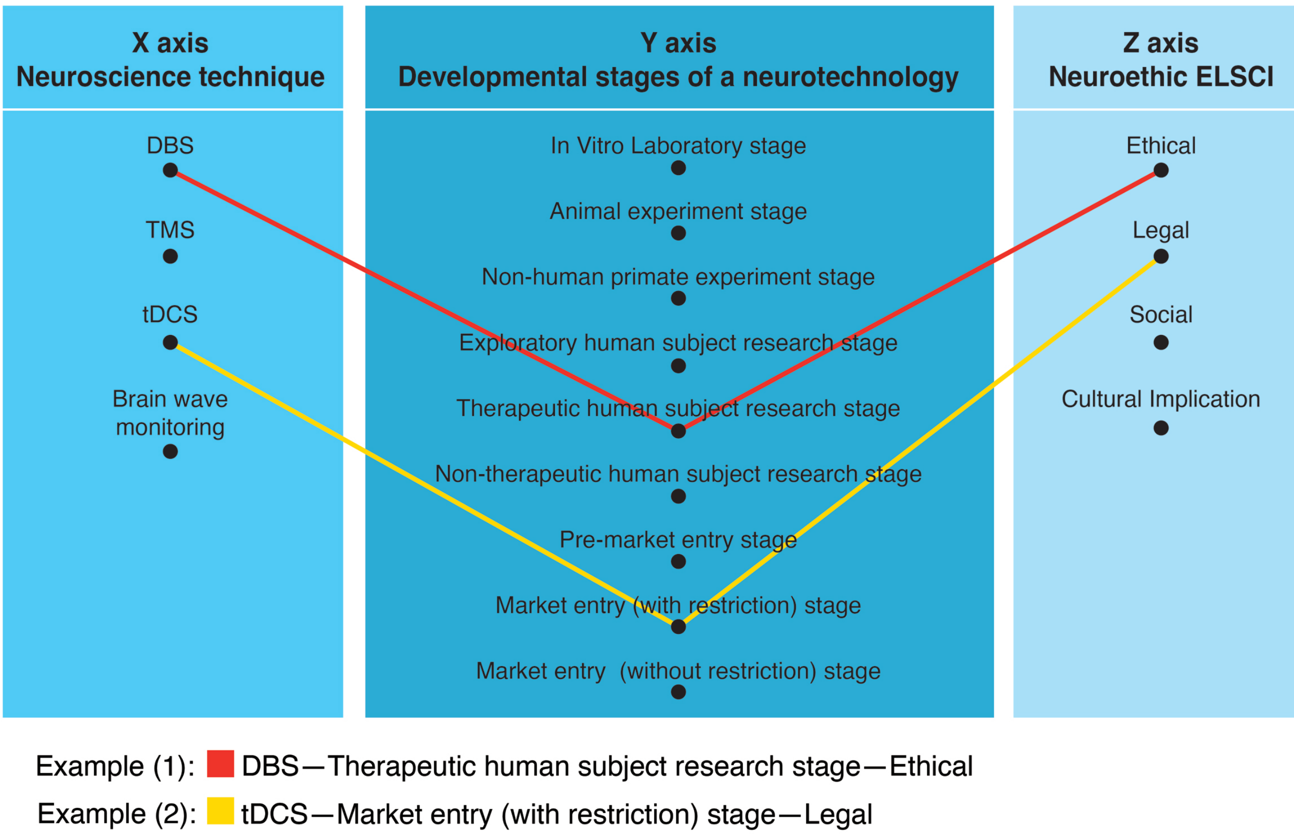

Fig. 3. The New XYZ Matrix Approach shown in a Table Format. The left column represents the X axis (a specific target neurotechnology), the middle column indicates the Y axis (the nine developmental stages of a target technology), and the right column represents the Z axis (the four major areas of neuroethics investigation). As in Fig 2-1, the yellow line shows neuroethics research on legal issues regarding the use of tDCS and the red line shows neuroethics research on ethical issues regarding the use of DBS.

laws and regulations (Step 4).

Members of the panel will then conduct an ELSCI analysis of the area or topic they are assigned (Step 5) and prepare their opinions to be collected and shared within the panel (Step 6). The whole panel will meet again to discuss the opinions on each topic (Step 7), and per this discussion, the opinions will be revised and updated (Step 8). The panel will also hold a public hearing and promote discussion among other stakeholders (e.g., neurotech companies, media, and policy makers) (Step 9). Incorporating the outcome of the public hearing and stakeholder discussion, the revised panel opinions will be published as a final report (Step 10). The panel will further disseminate the findings and recommendations in the final report through various public outreach activities, which may include creating a neuroethics training program at all levels of education, developing a lecture series, or publishing introductory books and booklets for the public. For example, some of the ongoing outreach activities conducted as part of the NRF-funded neuroethics research project in Korea [52] include writing and performing a play, publishing a comic book, and developing a discussion program on non-therapeutic use of tDCS (e.g., for cognitive enhancement) [53]. Emphasis on the public engagement in the workflow also distinguishes our approach from that of the IEEE Neuroethics Framework, one intended primarily for engineers, scientists, and neurotech companies. Promoting participation and engagement of the public through various educational programs and outreach activities will enable people to gain a more balanced view on the risks and benefits of a neurotechnology and to make informed decisions regarding the potential use of the technology.

With the completion of these 10 steps, the ELSCI study of a target technology will be concluded. Yet it should be noted that it is always possible, and even necessary, to revisit the implications of the technology as the technology itself and its potential application evolve. This workflow will provide detailed guidance for researchers to successfully conduct government-funded neuroethics projects. More specifically for practitioners in neuroscience, it will inform them when and how they can join and contribute to these neuroethics projects (e.g., by providing an initial technical analysis of the current state of a target technology (Step 3) or devising a

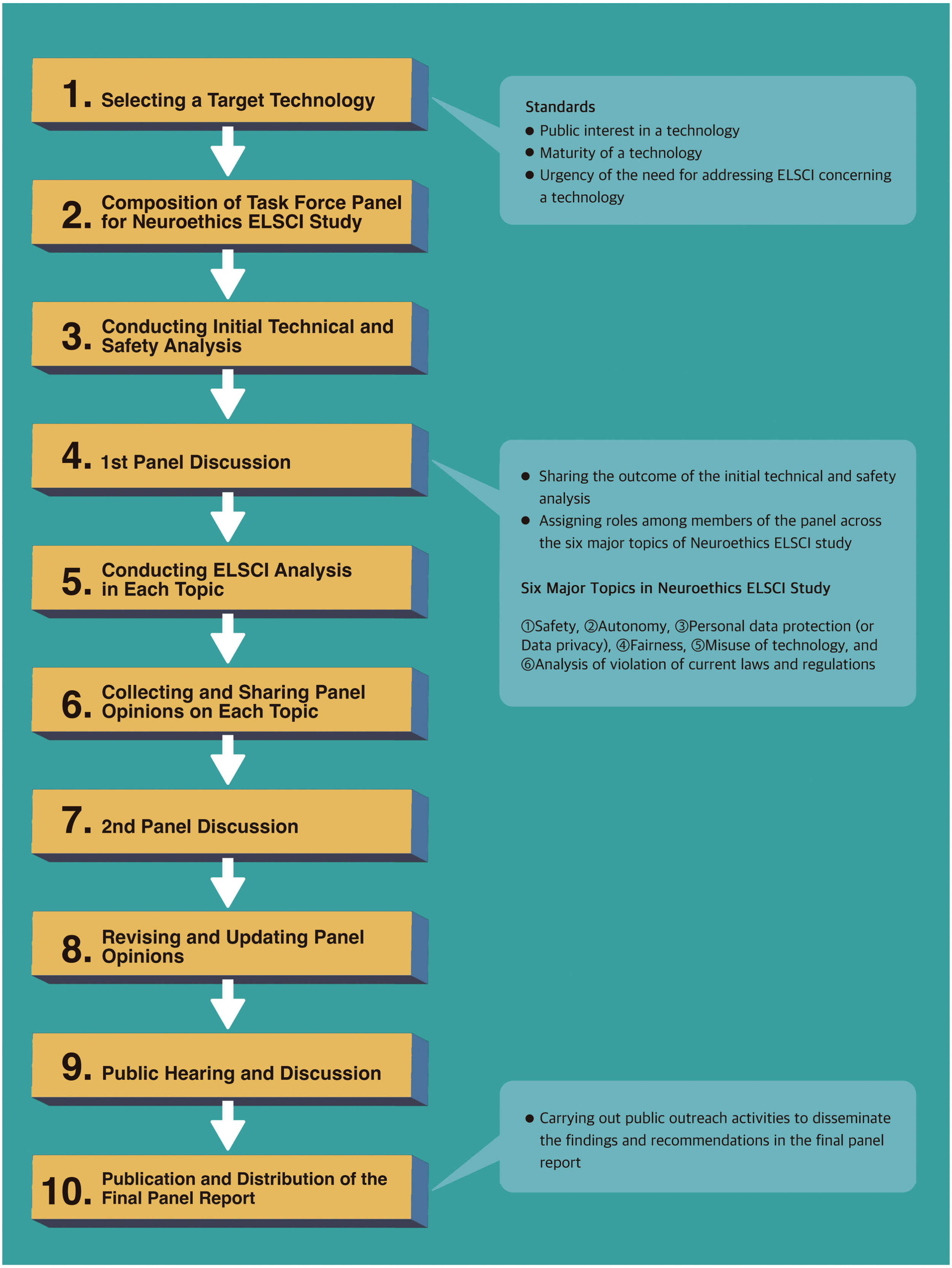

Fig. 4. A Step-by-Step Workflow for the Implementation of the New XYZ Matrix Approach.

guideline for the responsible conduct of research on the technology (Step 10)).

TOWARD MORE RESPONSIBLE INNOVATION IN NEUROSCIENCE AND NEUROTECHNOLOGY

Recent rapid advancement in neuroscience calls for the integration of neuroscience and neuroethics. States and international initiatives have made efforts to achieve the integration, such as the US BRAIN Initiative or EU Human Brain Project, which have incorporated ELSCI analysis as part of their research programs. However, scientists and scholars of the humanities often seem to speak in different languages, making it difficult for them to effectively communicate with each other. Particularly in countries that lack experience in interdisciplinary research of science and ethics, it has been challenging for researchers to even understand where and how to begin the process of integration. The lessons learned from experiences in South Korea revealed a pressing need for a clear and well-defined operational framework to integrate neuroscience and neuroethics. The new XYZ axis framework we have presented here, along with the step-by-step workflow designed to apply this framework, is expected to lower the barriers for researchers in various fields to engage in ELSCI analysis and to facilitate the integration of neuroscience and neuroethics. By including the maturity of neurotechnology as one axis to consider in conducting ELSCI analysis and requiring proactive engagement with the public and other stakeholders, this framework also aims to fill some of the gaps in other existing neuroethics frameworks. Given that neuroethical inquiry on emerging neurotechnologies is still a relatively new area in a majority of the world outside the global north, we believe that our new framework and the workflow will have a more general application beyond the case of South Korea. Our approach will benefit countries that lack experience and trained experts in neuroethics ELSCI research by enabling them to avoid unnecessary trial and errors in their efforts to achieve the integration and by allowing for a more efficient use of time and costs invested in government-funded research programs. To promote this new framework, we plan to conduct and publish a series of case studies to demonstrate the value of the framework, starting from the one that tackles tDCS as a target technology. We will also present our experience in implementing the framework in various international conferences and symposia [24, 25] to foster collaboration with other countries and help them refine the framework to be more attuned to their unique socio-cultural background. Ultimately, we hope this new matrix approach will contribute to responsible innovation in neuroscience and neurotechnology by minimizing harm to individuals and society across the globe while maximizing the benefits of neurotechnology.

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