

Evidence-Based Neuroethics for Neurodevelopmental Disorders

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Many neurodevelopmental disorders affect early brain development in ways that are still poorly understood; yet, these disorders can place an enormous toll on patients, families, and society as a whole and affect all aspects of daily living for patients and their families. We describe a pragmatic, evidence-based framework for engaging in empiric ethics inquiry for a large consortium of researchers in neurodevelopmental disorders and provide relevant case studies of pragmatic neuroethics. The 3 neurodevelopmental disorders that are at the focus of our research, cerebral palsy (CP), autism spectrum disorder (ASD), and fetal alcohol spectrum disorder (FASD), bring unique and intersecting challenges of translating ethically research into clinical care for children and neonates. We identify and discuss challenges related to health care delivery in CP; neonatal neurological decision making; alternative therapies; and identity, integrity, and personhood.

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Many neurodevelopmental disorders affect early brain development in ways that are still poorly understood. The scope of adverse events in early neurodevelopment partly accounts for the wide range and severity of deficits observed between disorders. As is the case with many brain disorders, neurodevelopmental conditions have known environmental and genetic influences. These disorders can place an enormous toll on patients, families, and society as a whole and affect all aspects of daily living for patients and their families. In the absence of effective medical therapies, neurodevelopmental disorders also create enduring personal and economic burdens. Although the needs of patients are met with a range of health, social, and educational services, there is a lack of evidence about ethical challenges faced by

patients and families in the context of research and health care. In fact, for 3 neurodevelopmental disorders that are at the focus of our research, cerebral palsy (CP), autism spectrum disorder (ASD), and fetal alcohol spectrum disorder (FASD), the unique and intersecting challenges of ethically translating research into clinical care for children and neonates is virtually untouched terrain. To address this gap, we describe a pragmatic, evidence-based framework for engaging in empiric ethics inquiry for a large consortium of researchers in neurodevelopmental disorders and provide relevant case studies of pragmatic neuroethics.

Ethical and Philosophic Underpinnings of NeuroDevNet

NeuroDevNet is a Canada-wide, multidisciplinary research network dedicated to accelerating the understanding of neurologic conditions that affect children, with a specific focus on CP, ASD, and FASD. Consistent with the general philosophy of the Networks of Centres of Excellence of Canada of which NeuroDevNet is part of the network strives to improve the economic and social well-being of Canadians. Basic and clinical researchers in the Net explore how the normal brain develops, pursue better methods for detecting abnormalities, and strive to uncover new strategies to repair the injured brain. NeuroDevNet also builds new investigator capacity by training the next generation of researchers in pediatric developmental neuroscience and seeks to disseminate new knowledge to inform health care delivery as well as policy decisions.

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Given the unique translational goals of the Net, questions related to human values and respect for persons surface both upstream and downstream of research. Therefore, the complexity and sensitivity of the context in which the Net operates calls for a practical and flexible ethics approach responsive to the wide range of issues and stakeholders at play. As leaders and members of the neuroethics Core for NeuroDevNet, we have adopted a pragmatic neuroethics framework to achieve this goal.

Pragmatic Neuroethics for Neurodevelopmental Disorders

Neuroethics is a relatively new field that lies at the intersection of bioethics and neuroscience. Neuroethics focuses on the ethics of neuroscience research and the ethical issues that emerge in the translation of neuroscience research to the clinical and public domain.¹ This field “aligns the exploration and discovery of neurobiological knowledge with human value systems.”² The neuroethics core for NeuroDevNet puts a particular emphasis on the importance of including all stakeholder views in informing these ethical perspectives including patients, researchers, families, community groups, advocacy groups, and physicians. Similarly, we strive to anticipate ethical challenges, acquire empiric evidence to understand them, and deliver practical solutions in the form of recommendations and guidelines.

Some of the key reflections on this approach come from philosopher John Dewey, who characterized major aspects of ethics as follows (for a more extensive review, see Racine³): (1) situationalism, the importance of context to understand human behavior and its possible universal implications; (2) (radical) empiricism and experientialism, the importance of empiric knowledge and experience to understand the nature of ethical behavior and the real-world consequences of human acts; (3) social nature of ethics, ethics being shaped by social networks and systems; (4) interdisciplinarity, ethics being the application of knowledge to human situations rather to a particular province of knowledge or expertise; and (5) practical focus, ethics as guidance for practical action in daily life.

Openness to different ethical approaches in light of their consequences is perhaps one of the most distinctive features of a pragmatic approach to ethics. In fact, pragmatism declines a commitment to any a priori set of ethical principles or virtues. Instead, pragmatism builds on empiric research to inform ethics in substantial ways. Within a pragmatic framework, empiric research and inquiry are part of a feedback loop that includes an assessment of whether actions have their intended effects. In addition, the approach allows for the integration of stakeholder perspectives regarding ethical and social issues and aims to apply current evidence to guide and inform best practices in ethics.

Some scholars have argued that bioethics is implicitly inspired by forms of pragmatism,^{4,5} but the commitments to social justice and social progress inherent in Dewey’s writing have not always been captured in modern bioethics discourse.^{6,7} By contrast, neuroethics has come to rely explicitly,

at least in part, on some of these features^{3,5} because it tackles practical ethical issues surfacing in neurologic and psychiatric care and research.^{8,9} Much of neuroethics also shares with pragmatism an approach grounded in radical empiricism and situationalism by embracing the social nature of ethics. Indeed, the pragmatic approach we have explicitly adopted seeks to identify practical starting points and alternatives to resolve difficult ethical challenges through a negotiated scientific and social process. It is a systematic approach that spans the process of issue identification, discovery, ethical analysis, development of tools, and evaluation of impact. It incorporates the philosophy that knowledge and communication about neuroscience are both multidimensional and multidirectional.^{3,10}

We argue that any complete model for understanding neurodevelopmental disorders must include an understanding of the ethical and social challenges that individuals with neurologic disorders face on both a daily and acute basis. Accordingly, the pragmatic approach we have (1) brings the voice of people affected by neurodevelopmental disorders to the foreground of discoveries and translation in health research and care; (2) shifts the ethical perspective to the “agent in context” from ethical frameworks that focus on the individual to capture the complex interactions of genetics, social contexts, and disability; and (3) provides a platform for the integration of social science and biomedical research.

Case Examples

Health Care Delivery in CP

Individuals with CP represent one of the largest cohorts of children with physical disability; yet, the nature of the ethical challenges they face with regard to access to health care, respect for autonomy, communication of health information, respect for confidentiality, and research participation are poorly understood. Adolescents and young adults with CP experience particular challenges when making the transition from the pediatric to adult health systems, including a lack of preparation for the transition¹¹⁻¹⁴ and a lack of integrated care in adult-centered settings.^{12,14-16} These challenges are compounded by the limited recognition of the active role that health care providers have in helping patients get access to health care services and educational and employment opportunities.¹⁷⁻¹⁹ In a recent pilot study, we showed that adolescents and young adults with CP experience a range of challenges with ethical implications during medical consultations (manuscript in preparation). Patients reported feeling a lack of trust and respect from their physicians and complained that information is communicated largely to their parents or caregivers rather than to them. They also reported difficulty in exercising autonomy in decision making and are often faced with prejudice from medical personnel who conflate motor disability with cognitive disability. Through the lens of pragmatic neuroethics, we are able to provide evidence-based recommendations to enhance ethics in health care delivery for this population. Our efforts will further support programs to incorporate ethics best practices in health care

delivery and capture challenges for research participation in trials for novel therapeutics.

Results of this work may also directly translate to the ASD and FASD groups that are also the focus for the Net. For example, by yielding an understanding of autonomy in one group, a well-developed method can then be used to explore autonomy in the others. Similarly, results that yield specific recommendations for better communication in CP can form the basis for piloting, testing, and tailoring of strategies for the other conditions. Overall, we have a limited understanding informed by stakeholder perspectives of the ethical and social challenges faced by patients, providers, and families in health care delivery for neurodevelopmental disorders. There is a need for an exploration of the shared and unique ethical challenges to inform best practices.

Neonatal Neurological Decision Making

One of the most enduring challenges for physicians working in the neonatal care context is prognosticating future outcomes for fetuses and neonates, especially when adverse events are indicated to have occurred antenatally or early after birth. The challenges that are created by uncertainty in prognostication are amplified by a rapid growth of genetic and imaging technologies that have improved the survival of infants and changed the landscape of prenatal testing without a clear consensus about what these technologies mean for future prognosis. This gap underscores how important a better understanding of diagnosis and prognostication is in the neonatal context. Some situations can be clearly identified as futile, such as prolonging inevitable death or protracted suffering. Others are much more challenging to identify, for example, when the likely outcome to be achieved is considered overwhelmingly poor, but the degree of severity is uncertain.²⁰ The challenges related to the determination of futility are especially acute at the beginning of life, such as in severe cases of birth asphyxia.²¹ In this context, life-support decisions require the use of parental proxy decision makers often caught between the emotional crushing of hopeful parental expectations for their child and the dehumanized technical environment of a neonatal intensive care unit. Furthermore, physicians involved in the care of sick newborns are hampered in their communication by an intrinsic lack of certainty regarding predicting potential outcomes and the probabilities of the occurrence of neurodevelopmental disorders and severe symptoms.²² Such situations are fraught for potential misunderstanding and conflict despite the best of intentions. Deciding “when is enough, enough?” in the neonatal intensive care unit simply eludes the ability to elaborate simple consistent universally applicable guidelines or algorithms.²³

The conditions in which end-of-life decisions take place, especially in the pediatric severe brain-injury context, leave a heavy burden on specialty physicians who must participate in decisions typically made on the patients' behalf. There is a clear need to closely examine prognostication practices for severely brain-injured pediatric patients, particularly in the context of variable decision making in the treatment of brain

injury and the interacting factors that complicate end-of-life decision making in this population. Close attention to these issues will yield new empirical support for decision making in difficult matters of diagnosis and treatment.

Alternative Therapies

No single intervention, either conventional or unconventional, has yet been proven to be effective in eliminating the symptoms of CP, ASD, or FASD. As a result, families of children with chronic disabilities are faced with many uncertainties regarding the risks, benefits, and outcomes of current treatment strategies. In response to dissatisfaction with current practices, many parents have turned to alternative or complementary medicines (CAMs) based on the belief that they may confer additional health benefits, including a sense of autonomy over which interventions to use with their children and a hands-on approach to care that is perceived as less invasive.²⁴⁻²⁶

The use of alternative therapies can generate ethical dilemmas and attempts to incorporate CAM into standard pediatric practice have proven challenging.²⁷ The underlying reasons are significant. First, alternative treatments may in time prove effective or have placebo effects that bestow additional therapeutic effects. However, scientific research on the safety and efficacy of many unconventional therapies is lacking, leading to concerns about patient safety and legal liability when recommending CAM therapies or therapists.^{28,29} Second, despite estimates that over half of children with autism and CP use some form of CAM,³⁰⁻³² many parents neglect to inform their pediatricians about the use of these treatments,³³⁻³⁵ and physicians often report that they lack sufficient training or knowledge about CAMs to appropriately guide patients on their use.³⁶ Physician guidelines on how to talk to patients and families about CAM have been published³⁷ and CAM training programs are now being offered at some medical schools and hospitals,³⁸ but uncertainties remain about the scope of practice, licensing requirements, and credentialing of nonphysician CAM providers.³⁸ Moreover, clinical guidelines on incorporating CAM into standard treatments have yet to be developed.³⁹ Third, the prevalence of false or misleading information on the Internet about the safety and efficacy of treatment products and services for children with disabilities has raised concerns.^{37,40-42} Currently, the Internet is the second most prevalent way for parents to access health information and learn about CAMs.³⁵ Given that parents are likely to trust online information, at least to some extent, and are influenced by it when making medical decisions for their children,⁴³ it is important that evidence-based information, not merely the marketplace, guides families and clinicians on the best treatment options for children with disabilities.^{32,42} Fourth, ethical concerns with respect to informed consent exist across a broad range of CAM practices.⁴⁴ Unfortunately, it is difficult to measure how treatment information is interpreted and understood by families and advancements in research such as stem cell therapy, genetic testing, and neuroimaging will make informed consent about treatment options

increasingly difficult because parents are required to understand exceedingly complex medical procedures.

The controversies surrounding the use of alternative therapies within the context of pediatric care are significant. An examination of stakeholder perspectives that takes into account cultural beliefs and values is needed both to inform policy on how to incorporate CAM into standard practice and on appropriate guidelines for delivery into the open marketplace.

Identity, Integrity, and Personhood

A pragmatic approach to neuroethics in neurodevelopmental disorders places an emphasis on better understanding the challenges and ethical imperatives for individuals with disabilities from the perspective of patients. The examination of patient perspectives has already shed some light on how issues such as self-identity may be affected by emerging neuroscience understandings of neurodevelopmental disorders. In the case of ASD, patient accounts of the experience of living with autism have revealed a view of autism that stands in stark opposition to the biomedical model, which is perceived as reinforcing a negative attitude toward autistic individuals and overlooking patient-centered goals in favor of service-related ones.⁴⁵ In contrast, narratives provide an understanding of individuals with ASD whereby unique skills and ways of experiencing the world are attributed to their autistic self-identity and are viewed positively (eg, those found in *The Ethics of Autism*⁴⁶). Accordingly, some scholars have suggested that there is a need for the medical community to acknowledge the “importance of autism as a self-identity.”⁴⁵ Given adequate consideration, these personal reflections may have a grave bearing on the research effort to find a “cure” for ASD. For example, Temple Grandin once stated, “If I could snap my fingers and be nonautistic, I would not—because then I wouldn’t be me. Autism is part of who I am.”⁴⁷

The importance of such personal accounts lies in their ability to allow us to measure whether researcher and clinician priorities are in line with the priorities and preferences of the individuals themselves. The indication of such gaps is increasingly important because a steady stream of media reports bring more attention to research that is paving the way for the development of potential “cures” and genetic tests. For example, new drugs aimed at the treatment of fragile X syndrome are being lauded as potential cures for ASD because 30% of individuals with fragile X syndrome also have an ASD.⁴⁸ To best serve this population of individuals and their families we must ask questions, such as what aspects of a person’s identity, integrity, and sense of personhood would these drugs bring about? What, if any, level of change is ethically appropriate? The inclusion of patient perspectives in the conduct of research will help ground research within a concerted and collaborative framework to respect values and social diversity.

Conclusions

Neuroethics has joined NeuroDevNet in a partnership that addresses the challenges of CP, ASD, and FASD in pragmatic

and innovative ways. We emphasize practical, in-context solutions to difficult challenges. We are starting to gain traction on some of these problems in 4 areas at the outset: health care delivery, neonatal neurologic decision making, alternative therapies, and self-identity. In this sense, neuroethics promises to align human values with cutting-edge research to improve treatment and understanding of neurodevelopmental disorders.

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