
SPECIFIC AIMS

More than 500,000 children in the USA and Canada suffer from epilepsy today, with 30% of these having drug resistant epilepsy (DRE). Unmanaged, epilepsy can result in cognitive decline, social isolation and poor quality of life, and has substantial economic impact on families and society. Properly selected, up to 70% of DRE patients become seizure-free after surgery (Muh, 2016). Nevertheless, epilepsy surgery carries with it risks proportional to its level of invasiveness: infection, damage to adjacent areas of the brain, memory impairment, stroke and hemorrhage, as well as a hospital stay and recovery phase. As a result, less invasive interventions such as MRI-guided laser interstitial thermal therapy, stereotactic radiosurgery, and responsive neurostimulation have been developed. While the outcomes and complications of conventional epilepsy surgery, especially temporal lobectomy, have been well studied, the short- and long-term efficacy and side effects of these newer interventions for DRE are less understood. Moreover, unlike novel pharmaceutical treatments, these interventions are rarely put through the rigors of a randomized control trial, nor are the outcomes of adult trials clearly generalizable to children. **To address the knowledge gap and related ethical considerations in the pathway to the adoption of novel neurotechnologies for pediatric DRE**, we will use a pragmatic neuroethics framework to:

Aim (1) Engage affected families and clinicians to identify critical features for choices about procedural trade-offs, values, and concerns for decision-making and communication about neurotechnological interventions for pediatric DRE. Using purposive sampling methods, we will recruit carers of children with DRE (parents and primary caregivers) through epilepsy clinics that have an established epilepsy surgery program. We will use both purposive and convenience sampling to recruit pediatric neurologists and neurosurgeons and invite them by email to attend one of four focus groups that will be held at key national conferences. We will use qualitative focus group methodology to explore attitudes towards different neurotechnological interventions and generate key ethics attributes around choice and decision-making.

Aim (2) Apply the findings from Aim 1 to a discrete choice experiment (DCE) online survey to determine the value placed on key attributes (e.g., risks, compliance, reversibility) of decisions surrounding conventional and novel DRE interventions among families affected by DRE, and clinicians who care for them in the USA and Canada. DCEs have been used extensively to understand health care preferences and treatment (de Bekker-Grob et al., 2015), and their likely acceptability in practice, even before they are introduced. We will develop and implement an online DCE study, and analyze responses using the conditional logit model (McFadden, 1973). Estimating at least 120 total responses (60 from parents and 60 from clinicians across North America), we expect that the willingness of affected families to choose and the willingness of a physician to recommend a certain intervention will depend on expected risks of long-term neurologic morbidity and trade-offs between the benefits (e.g., likelihood of seizure control/reduction, risk reduction) and the risks from the intervention. We expect that parents will value higher risk of morbidity for a higher likelihood of freedom from seizure, but that will correlate with the severity of their child's epilepsy (i.e., frequency and nature of seizure). We will identify the characteristics of parents and clinicians who would prefer maximally invasive, low-maintenance, higher seizure freedom interventions over less invasive surgical neuromodulatory interventions requiring ongoing maintenance or multiple interventions.

Aim (3) Integrate the findings from Aims 1 and 2 to develop, evaluate, and deliver patient-directed resources in the form of infographics and informational materials and videos, and clinician resources for family decision-making, clinician counseling and care. Modern informational resources will focus on the key attributes identified in Aim 2 for supported decision-making for neurotechnology for DRE. They will use images prominently, and language consistent with a 5th grade reading level (Weiss, 2007), and will be piloted and evaluated using visual analogue scales and open commentary by focus groups participants from Aim 1 who agree to recontact.

The **significance of this work** is in the unique ethical challenges for children with DRE whose bodies, brains, experiences, and goals are still evolving, and for whom neurosurgical innovations are imminent. The focus on children speaks directly to the goals articulated in the visions of the RFA and BRAIN 2025 pertaining to advances in neurotechnology and its effects on personal identity, agency, and perception of normality,

risk/benefit analyses and consent issues, ethical implications of evolving neuromodulation technologies, invasiveness, and special populations.