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Neuroethics: Defining the issues in theory, practice, and policy (2nd edn)

Judy Illes (ed.)

<https://doi.org/10.1093/acprof:oso/9780198567219.001.0001>

Published: 08 Apr 2004

Online ISBN: 9780191724084

Print ISBN: 9780198567219

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15 Functional neurosurgical intervention: neuroethics in the operating room

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<https://doi.org/10.1093/acprof:oso/9780198567219.003.0015> Pages 213–228

Published: April 2004

Abstract

This chapter covers ethical challenges faced by surgeons practicing functional neurosurgery. The exploration of issues surrounding this set of surgeries presents especially interesting problems given the effects, potential or actual, on patient's quality of life in the attempt to restore or normalize a function. The chapter sets the context by briefly discussing the special challenges of surgical ethics in general, defines 'functional neurosurgery', and reviews the past, present, and expected future of functional neurosurgery. After setting this context, it addresses a variety of prominent ethical issues. It pays special attention to the context in which issues arise and reflect on ethical challenges to functional neurosurgery as a discipline.

Keywords: [functional neurosurgery](#), [neuroscience](#), [ethics](#), [brain surgery](#)

Subject: [Cognition and Behavioural Neuroscience](#)

Collection: [Oxford Scholarship Online](#)

Introduction

Evaluating ethics in neurosurgical practice requires a re-evaluation and recalibration of the analysis found in other areas of neuroethics. Neurosurgical practice adds complexities to the neuroethics discussion because of the structure of surgical teams, popular perceptions of surgery and surgeons, and the relatively transitory nature of patient-surgeon relationships. Although neurosurgical ethics does not constitute an ethic separate from general medical ethics, surgical ethics, or neuroethics, significant unique textures must be taken into account. Neuroethical issues discussed in other chapters of this book have relevance and must be recognized when evaluating ethically appropriate neurosurgical practices. For instance, the ethical implications of emerging neuroimaging cannot be ignored if neurosurgeons rely upon these images for guidance in surgery. Similarly, the issues of cognitive capacity must be understood in order to evaluate informed consent processes (see also Chapter 9). The interesting challenges come in integrating these concerns into the events of neurosurgery.

In order to focus the discussion even further, this chapter covers ethical challenges faced by surgeons practicing functional neurosurgery. The exploration of issues surrounding this set of surgeries presents especially interesting problems given the effects, potential or actual, on patient's quality of life in the attempt to restore or normalize a function. In order to elucidate these issues, we set the context by briefly discussing the special challenges of surgical ethics in general, define 'functional neurosurgery', and review the past, present, and expected future of functional neurosurgery. After setting this context, we address a variety of prominent ethical issues. We pay special attention to the context in which issues arise and reflect on ethical challenges to functional neurosurgery as a discipline.

General surgical ethics

Until recently, particular ethical issues of surgery were largely ignored. Professional journals describe the need both to develop ethics curricula tailored specifically for surgical residents and to include more ethics discussions in journal publications (Hanlon 2004; Polk 2004). Regulations mandating ethics content in resident education have prompted further attention to the ethical issues of subspecialties such as surgery. In the small literature that exists, the established issues of surgical ethics include such things as:

informed consent, confidentiality, advance directives, and the determination of death—through the range of surgical patients, from elective and high-risk patients to poor-risk and dying patients, to intra-professional and inter-professional issues, surgical innovation and research, and financial aspects of surgery... (McCullough *et al.* 1998)

These elements play significant roles in the treatment of surgical patients. Given the complexities of patients and health care systems, there are no formulaic ways of addressing ethics problems for all cases. The surgeon and other relevant providers must first be able to identify when ethical challenges arise. The problems quoted above provide a valuable list of classes of potential problems. Subsequently, participants must reflect on and balance salient ethical features of each particular case in order to resolve identified dilemmas well.

The complex processes of surgery provide one type of ethical texture that should be considered. Surgical ethics begins at the time of a patient's referral and continues through postoperative follow-up. Ethical practice relates not only to activities in the operating room, but also to activities of accepting a patient for surgery, preoperative preparation, and postoperative care. Clearly, ethical considerations are fundamentally rooted in what will, is, or has happened in the operating room under the direction of the surgeon(s). However, those activities fall within the context of a temporally related group of activities. Many ethical dilemmas can be avoided by having

appropriate preparation or good processes in place. Considering 'ethics in the operating room' means considering the ethics of practice for the entire time surrounding the actual operating room event.

Given the complexity of contemporary health care, surgeons navigate intricate webs of professional and patient relationships. The surgeon relies on the patient both as a patient and as a paying client (or at least as a billing unit). The surgeon relies on other physicians for referrals of potential surgical candidates and for collaboration in research. Conflicts of interest may take the form of financial incentives as well as professional obligations that may be contrary to patient interests. These matters must be transparent when considering surgical options, both in deciding the type of surgery as well as whether to offer any surgery.

Surgeons can be challenged in leading teams and in negotiating interprofessional roles. These complex roles include professional reputation as well as economic incentives. Ethical land mines litter the pathway of these interactions. Much of the surgeon's information relies on subspecialty advice and interpretation. In neurosurgery this can be the neurologist, neuroradiologist, neurophysiologist, or neuropsychologist. Surgeons need to acknowledge the influences, positive and negative, that these subspecialties may have on decision-making.

Further, in considering a patient's best interests and desires, surgeons must recognize the competing interests of patients and their social supports. Patients and their social supports interact with surgeons only during a relatively well-defined window of time. The swing of Western bioethics has been toward viewing patients as needing to make autonomous decisions that are uninfluenced by the interests of others. However, humans seldom make decisions isolated from a social structure and continue to have obligations to others throughout their lives. This translates into health care choices. Recognizing the important role of those who are relationally close (usually families/caregivers) in decision-making is important. (Seaburn *et al.* 2004) These relations can elucidate patient values and best interests given a particular social milieu (Neil-Dwyer *et al.* 2001). Although good ethical practice dictates that patients are not unduly influenced, i.e. coerced, this does not mean that patients should have their regular influences removed while giving consent for surgery. Generally, the small window of interface prior to surgery does not give the surgeon ample time to make a full evaluation of complex relations and how they interface with a patient's decision-making or health. Although surgical teams rely a great deal on referring physicians to identify these conflicts, it is important to watch for warning signs that ethical problems may be present. This is particularly true when dealing with 'functional' surgeries that have a potential to alleviate the caregiver's burden at the expense of other aspects of a patient's health.

The complex surgical dynamic also includes interface with pharmaceutical and device manufacturers. Conflicts of interest in commercial enterprises continue to concern many in the health care community (Trojanowski 1999; Morreim 2004). Balancing patient benefits, societal needs for collaborative work with industry to improve surgery, and commercial interests of companies and surgeons requires great care. Again, transparency and disclosure of conflicts of interest provide necessary, but not always sufficient, conditions for good ethical surgical practice.

Since the anatomy of individual patients and the surgical techniques of individual surgeons vary considerably, standards of practice can be difficult to characterize. Often a surgeon must improvise during surgery. Deciding whether the alterations are simply an exercise of professional judgment or part of a research innovation can be difficult. Those improvisations/innovations do not necessarily lend themselves well to standard research methods developed to govern drug development. These elements of surgical practice have given rise to discussions about appropriate process and regulation of innovative practices in surgery (Gillett 2000). A surgeon's professional prerogative to employ his skill and judgment in unique cases must be balanced against a need to generalize knowledge and provide best care for groups of patients.

Surgical education and training present challenges to informed consent, patient trust, and good individual care. In medical practice, treatment by a resident physician can usually easily be reviewed and reversed if necessary.

However, in surgical procedures (as well as in some diagnostic medical procedures) errors are generally more difficult to reverse. This raises the challenge of training new surgeons while retaining patient safety and trust. Training provides a societal benefit that may have some cost to individuals. Although most training programs occur in high-volume centers, and recent correlations have been made between better outcomes and higher volumes of surgeries (Birkmeyer *et al.* 2002), significant issues remain about the level of disclosure to patients about who actually makes the incision that is ethically necessary.

Gaining informed consent for surgical procedures contains a number of generic challenges. First, a patient needs to have confidence in his surgeon while still understanding that complications may actually occur. This necessitates a balance of optimism with reality. Secondly, a surgeon should have confidence in his practice. Thirdly, the procedure itself may not have clear boundaries in duration or scope. The consent process should cover not only the actual time in the operating room, but also the preoperative evaluations and postoperative recovery. Finally, informed consent involves the patient's understanding and agreeing to go forward with the therapeutic modality and not simply signing a complex legal form. These elements apply to therapy as well as research in differing degrees. We will discuss this at greater length in the later section on neurosurgical ethics.

As addressed in the next section, functional brain surgery has an interesting and somewhat checkered past. When the brain is involved in surgery, there are special overlays of issues both technically and perceptively. Brain function remains somewhat mysterious, with small variations in individual brains making significant functional differences. Recognizing that the brain has a central importance in the organization of patients as persons makes performing brain surgery perceptively different from other types of surgeries. Given that cognition and independence are privileged traits in our cultural understandings, a sense of desperation can deeply influence patients in their desire to go forward with risky neurosurgical procedures or to decline relatively benign neurosurgical procedures. As we discuss in later sections, it can be difficult for patients to weigh the potential of a decrease in cognition, change in personality, or loss of memory as complications of surgeries. The public perceptions of neurological surgeries are deeply influenced by such stories as that of Phineas Gage, people waking after being 'brain dead', and the proliferation of frontal lobotomies (as described below). These elements add interesting textures to the ethics issues in functional neurosurgery, since they cultivate both fascination and distrust.

Functional neurosurgery: past, present, and future

Functional neurosurgery aims to improve the function of the nervous system by altering the underlying physiology by either destruction or augmentation of the various pathways involved in normal nervous system function. This contrasts with anatomical procedures, in which anatomical lesions are removed regardless of the potential effect on the underlying function of the nervous system. As defined by Iskandar and Nashold (1995), there are six broad categories of functional disorder: abnormal involuntary movements, spasticity, pain, psychiatric disorders, epilepsy, and neuroendocrine disorders. The first five of these are most relevant to our discussion.

Movement disorders

Surgeons began manipulation of the nervous system for the treatment of movement disorders around the turn of the twentieth century. In 1909, Sir Victor Horsley excised portions of the motor cortex in a patient with continuous uncontrolled involuntary movements (Horsley 1909). The patient's condition improved, ushering in the age of surgical treatment for movement disorders. Other surgeons, encouraged by Horsley's success, performed destructive procedures in other parts of the motor system with mixed success. Browder described sectioning the internal capsule via a transventricular approach. Unfortunately, this procedure universally created motor weakness and spasticity, and in the majority of cases the abnormal movements recurred with time. In 1939, Meyers resected the head of the caudate nucleus in a patient with tremor, with subsequent dramatic improvement in symptoms and no hemipar-esis. He then embarked on a series of experiments in the destruction of various deep nuclei, achieving relatively good results but with a surgical mortality of 15 percent (Meyers 1958).

In 1952, Irving Cooper was performing a pedunculotomy in a patient with parkinsonian tremor when he accidentally severed the anterior choroidal artery, which supplies portions of the basal ganglia. He aborted the procedure and the patient subsequently awoke from surgery with marked reduction in tremor. This led Cooper to embark on a series of anterior choroidal artery ligations, with good relief of tremor in 65–75 percent of patients, but with a mortality rate 10 percent (Cooper 1954). Although these results strongly suggested that the basal ganglia could be an effective target for the treatment of movement disorders, it was clear that less invasive methods were necessary.

The use of precise mathematical methods for targeting deep-brain structures had previously been described by Horsley and Clarke (1908). Their apparatus for recording from the deep cerebellar nuclei in monkeys was based on skull landmarks and the relationship of these landmarks to an atlas of brain structures. The technique was called stereotactic surgery, a compound word derived from the Greek *stereos* (solid or three-dimensional) and the Latin *tactus* (to touch). Unfortunately, the variability of the human brain and skull prevented the use of such an apparatus for human neurosurgery until a method could be devised for relating the structure of the brain to the coordinate system of the stereo tactic device. In the late 1940s, Spiegel and Wycis linked skull radiography with a stereotactic instrument to produce the first practical system for human stereotactic surgery (Spiegel *et al.* 1947). Other investigators soon followed suit, with rapid application of stereotactic techniques to the treatment of movement disorders.

Stereotactic interventions such as pallidotomy and thalamotomy soon became standard treatment for Parkinson's disease and tremor. Although their efficacy for the treatment of movement disorders was modest, the morbidity was relatively low compared with the highly invasive procedures that had preceded them. The landscape of Parkinson's disease treatment changed dramatically in the late 1960s with the introduction of l-dopa. Stereotactic surgery declined dramatically with the realization that l-dopa was both safer and more effective. However, the limitations of medication became apparent after years of treatment. Patients began to develop abnormal involuntary movements (dyskinesia) and wide fluctuations in motor symptoms. In the late 1980s, Laitinen re-introduced pallidotomy as an effective treatment for patients who had developed motor complications from medication (Laitinen *et al.* 1992). Stereotactic surgery for movement disorders again became viable.

Stimulation of the brain was first attempted in patients with chronic pain and psychiatric disorders (Heath and Mickle 1960). Several investigators reported on targets for pain, and patients had electrodes implanted which were intermittently stimulated. It had long been known that stimulation of a structure before lesioning could help predict the eventual effect of a particular lesion placement. It was this observation that led Benabid and colleagues to chronically implant electrodes into the thalamus of a patient who had a prior contralateral thalamotomy in order to avoid the known risks of bilateral lesioning (Benabid *et al.* 1987). By this time, technology had advanced to the point that a fully implantable stimulation system, based on cardiac pacemaker

technology, was feasible. Chronic deep-brain stimulation has subsequently proved to be an effective treatment for medically refractory Parkinson's disease (Krack *et al.* 2003).

Epilepsy

Surgery for epilepsy has been practiced since the early part of the nineteenth century, when trephination was used for post-traumatic epilepsy. However, epilepsy surgery truly began when the electrical nature of the brain was demonstrated convincingly in animal studies. Fritsch and Hitzig (1870) showed that stimulation of the motor cortex of the dog could cause movements of the contralateral body (Fritsch and Hitzig 1870), leading the way to Penfield's detailed studies of human motor and sensory function in the early twentieth century. The discovery of electroencephalography by Berger in 1929 was eventually validated in 1935 by Adrian and Matthews, with the result that epileptic foci could be reliably localized in the brain. Localization of function with recording and stimulation became commonplace (see also Chapter 11), and mapping procedures are now routinely carried out to characterize electrically responsive sites in patients undergoing brain surgery. In patients with pathology close to critical brain areas, these operations are often carried out with the patient awake, allowing test stimulation of such vital functions as speech, vision, and cognition. Resective surgeries for epilepsy have a significant range of invasiveness that includes corpus callosotomy (a disconnection of communication between hemispheres), lesionectomy, lobectomy, and hemispherectomy.

Pain

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Pain is an integral part of human experience. Thus it is not surprising that attempts to treat pain date back to the beginning of recorded history. For instance, electric fish were used by the ancient Egyptians after it was discovered that electric shocks could relieve pain. Several societies, including the Assyrians, Babylonians, and Egyptians, practiced trephination and other physical procedures.

Pain treatment advanced very little during the Middle Ages, although electrotherapy, massage, and exercise were still practiced. The roots of contemporary surgical treatment of pain can be traced back to a report by Ambroise Pare (1598):

In the course of bleeding King Charles IX for the smallpox, Antoine Portail's lancet had injured a superficial nerve with the production of intense pain and contraction of the arm. After more than three months of suffering the king happily recovered, but Pare stated in his commentary that, had other remedies not been successful, he was prepared to use boiling oil in the wound or to have severed the nerve completely...Marechal, surgeon to Louis XIV, inaugurated neurotomies for tic douloureux toward the end of the seventeenth century. (White and Sweet 1955)

The beginning of a modern understanding of pain has been attributed to Descartes, who produced the first depiction of the pain pathway as a string connecting the skin to the brain. As knowledge of neuroanatomy and neurophysiology grew, the existence of a separate pathway dedicated to pain became more clearly defined. Many different types of destructive procedure were designed to interrupt these pathways, with greater or lesser efficacy depending on the painful disorder being treated. These ablative procedures sometimes produce lasting cures, but more frequently merely add a sensory deficit without relieving pain.

In 1965, Melzack and Wall published their influential gate control theory which revolutionized the understanding and treatment of pain (Melzack and Wall 1965). Simply stated, the theory describes a gating mechanism in the spinal cord by which painful stimuli can be overridden by innocuous stimuli. By electrically stimulating sensory nerves, this gate can be 'closed', leading to pain relief. This theory formed the basis for peripheral nerve and spinal cord stimulation, which have been successfully used to treat a wide variety of neuropathic pain syndromes.

Even before these experiments, neurosurgeons had learned that stimulation of the central nervous system could alleviate pain. Heath (1954) reported pain relief in patients who had undergone stimulation of the septal region for treatment of psychiatric disorders. Mazars *et al.* (1960) used anatomical knowledge of nociceptive pathways to devise a procedure to stimulate the termination of the spinothalamic tract in the thalamus. This technique was later used by several investigators to treat many types of neuropathic pain. For a time, deep-brain stimulation was used for a variety of pain syndromes. Despite reasonably good successes in some conditions, there was insufficient evidence to support its widespread use for the treatment of pain, and the FDA re-classified deep-brain stimulation for pain as an experimental procedure (Bendok and Levy 1998).

Psychiatric disorders

The treatment of psychiatric disorders may arguably have been among the first uses of neurosurgery. Stone age skulls have been found with well-healed trephinations, and written records of trephining to release demons or evil humors date back to 1500bc (Feldman and Goodrich 2001). However, intentional lesioning of the brain to treat psychiatric disorders was based on observations in patients who had sustained brain injuries with subsequent changes in personality. Perhaps the most famous case of this type is that of Phineas Gage, a 25-year-old railroad worker. On 13 September 1848, an accidental explosion drove a 3 cm steel rod into his left cheek, through both frontal lobes, and out through the skull near the sagittal suture. He was treated by a local physician, John Harlow, who reported the case in a letter to the *New England Journal of Medicine* in 1848 (Harlow 1848). According to Harlow, Gage's personality was now

...fitful, irreverent, indulging at times in the grossest profanity (which was not previously his custom), manifesting but little deference for his fellows, impatient of restraint or advice when it conflicts with his desires, at times pertinaciously obstinate, yet capricious and vacillating, devising many plans of future operation, which they are no sooner arranged than they are abandoned in turn for others appearing more feasible.

Observations in patients such as Gage, coupled with experimental work showing specialization of the cerebral cortex in laboratory animals (Fritsch and Hitzig 1870), led to the consideration of surgical interventions for psychiatric disease in humans. Gottlieb Burckhardt was the first investigator to publish the results of cortical excision for psychiatric disease. In his initial report of six patients, three were considered successes, two were considered partially successful, and one patient died (Burckhardt 1891). Burckhardt's results were not received enthusiastically, and he performed no further operations. However, the social climate of the early 1900s provided a fertile environment for the further development of surgical procedures for psychiatric disease. In the early years of the twentieth century, there were few available treatments for patients with psychiatric illness. Asylums became overcrowded, and physicians caring for the hundreds of thousands of intractable patients were desperate for any method which might offer hope of returning them to a useful life. Thus, when Egas Moniz introduced prefrontal leucotomy in 1935 (Moniz 1937), there was widespread enthusiasm for the procedure. Moniz eventually won the Nobel Prize for the development of this surgical technique, and frontal lobe surgery was heralded by the popular press. In 1936, Freeman and Watts performed the first lobotomy in the United States. By 1942 they had performed 200 lobotomies, with a reported 63 percent of patients showing improvement (Freeman and Watts 1942). At about this time, Freeman developed a technique for performing lobotomies using an icepick-like device called an orbitoclast. The instrument was introduced through the orbit with a mallet, and the frontal lobe was severed with a back-and-forth movement. The entire procedure took only 15–20 min, and Freeman visited hundreds of hospitals and asylums performing thousands of lobotomies. Non-surgeons and even personnel without medical training began performing the procedure, with the result that 60 000 psychosurgical procedures were performed between 1936 and 1956. Because of the indiscriminate use of psychosurgical procedures, many neurosurgeons and psychiatrists began expressing grave concerns that presaged the eventual abandonment of psychiatric surgery in all but a few centers. The introduction of

chlorpromazine in 1954 provided a medical alternative which was safer, cheaper, and more effective than the available surgical options, and marked the beginning of the end for psychosurgery (Feldman and Goodrich 2001).

The future of functional neurosurgery

Future advances in functional neurosurgery grow from two major parallel avenues of investigation: understanding of brain function and advances in therapeutic interventions. Although major progress has been made in the understanding of neurodegenerative diseases, our knowledge of the intricacies of brain functions such as movement, speech, cognition, and perception remain woefully inadequate. As basic science research reveals more precisely how these systems function normally and how they fail, targets for therapeutic interventions will become evident. Stem cell transplantation, gene therapy, and targeted delivery of medications will continue to advance in sophistication, with the eventual goal of complete restoration of normal nervous system structure and function. Marked advances in technology for brain-machine interfaces have already led to paralyzed persons controlling devices by brain signals alone, i.e. implantable chips. This technology will advance to the point not only of restoring lost brain function, but also of augmenting the function of the normally functioning brain. Ethical concerns will thus play an ever-increasing role as our power to affect the function of the nervous system continues to grow at a rapid pace.

Ethics in functional neurosurgery

The review of growth of functional neurosurgery and surgical ethics now allows for a further discussion of particular ethical challenges. The selected topics below give a brief account of challenges faced in functional neurosurgery that add further detail to some of the issues raised in general surgical ethics. Similar to all surgical ethics, informed consent and balancing of risks and benefits are central. Equal to these in importance are societal and research issues as further functional neurosurgical procedures and devices develop.

Informed consent

Informed consent is a continuous activity formally signified by a document or an initial conversation, i.e. informed consent involves a continuous agreement to go forward with a particular treatment modality. A patient or surrogate must be informed of all relevant information, voluntarily wish to proceed, and have the capacity to understand the implications of the particular decision (Scarow and Scarow 2002). The burden of consent varies depending on a number of factors that include potential benefits, risks, degree of understanding, and time sensitivity. The level of consent required in order for a patient to agree to a procedure also varies depending on whether the procedure deals with research, therapy, or some combination thereof. Most functional neurosurgeries are elective procedures for a chronic or degenerative disorder. They are elective in that they are not life saving (although selected epilepsy surgeries have the potential to decrease mortality rates from seizures). Since the problems corrected by functional neurosurgery involve the central nervous system, and the central nervous system influences the way people think, evaluating a patient's capacity to make decisions can be difficult. As discussed below, this becomes even trickier when the potential risks involve psychological impairment or cognitive loss as well as motor or sensory loss. The psychological state of a patient who has functional impairments, especially chronic pain, can make a robust informed consent process challenging.

Neurosurgeons perform some functional neurosurgical procedures while the patient remains awake. This is done for preservation of valued patient function through brain mapping or to evaluate the most effective placement of stimulators and lesions. The most common instances of awake craniotomies involve resections

near the eloquent or motor cortices for tumors or focal epilepsy and lesioning or deep-brain stimulation for movement disorders. Revoking consent during awake surgery provides an interesting vehicle to elucidate a number of ethical challenges to informed consent, since the patient may attempt to revoke consent in the midst of the surgical procedure. During most of these awake surgeries, the patient retains a significant level of decision-making capacity. If a patient requests that the surgery be discontinued, the surgeon must make a number of important decisions about whether to halt the procedure and, if so, how quickly and in what way. In reacting to this situation, the surgeon could invoke 'therapeutic privilege' in order to override the need for patient consent to continue. This is a paternalistic principle that allows a medical practitioner to ignore the patient's wishes for some obvious and greater good. Although it is seldom appropriate to invoke therapeutic privilege, in a clearly harmful situation it can be utilized. Since functional neurosurgery usually involves quality of life rather than mortality prevention, this invocation does not generally apply. However, before allowing a patient to halt such a procedure, the surgeon has an ethical obligation to inform the patient of the potential loss of benefit, be certain that the patient is reasonable in his request, and make it clear to the patient that the surgery can only be discontinued in a safe manner. In this way, the surgeon looks for an informed revocation of consent. If the surgeon believes that the surgery has not been the cause of a temporary loss of capacity and that the patient is making an informed revocation, then he must decide whether halting the procedure would egregiously harm the patient. If halting the procedure can be performed safely, there is not a significant increase in mortality risk, and halting would not constitute an unacceptable deviation from standards of practice, then the surgeon is on weak ethical grounds if he continues. It must be understood that a particular expression of a desire to stop does not force the surgeon to discontinue the procedure. Clear procedures should be in place and known by the patient regarding how this type of expression will be handled.

This instance of intraoperative revocation of consent provides an example of the challenges of ethics in the operating room as well as prior to the instance. In the midst of surgery is a poor time to attempt to make an important ethical decision because of time constraints and stress. However, the surgeon still needs to undertake a quick balancing of harms, benefits, respect for persons, and justice to the degree possible. Once this instance arises once in the operating room, it is important to review the processes in place for consent to elucidate whether better ways may be implemented to avoid this dilemma.

The question of how to handle a request to halt surgery becomes slightly more complex when part of the neurosurgery involves a research protocol. Generally consent can be more easily revoked during research procedures than during proven therapeutic endeavors. The researcher/ surgeon performing the procedure under a protocol needs to be concerned with what parts of the remaining surgery have known benefit and what parts are experimental. These elements should be clearly outlined in the informed consent process and rediscussed as the surgeon evaluates an informed revocation. As mentioned above in the section on general surgical ethics, good process and preparation can help to avoid these types of problems in both the therapeutic and research areas.

At times, functional neurosurgery involves the implantation of devices that modulate neural functioning. Those neuromodulators may have side effects that have a detrimental impact on a patient's social life without the patient having the ability to recognize the change as a problem. For instance, an induced mania may make a patient feel great, but impair his quality of life because of severely impaired decision-making. An internal device is somewhat different from psychiatric medications that can be discontinued without the consent of the patient. This poses a conflict between medical paternalism and patient autonomy in who controls the settings of the internal device. To avoid these issues, consent should be sought in advance for follow-up and postoperative care. The ethical questions about functional neurosurgical devices continue to evolve alongside the technological advances. The implementation of 'Ulysses contracts', documents that waive the right to change one's mind, may be well intentioned but are not generally enforceable. A competent patient's ability to control his body remains and cannot be waived.

Between control of programming neuromodulators and revocation of intraoperative consent, many neurosurgical programs build safeguards into patient selection criteria to exclude patients at risk of either declining to continue surgery or refusing to have stimulator settings altered. Since there are no definitive tests to predict whether a patient will change his mind or will not be able to handle a surgery, a justice question arises about unfairly excluding patients who would not be a problem balanced against including patients who would have a problem. For instance, excluding all parkinsonian patients with an anxiety disorder from neuromodulation would exclude many patients who only have a very mild anxiety directly related to their frustrations about lack of function. This blanket exclusion would probably not be appropriate since many patients with mild anxiety have had no problems undergoing awake procedures. However, too lax a restriction would cause patients with severe anxiety to undergo only partial operations. Neurosurgical ethics includes the careful and consistent selection of patients who are likely to continue to consent to the entire process of therapy.

Finally, functional neurosurgery often comprises last-chance therapy for patients. These are often experimental or off-label procedures. The desperation of a patient in intractable pain, who can no longer care for himself because of Parkinson's disease, or who cannot leave his house because of obsessive-compulsive disorder should not be underestimated. Although desperation does not necessarily cause a patient to formally fall into the 'vulnerable population', health care providers should be particularly careful that patients have full understanding of the risks and that the health care provider undertakes the procedure with good conscience.

Risk-benefit: the surgeon's responsibility beyond informed consent

Although informed consent constitutes the bedrock of current ethical practice, informed consent does not make everything permissible or required. Ethical guidelines for health care always include some articulation of a responsibility to benefit patients and to avoid harming them (beneficence/non-maleficence). In this way, neurosurgeons have obligations to use professional judgments in excluding patients from surgery even if patients or their families demand the procedure. There are limits to patients' choices, just as there are limits to surgeons' paternalism. The above discussion of therapeutic privilege begins to address this point. There are at least two very difficult types of scenarios that demonstrate these limits: suspicion of psychogenic causes and innovation.

Psychogenic causes of diseases provide particularly difficult confounding elements to functional neurosurgery for a number of reasons. First, a psychogenic cause of a functional problem may be wrongly classified as non-organic simply by means of elimination of known organic causes. Secondly, there may be an organic disease present with a psychogenic overlay. For most neurofunctional disorders, there exists no definitive way of deciphering whether a disease is primarily psychogenic or organic. Fortunately, with regard to epilepsy surgery there are clear correlations between EEG patterns and epileptic seizures (Kellinghaus *et al.* 2004; Papavasiliou *et al.* 2004). By careful evaluation, psychogenic seizures can be distinguished from actual seizures. However, diseases such as dystonia, Tourette's syndrome, or trigeminal neuralgia do not have clear physiological indications to discriminate psychogenicity. These present true ethical dilemmas where values come into conflict. The surgeon does not want to keep beneficial therapy from those who could have their suffering alleviated. Also, the surgeon does not want to unnecessarily harm patients for whom no real chance of benefit may be obtained from the surgery. These must be balanced in some way by the surgeon, given informed consent does not dissolve the problem.

The above ethical dilemma could be avoided by developing better ways of differentiating organic from psychogenic causes. Two types of patient deception need ethical mention in this respect. First, a team may consider performing the procedure, or some semblance of it, as a placebo. However, a placebo effect may be very transitory, given the risk of transference of cured symptoms to other manifestations. Given the risks of many functional neurosurgical procedures, this risk-benefit does not generally balance. Secondly, an

evaluation using deception may be considered. This may be ethically acceptable, but the patient still needs to be informed to the degree possible while still making the evaluation effective. For example, a patient could be told: 'Sometimes I will be giving you a test of pills that actually do not contain medication'. A great deal of uncertainty may still exist even with the use of the second type of deception. Neurosurgeons must balance elements of risks and benefits in light of significant uncertainty.

Our society's strong belief in 'doing' must be balanced with recognizing the limits of our abilities. This belief invokes the metaphor of galloping in on a white horse with a last-ditch effort to apply an innovative procedure. Relating back to the history of functional neurosurgery, we should question the risk-benefit ratio of Meyer's resections of the head of the caudate nucleus to reduce tremor. His mortality rate of 15 percent appears unjustifiable in comparison with the potential benefits (see above). Likewise, Cooper's anterior choroidal artery ligation with a mortality rate of 10 percent appears to have unbalanced risks. Just because a patient's tremor has been refractory to all known effective treatments does not mean that we should try procedures that have not been shown to be effective or that have significant mortality risks. This is particularly true when the functional neurosurgery is primarily a cosmetic neurosurgery for social purposes. These are considerations of risk-benefit as well as appropriate processes for innovating.

A surgeon may ethically turn down a patient for surgery based on conscience or professional judgment that risks are unbalanced. When a surgeon comes to this conclusion he must then decide whether or not to help the patient to find a surgeon who will perform the surgery. An example would be a pain patient asking for his arm to be amputated when the surgeon is convinced that amputation would not help, would be outside standard surgical practice, and would be harmful to the patient. The ethical values to be balanced in these cases revolve around patient abandonment, professional obligation to facilitate patient transfer, and not being party to unnecessary patient harm.

Societal consideration: economics and enhancement

Functional neurosurgeries, especially those involving complex devices, can be very expensive. All health care systems have limits to resources with implicit or explicit rationing built into the systems. As a matter of social justice, explicit conversations need to take place concerning which patients should have priority. Much of this depends on selecting a view of justice/fairness. For some, the sickest patients impose greater obligations on us to relieve their suffering than those who are less sick. Others would take the stance that the less sick can be maintained as active workers and members of society and thus will benefit everyone by keeping them more functional. Yet others would consider justice as being served by random selection from all of those who could garner some benefit from the intervention. One example of explicit rationing is the Australian governmental advisory committee report that recommends supplying deep-brain stimulators only for the sickest Parkinson's patients. This is recommended because the system could not afford to have everyone receive the treatment modality (Medical Services Advisory Committee 2001). Explicit recognition and discussion of the underlying views of justice conform to good ethical standards. Societal costs of futile neurosurgical interventions need to be balanced against our respect for patient preferences and goals (Toms 1993).

p 224 A particularly interesting subquestion of rationing involves whether a patient with a terminal condition should receive expensive functional neurosurgery if it will provide palliation for only a matter of months. Many deem this to be cost ineffective and thus an unethical use of resources. Yet, many surgeries could conceivably enhance a person's life for that short period through improvement in cognition or physical mobility. Any guiding ethical principle keeping terminal patients from these surgeries needs to be consistent with criteria for non-terminal patients, which would include the length of potential benefit. This is not only an economic concern, but also a concern for the amount of operative harm/suffering persons should be exposed to when they have a limited life expectancy. This question resides at the intersection of societal interests, individual autonomy, and professional judgments of risk and benefit.

The newest and most innovative treatment may not be the most effective or have the most responsible cost-benefit ratio. This can be seen in the aggressive use of spinal instrumentation (plates, screws, and pins) as well as robotic or stereotactic surgery. Often device companies aggressively market products to surgeons and patients (Trojanowski 1999). Patients will often believe that the newest and highest technology solution is the most effective solution. The efficacy of the surgery depends a great deal on the comfort and training of a surgeon, i.e. the tool is only as good as the workman. Although industry provides an important component for improvement in neurosurgical intervention, there are ethical challenges to the degree of influence that companies have on patient and surgeon decision-making.

Enhancing function by means of neurosurgery provides the final social issue of this section. Surgery's goal is to improve patients' lives. In general, functional surgery aims at alleviating suffering and restoring function to a 'normal' state. However, some of the procedures now, or in the future, could be adapted to enhance one's abilities beyond the normal. Like genetic enhancement, concerns involve social injustice, devaluation of traits within boundaries historically considered to be normal, uncertainty about long-term consequences, and use of resources for unnecessary or vain purposes (Parens 1998). These questions of enhancement and justice figure prominently in the development of future neurosurgical innovations.

Research and innovation

Improvements in functional neurosurgery have depended on experimentation, innovation, and often leaps of faith. As with all research, current functional neurosurgery research is expected to comply with principles articulated in the *Declaration of Helsinki* (World Medical Association 2002) and the *Belmont Report* (United States National Commission 1979). In reviewing the history of functional neurosurgery, it becomes apparent that these principles have not always strongly held sway in practice. The processes that brought about many of the improvements and breakthroughs in neurosurgery would no longer be considered ethically justified. Current regulations are much more stringent on the ways in which innovation can take place. There is an expectation that a surgeon will not explore brain areas unrelated to the immediate purpose of the operation during procedures, and that there will be a clear pre-operative explanation of the planned surgery, i.e. informed consent, and good evidence for a positive risk-benefit ratio.

p 225 Ethical issues in research on functional neurosurgery differ greatly from many other types of human systems since the brain remains imperfectly understood, there is significant variation in the mapping of functional locations between individuals brains, and the brain is central to a person's identity and cognition. Although functional imaging, such as functional MRI, continues to help surgeons map individual patient's brains better, a great deal remains unknown ↪ (see Chapter 11). Because of the complexity of human brains, animal models can be of only limited help. This complexity has kept us from having a robust and accurate theoretical foundation on which to build research. Functional neurosurgical research often occurs through happenstance or clinical observation of what works. Historically, this is exemplified by Cooper's accidental severing of an artery and Benabid's application of continuous electrical stimulation. Finally, because of the high cost of research and the difficulty in standardizing surgical procedures across institutions, the research agenda of functional neurosurgery is plagued with small numbers of enrolled patients which poses challenges to the generalizability of research results. Many surgical devices are approved after relatively small trials and thus fairly weak evidence (Bhandari *et al.* 2004). All these elements make these research endeavors fraught with ethical challenges of providing good generalizable data in an efficient and beneficial way that minimizes harm.

An editorial exchange between Cosgrove and Aouizerate and colleagues provides an example of the types of challenges to expanding functional neurosurgical practice by means of research. In discussing a case report on the effectiveness of deep-brain stimulation for medically refractory obsessive-compulsive disorder with severe depression, Cosgrove (2004) warns of the challenges in appropriately performing further research while urging researchers to grasp this opportunity to learn more: 'These early efforts must go forward only with the

highest ethical, moral, and scientific standards to ensure that this historic opportunity is not wasted'. Aouizerate *et al.* (2004) respond with a list of ethically necessary conditions to perform the research. Two conditions of particular interest are 'DBS [deep-brain stimulation] procedures being performed by extensively experienced neurosurgical teams' and 'collaboration of multi-disciplinary investigative teams'. Part of the backdrop of these cautionary comments includes the worry that a technique will be adopted before being fully and rigorously explored. Historical examples of technologies being adopted too hastily include Moniz's leucotomy and Horsley's motor cortex excisions (discussed above). Cosgrove shows an intense curiosity and belief that the potential to explore new therapies should not be lost, while still tempering this with good processes that protect patients. This example is textured even further given the challenges of past psychosurgery. Moving forward in neurosurgical research needs to be cognizant of the accusations of past attempts at social control as well as overzealous application (Pressman 1998; Fins 2003).

Research methods in functional neurosurgery themselves create significant challenges. Double-blind placebo-controlled trials, derived from pharmaceutical research, have become the gold standard for research in general. Recent studies, such as the transplantation of fetal cells for Parkinson's disease, have further supported the usefulness of placebos in neurosurgical research. The use of placebos allows for a very robust type of knowledge. However, there are lesser types of knowledge that can be usefully gained without placebos that minimize harm to human subjects. A great deal of debate surrounding placebo procedures in neurosurgical research continues (Bernat 2002). More appropriate for most types of surgery is either the use of historical controls or the implementation of a cross-over designs where a device is turned on or off.

Even before ethical research methods come into play, a research question must be selected. There are ethical challenges regarding which questions are worth pursuing and what priority is given to the various worthy research questions. Restoring function to something like a normal state is a type of enhancement for an individual. If a person can have their function enhanced to a normal state, is it appropriate to research ways of enhancing function to a greater than normal state. The ethical question comes in how many resources should be applied to ↵ technologies that will make average people's lives better instead of focusing on improving the lives of those who endure horrible suffering or lack average functions. Again, this question involves a stance on what justice means in this context.

An equivalent issue to the funding of enhancement research lies in the problems of orphan diseases. Functional neurological diseases that are rare may not be lucrative for industry to explore. Hence these diseases may be ignored even if patients suffer horribly. It is important that research agendas maximize the general good, be economically viable, and address those who suffer most. Treatment for orphan neurological diseases should not be ignored in favor of more lucrative diseases. The open ethical question is: Who funds these very expensive neuro-surgical trials?

Finally, there is the question of convenience and exploration outside a protocol during a surgery, i.e. exploring brain areas unrelated to the immediate purpose of the operation. These explorations need to conform to best current standards of practice and should be avoided unless they are either under protocol or for the individual patient's best interest. This means respecting the need for review boards to vet research, while recognizing that review boards depend on individual researchers/innovators to consider carefully the burden of risk of each change and evaluation of standard practice.

Conclusion

Functional neurosurgeons must be cognizant of a multitude of ethical concerns in standard practice, innovation, and research. The privileged status of the brain, the uncertainty involved in outcomes, and the complexity of cases add significant textures to the ethical concerns of functional neurosurgery. The ethical issues cannot be reduced to or solved by impeccable informed consent or some formulaic ethics process. Good standards of practice need to be developed, and surgical teams need to be attentive in identifying special ethics problems. The further development of functional neurosurgery needs to be undertaken with a clear understanding of the costs and ethical implications.

References

Aouzerate B, Cuny E, Guehl D, Burbaud P (2004). Response to: Deep brain stimulation and psychosurgery. *Journal of Neurosurgery* **101**, 575–6.

[WorldCat](#)

Benabid AL, Pollak P, Louveau A, Henry S, de Rougemont J (1987). Combined (thalamotomy and stimulation) stereotactic surgery of the VIM thalamic nucleus for bilateral Parkinson disease. *Applied Neurophysiology* **50**, 344–6.

[WorldCat](#)

Bendok B, Levy RM (1998). Brain stimulation for persistent pain management. In Gildenberg PL, Tasker RR (eds) *Textbook of Stereotactic and Functional Neurosurgery*. New York: McGraw-Hill, 1539–46.

[Google Scholar](#) [Google Preview](#) [WorldCat](#) [COPAC](#)

Bernat J (2002). *Ethical Issues in Neurology* (2nd edn). Boston, MA: Butterworth-Heinemann, 469–94.

[Google Scholar](#) [Google Preview](#) [WorldCat](#) [COPAC](#)

Bhandari M, Busse JW, Jackowski D, et al. (2004). Association between industry funding and statistically significant productivity findings in medical and surgical randomized trials. *Canadian Medical Association Journal* **170**, 477–80.

[WorldCat](#)

Birkmeyer JD, Siewers AE, Finlayson EV, et al. (2002). Hospital volume and surgical mortality in the United States. *New England Journal of Medicine* **346**, 1128–37. [10.1056/NEJMsa012337](#)

[WorldCat](#) [Crossref](#)

Burckhardt G (1891). Über Rindenexcisionen, als Beitrag zur operativen Therapie der Psychosen. *Allgemeine Zeitschrift für Psychiatrie psychischgerichtliche Medizin* **47**, 463–548.

[WorldCat](#)

Cooper IS (1954). Surgical occlusion of the anterior choroidal artery in parkinsonism. *Surgical Gynecology and Obstetrics* **99**, 207–19.

[WorldCat](#)

Cosgrove GR (2004). Deep brain stimulation and psychosurgery. *Journal of Neurosurgery* **101**, 574–5. [10.3171/jns.2004.101.4.0574](#)

[WorldCat](#) [Crossref](#)

p 227 Feldman RP, Goodrich JT (2001). Psychosurgery: a historical overview. *Neurosurgery* **48**, 647–59. [10.1097/00006123.200103000.00041](#)

[WorldCat](#) [Crossref](#)

Finn JJ (2003). From psychosurgery to neuromodulation and palliation: history lessons for the ethical conduct and regulation of neuropsychiatric research. *Neurosurgery Clinics of North America* **14**, 303–19. [10.1016/S1042-3680\(02\)00118-3](#)

[WorldCat](#) [Crossref](#)

Freeman W, Watts J (1942). *Psychosurgery: Intelligence, Emotion and Social Behavior Following Prefrontal Lobotomy for Mental Disorders*. Springfield, IL: Charles C. Thomas. [10.1037/11151000](#)

[Google Scholar](#) [Google Preview](#) [WorldCat](#) [COPAC](#) [Crossref](#)

Fritsch G, Hitzig E (1870). Über die elektrische Erregbarkeit des Grosshirns. *Archives of Anatomical Physiology* **37**, 300–32.

[WorldCat](#)

Gallet G (2000). How should we test and improve neurosurgical care? In: Zeman A, Emanuel L (eds) *Ethical Dilemmas in Neurology*. London: Harcourt Brace, 87–100.

[Google Scholar](#) [Google Preview](#) [WorldCat](#) [COPAC](#)

Hanlon CR (2004). Surgical ethics. *American Journal Surgery* **187**, 1–2. [10.1016/j.amjsurg.2003.09.007](#)
[WorldCat](#) [Crossref](#)

Harlow JM (1848). Recovery from the passage of an iron bar through the head. *Boston Medical and Surgical Journal* **39**, 389–92. [10.1056/NEJM184812130392001](#)
[WorldCat](#) [Crossref](#)

Heath RG (1954). *Studies in Schizophrenia*. Cambridge, MA: Harvard University Press.
[Google Scholar](#) [Google Preview](#) [WorldCat](#) [COPAC](#)

Heath RG, Mickle WA (1960). Evaluation of 7 years' experience with depth electrode studies in human patients. In: Ramey ER, O'Doherty DS (eds) *Electrical Studies in Anesthetized Brain*. New York: Harper and Row, 214–17.
[Google Scholar](#) [Google Preview](#) [WorldCat](#) [COPAC](#)

Horsley V (1909). The function of the so-called motor area of the brain. *British Medical Journal* **2**, 1286–92. [10.1136/bmj.2.2444.1286](#)
[WorldCat](#) [Crossref](#)

Horsley V, Clarke RH (1908). The structure and functions of the cerebellum examined by a new method. *Brain* **31**, 45–124. [10.1093/brain/31.1.45](#)
[WorldCat](#) [Crossref](#)

Iskandar BJ, Nashold BS Jr (1995). History of functional neurosurgery. *Neurosurgery Clinics of North America* **6**, 1–25.
[WorldCat](#)

Kellnerhaus C, Loddenkemper T, Danner DS, Lachhwan D, Luders HO (2004). Non-epileptic seizures of the elderly. *Journal of Neurology* **251**, 704–9. [10.1007/s00415-004-0406-3](#)
[WorldCat](#) [Crossref](#)

Krack P, Batra A, Blercom NV, et al. (2003). Five-year follow-up of bilateral subthalamic nucleus in advanced Parkinson's disease. *New England Journal of Medicine* **349**, 1925–34. [10.1056/NEJMoa035275](#)
[WorldCat](#) [Crossref](#)

Laitinen LV, Bergenheim AT, Hariz MI (1992). Leksell's posterovenral pallidotomy in the treatment of Parkinson's disease. *Journal of Neurosurgery* **76**, 53–61. [10.3171/jns.1992.76.1.0053](#)
[WorldCat](#) [Crossref](#)

McCullough LB, Jones JW, Brody BA (1998). Principles and practice of surgical ethics. In: McCullough LB, Jones JW, Brody BA (eds) *Surgical Ethics*. New York: Oxford University Press, 3–14.
[Google Scholar](#) [Google Preview](#) [WorldCat](#) [COPAC](#)

Mazars G, Roge R, Mazars Y (1960). Stimulation of the subthalamic fasciculus and the bearing on the pathophysiology of parkinsonism. *Revue du Praticien* **103**, 136–8.
[WorldCat](#)

Melzack R, Wall PD (1965). Pain mechanisms: a new theory. *Science* **150**, 108–9. [10.1126/science.150.3699.971](#)
[WorldCat](#) [Crossref](#)

Medical Services Advisory Committee (2001). *Deep Brain Stimulation for the Symptoms of Parkinson's Disease*. Canberra, Australia: MSAC.
[Google Scholar](#) [Google Preview](#) [WorldCat](#) [COPAC](#)

Meyers R (1958). Historical background and personal experiences in the surgical relief of hyperkinesia and hypertonus. In Felds

WS (ed) *Pathogenesis and Treatment of Parkinsonism*. Springfield, IL: Charles C Thomas, 229–70.

[Google Scholar](#) [Google Preview](#) [WorldCat](#) [COPAC](#)

Moniz E (1937). Prefrontal leucotomy in the treatment of mental disorders. *American Journal of Psychiatry* **93**, 1379–87.

[WorldCat](#)

Morreim HE (2004). High profile research and the media: the case of the AbioCor artificial heart. *Hastings Center Report* **34**, 11–24. [10.2307/3528247](#)

[WorldCat](#) [Crossref](#)

Nell Dwyer G, Dorthey L, Garfield J (2001). The realities of postoperative disability and the carer's burden. *Annals of the Royal College of Surgeons of England* **83**, 2145–8.

[WorldCat](#)

Papavasiliou A, Vassilakis N, Paraskevoulakos E, Kotsalis C, Bazgou H, Bardanis I (2004). Psychogenic status epilepticus in children. *Epilepsy and Behavior* **5**, 539–46. [10.1016/j.yebeh.2004.04.011](#)

[WorldCat](#) [Crossref](#)

Parens E (1998). Is better always good? The Enhancement Project. In: Parens E (ed) *Enhancing Human Traits: Ethical and Social Implications*. Washington, DC: Georgetown University Press, 1–28.

[Google Scholar](#) [Google Preview](#) [WorldCat](#) [COPAC](#)

p 228 Polk HC (2004). Is ATLS a mechanism for teaching core competency in ethics? *American Journal of Surgery* **187**,

6. [10.1016/j.amjsurg.2003.04.003](#)

[WorldCat](#) [Crossref](#)

Pressman JD (1998). Epilogue: the new syntheses. *Last Resort: Psychosurgery and the Limits of Medicine*. New York: Cambridge University Press, 401–42.

[Google Scholar](#) [Google Preview](#) [WorldCat](#) [COPAC](#)

Scarrow AM, Scarrow MR (2002). Informed consent for the neurosurgeon. *Surgical Neurology* **57**, 63–8. [10.1016/S0090-3019\(01\)00567-5](#)

[WorldCat](#) [Crossref](#)

Seaburn DB, McDanel SH, Kim S, Bassen D (2004). The role of the family in resolving bioethical dilemmas: clinical insights from a family systems perspective. *Journal of Clinical Ethics* **15**, 263–75.

[WorldCat](#)

Spiegel EA, Wyss HT, Marks M, Lee AJ (1947). Stereotactic apparatus for operations on the human brain. *Science* **106**, 349–50. [10.1126/science.106.2754.349](#)

[WorldCat](#) [Crossref](#)

Toms SA (1993). Outcome predictors in the early withdrawal of life support: issues of justice and allocation for the severely brain injured. *Journal of Clinical Ethics* **4**, 206–11.

[WorldCat](#)

Trojanowski T (1999). New technologies and methods in neurosurgery: ethical dilemmas. *Acta Neurochirurgica*, **74**, 83–87.

[WorldCat](#)

United States National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (1976). *Psychosurgery*. Washington, DC: US Government Printing Office.

[Google Scholar](#) [Google Preview](#) [WorldCat](#) [COPAC](#)

United States National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (1979).

Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects Research. Washington, DC: US Government

Printing Office.

[Google Scholar](#) [Google Preview](#) [WorldCat](#) [COPAC](#)

White JC, Sweet WH (1955). *Pain: Its Mechanisms and Surgical Control*. Springfield, IL: Charles C Thomas.

[Google Scholar](#) [Google Preview](#) [WorldCat](#) [COPAC](#)

World Medical Association (2002). *Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects*. World Medical Association General Assembly, Washington 2002. New York: World Medical Association.

[Google Scholar](#) [Google Preview](#) [WorldCat](#) [COPAC](#)