Ethical Issues in Intraoperative Neuroscience Studies: Assessing Subjects' Recall of Informed Consent and Motivations for Participation

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Introduction

In recent years, an increasing number of intraoperative neuroscience studies have been supported by the National Institutes of Health (NIH) through the BRAIN initiative. In particular, intraoperative studies that make use of microelectrode recordings, often in deep brain stimulation surgeries (DBS) for Parkinson's Disease (PD), have been on the rise (Tekriwal et al. 2019). The use of neurosurgical patients as human research subjects raises important ethical considerations regarding undue influence, capacity, and informed consent (Chiong et al. 2018). However, to our knowledge, no study has empirically examined these considerations in a real-world context.

Objective

The present study aimed to empirically examine ethical concerns related to undue influence and recall of informed consent in PD patients undergoing DBS surgery who agreed to participate in an intraoperative neuroscience study. In particular, we sought to examine patient motivations for participating in an intraoperative research study, and assessed recall of study purpose, study protocol, risks, and benefits.

Methods

This study was conducted as an ethics supplement to a larger NIH-funded intraoperative study in PD patients undergoing unilateral or bilateral DBS placement in the subthalamic nucleus (3U01NS103799-02S1). The parent study sought to better understand how activity patterns of neurons in various structures of the human brain contribute to higher functions like learning and decision-making.

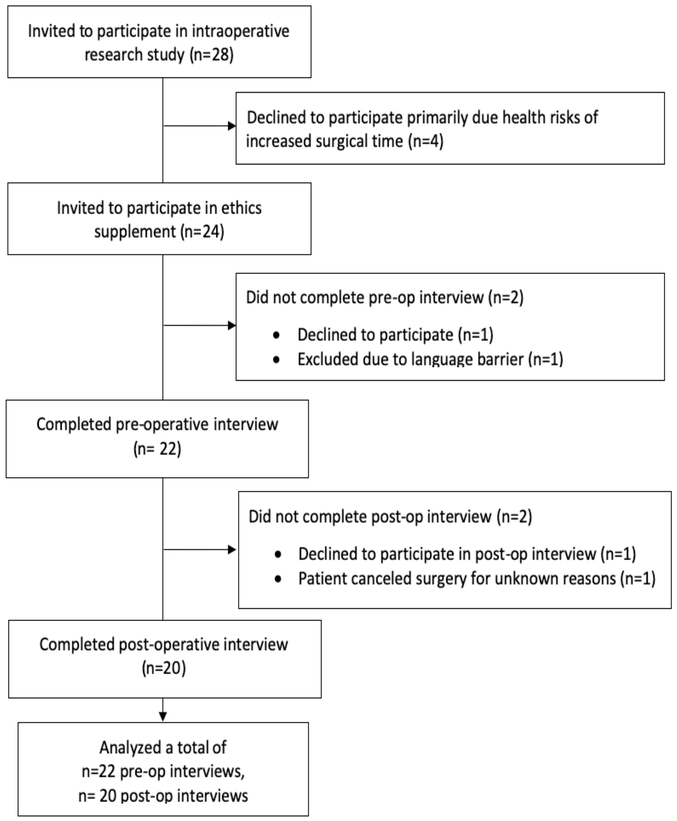
Between Oct 2018-Feb 2020, patients who consented to the parent study during an in-office visit were also asked to participate in the ethics study. Two semi-structured interviews of approximately 30 minutes in length were conducted preoperatively and postoperatively via telephone by an embedded ethicist. Patients were not offered financial incentives for the parent intraoperative study but were provided with a $75 Amazon e-gift card following completion of each ethics interview.

Results

Study Timeline

Pre-op interviews were completed at a mean of 7.8 days following provision of informed consent. Patients underwent DBS surgery a mean of 5.2 days after the pre-op interview. A post-op interview was conducted a mean of 5 weeks after surgery.

Figure 1. CONSORT diagram (N=22).



Demographic Characteristics

A total of n=22 subjects were enrolled. The mean age (SD) of the study sample was 60.9 (10), and the average time since PD diagnosis was 8.9 years. Of the sample, n=17 subjects were male (87.3%). The majority of patients had an associate's degree or higher (n=14; 63.6%), and an annual household income of $75k or higher (n=13; 65%; missing n=2). Three patients had prior DBS implants, all unilateral.

Undue Influence

Table 1. Patient motivations for participation (N=22).

Reasons for participation cited as "very important" or "important"	N (%)
Help future Parkinson's disease patients	22 (100.0)
Help advance medical science	21 (95.5)
Trust in clinical team	18 (81.8)
Trust in hospital	14 (63.6)
Family might get PD	11 (50.0)
Advice of family/friends	11 (50.0)
Interesting experience	10 (45.5)
Extra time with clinical team	8 (36.4)

All patients reported that helping future PD patients was "very important" or "important" in their decision to participate in the intraoperative study. Other important reasons were helping advance medical science, and trust in the clinical team. The least important reason was extra time with clinical team. For patients who declined to participate in the NIH trial (n=4), the primary reason was due to health concerns of increased surgical time.

Informed Consent

Table 2. Summary of informed consent recall (N=22).

Informed Consent Components	% recalled correctly
Study Purpose	36.4
Study Protocol	50.0
Risk	22.7
Benefits	36.3

Overall, recall of informed consent was poor. Notably, only 22.7% of patients recalled at least one of two risks: 1) increased risk of infection due to additional time in the operating room; or 2) loss of confidentiality. While 36.4% of subjects correctly recalled that the study purpose was neuroscience-related, others could not recall (22.7%), remembered study tasks but not study purpose (22.7%), or thought it was Parkinson's related (9.1%). 63.7% of patients could not recall benefits, or said they were not mentioned during the informed consent process. Study protocol was coded generously, with any mention of intraoperative tasks coded as correct recall. There were no clear demographic patterns in recall results.

Discussion

All subjects correctly understood that the study would not confer a direct therapeutic benefit. Overwhelmingly, participants wanted "to help" others, including future patients and medical science in general. However, two of the three subjects who had prior experience with the neurosurgeon for unilateral DBS placement reported participating in the study because they wanted to "give back" to the neurosurgeon because the initial DBS surgery had dramatically improved their lives. Thus, undue influence may be of concern for this subgroup.

Furthermore, even though standard informed consent procedures were followed, subject recall of elements of the informed consent was poor. In our study, risk recall was markedly lower than previous studies assessing PD patients for recall. However, in prior literature, a variety of methods were used to assess risk, ranging from multiple choice questionnaires (Ravina et al. 2010) to yes or no questions (Valadas et al. 2011). Study methods and definition of risk, among other factors, may have contributed to inflated recall rates.

Given that the NIH has prioritized funding of intraoperative neurosurgical studies, future work should focus on: 1) ensuring subject understanding and retention of information presented during the informed consent process; 2) empirically assessing other ethical issues, such as capacity and risk, which remain relevant to intraoperative research in this patient population. Risks and post-op complications should be tracked across intraoperative studies, and compared to standard-of care outcomes.

References

Tekriwal A, Afshar NM, Santiago-Moreno J, Kuijper FM, Kern DS, Halpern CH, Felsen G, Thompson JA. Neural Circuit and Clinical Insights from Intraoperative Recordings During Deep Brain Stimulation Surgery. Brain Science. 2019; 9(7): 1-18.

Chiong W, Leonard MK, Chang EF. Neurosurgical Patients as Human Research Subjects: Ethical Considerations in Intracranial Electrophysiology Research. Neurosurgery. 2018; 83(1):29-37.

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