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Ethical and Legal Issues in Deep Brain Stimulation: An Overview

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ABSTRACT

As a treatment approved and certified for certain neurological diseases, Deep Brain Stimulation (DBS) sometimes produces spectacular results quickly. It is also a powerful research tool in neurology and psychiatry. It combines a highly technical surgical procedure with a complex active medical device that acts on the brain, the substratum of human thought and identity. It raises several ethical and legal questions. Some are not specific, and can be solved by applying the principles of medical ethics and law. Others appear to be more DBS-specific. Some arise from the intrication of research and treatment in its development, and from the need to tune the device. Some are related to its effectiveness and its occasional harmful side effects (including potential applications beyond the field of health care).

INTRODUCTION

High frequency Deep brain stimulation (DBS) delivers electrical impulses to specific areas of the brain (mainly the basal ganglia) by means of implanted electrodes that are connected to a battery-operated neurostimulator unit. The unit is implanted in the infraclavicular cavity via wires that go under the scalp and down under the skin of the neck [1]. In 2015, it was estimated that worldwide, over 100,000 patients had been treated with this technique. DBS is such an important treatment breakthrough that it continues to earn prestigious prizes and awards (like the European Inventor Award in 2016 and the Lasker Award, in 2014, with M. De Long) for its principal French inventor, Alim-Louis Bénabid. DBS is remarkably effective in relieving the motor symptoms of certain neurological diseases, especially Parkinson's Disease (PD) and essential tremor. It has also been shown to have a beneficial effect on epilepsy and certain psychiatric disorders, such as obsessive-compulsive disorders (OCDs). DBS also shows promising characteristics in the field of cognitive or memory capacities. Paediatric neuromodulation also represents a highly promising area of development of DBS for neurological and psychiatric illness in children, especially for dystonia. Therefore, at the same time, DBS is an accepted and approved treatment method for certain diseases, occasionally achieving quick and quantifiable results and a productive research tool for many others. Moreover, it has the great advantage of being a modulable and "reversible" solution. The area or areas of the brain that are implanted, the electrode poles that are activated, and the intensity of the stimulation can all be adjusted to the needs of each patient. Although brain surgery risks are real and despite the fact that implantation and stimulation may cause an adaptation in the brain over the long term, the stimulation can be stopped and the devices can be removed. From this standpoint, DBS is much safer and more reassuring than lesional or

ablative surgery, which causes definitive damage to tissue, but which is nevertheless a competing treatment option, in some cases [2]. However, like any surgical procedure, especially when it involves the brain, an eminently complex organ and the substratum of human thought and identity, DBS raises ethical and legal questions. Some of these questions are well known and call for the application of the principles of medical law and ethics. Others are more specific, resulting from the particular characteristics of DBS as an innovative and long term treatment. This paper proposes an overview of these issues from the standpoint of a French legal scholar. It will first address the issues raised by the development of DBS, which is generating new practices as an innovative and potentially beneficial treatment for certain patients and for certain pathologies (1). It will then discuss the issues related to (positive and negative) effects of DBS (including uses that go beyond the field of health care) (2).

DEVELOPMENT OF THE TECHNIQUE

DBS has earned regulatory approval or certification for the treatment of PD and essential tremor in the United States, Europe, Canada, Australia and Japan. In Europe, where medical devices are subject to a certification system, DBS is also a certified treatment for OCDs and epilepsy, whereas in the United States, it was granted a humanitarian device exemption (making it possible to use the device in the absence of FDA approval) for OCDs and dystonia. Thus, a first insight leads to the idea to differentiate between situations where DBS is a routine treatment with regulatory approval (PD, essential tremor); those where it is an innovative therapy still in the process of obtaining confirmation (OCD, dystonia, epilepsy); and those where it is still an experimental treatment (resistant depression, cocaine addiction, cases of obesity or severe anorexia that have not responded to other treatment options, bipolar disorders, Alzheimer's, etc.). In this perspective, it would be appropriate to present, on the one hand, the ethical and legal principles applying to care (patient' autonomy; informed consent; physician beneficence and non-malfeasance principle; medical deontology and liability; fairness in access to care) and, on the other hand, ethical and legal solutions suitable for clinical trials (principles governing research: scientific soundness of the experimental hypothesis and protocol, reproducibility of the results; preliminary experimental results in silico and/or in vivo to protect human participants; specific consent; procedural protection including opinion from a committee for the protection of participants and regulatory approvals). However, some specificities of DBS may disturb this presentation.

Intrication of research and treatment

For DBS in children, most of the applications are still on a research phase. As stated by Davidson & al., "given biological differences between adults and children, the procedure in paediatric populations can be considered a surgical innovation and is still investigational for all indications" [3].For adults, although it is possible to make a distinction between the uses of DBS as routine treatment and other, more experimental uses, the technique has features that make it a "mosaic tool" [4], potentially effective for treatment, but also "ideal for experimental goals" [5,6]. It offers access to human brain function with more limited irreversible effects than lesional or ablative surgery. The technique assumes and allows choices for implantation and adjustment and each test, try or tune is likely to give rise to a discovery. During the surgery, the patient is frequently awake in order to check the immediate effect of the actions carried out by the surgeon. In the aftermath of the surgery, later adjustments may also give rise to tests and discoveries. Consequently, more than in other medical fields, the categories of treatment and research appear to overlap easily [7]. Currently, it is especially in the field of psychiatry that this "intrication of treatment with research procedures" [8] is perceived, but in fact, it occurred continually while the technique was being developed. One particular sign that this is true is the importance of "case reports" in the literature on the topic [9]. For example, incidental discoveries gave rise to the idea that DBS could potentially be a treatment for OCDs, addiction, or memory disorders [5,10-12]. Case reports played such a decisive role in the matter that voices were raised to demand more centralized, systematic publication of these results obtained with individuals or very small cohorts [13].Even for PD, the technique continues to be the subject of research. Indeed, much still remains to be learned about the causal mechanisms of DBS [14,15].This intrication of research and treatment raises two types of questions: the first are related to the patient's status and to his or her perception of the difference between research and treatment; the second

concern the conditions under which the experiments are carried out, in terms of the epistemological and ethical requirements of research.

Firstly, regarding patient status, European and French law differentiate between, on the one hand, treatment applied for the purpose of caring or providing relief for a patient, as an individual, and, on the other hand, research projects carried out chiefly for the purpose of increasing our knowledge of the body and its functions and dysfunctions, for the common good [16,17]. Separate legal regimes have been designed in France (the Huriet-Serusclat Law in 1988, and the later Jardé Law in 2012). They enjoin that persons likely to consent to a treatment or to participate in a clinical trial be clearly and distinctly informed. Yet studies of trial participants' perceptions and motivations have demonstrated that confusion persists between treatment and research, particularly in relation to research on the treatment of psychiatric disorders [18,19]. Even when the participants have signed an agreement specifying that they are knowingly submitting to the limitations of a clinical trial, studies show that they opt in because they expect an improvement of their symptoms [20,21]. Difficulties also arise for the patient from a non-optimal adjustment between the trial period and its aftermath [22,23]. Sometimes, removal of the implant is the only course of action offered. Should the patient refuse, he may lose the entitlement to follow-up supposedly guaranteed by the study sponsor.

Secondly, the prominence of treatment in the research context also creates difficulty concerning the postulates of Evidence-Based Medicine (EBM), designed to be the practical consequences of the epistemological principles characterizing "good science." EBM demands that researchers set up double-blind trials in which the results of an innovative treatment are compared with those obtained with a control group. When this is applied to a clinical trial for DBS, it means that "sham surgery" or "sham stimulation" is performed on half of the participants: either the surgery is simulated or the device is implanted but not activated. As a result, an ethical controversy opposes researchers who consider that, no matter what, "sham stimulation" is necessary in order to assess the extent of the placebo effect [24] and those who consider "sham stimulation" ethically unacceptable [25,26].One method suggested to overcome the difficulty consists of creating two groups within the cohort, who will be stimulated on an alternating basis in two successive phases. The advantage of this solution is that it does not leave patients entirely untreated. However, it does not really meet the double-blind requirements of EBM. Another difficulty arises from the small size of the cohorts assembled by the researchers, prompting doubts about the statistical reliability of the results. That problem is usually solved by organizing multi-facility trials, in order to assemble larger cohorts. The disadvantage in a multi-facility trial, however, is that the patient-participants are not really in identical environments for the follow-up and supervision. DBS is a complex treatment, both at the time of the implant and in the ensuing follow-up. The surgical procedure and the knowhow of the healthcare team, as well as various human and material resources in the facilities, may indeed lead to distortions in the results. The US Food and Drug Administration (FDA) and the European authorities in charge of medical devices have drawn up more flexible objective evaluation criteria, in reference to the healthcare teams' expertise and knowhow [27], but the epistemological difficulty remains. The example of studies of DBS on treatment-resistant depression is informative. It yielded disparate results: fairly positive for a small cohort of patients supervised by their psychiatrist [28], fairly negative for two larger cohorts and multi-center trials that led to the abandonment of the trials [22]. The disparity was interpreted in several different ways: either as the result of a non-reproducible personal effect (linked to the psychiatrist), as an acknowledgement of the insufficient knowledge about the electrical stimulation parameters to be used [29], or as a sign that it may become necessary to abandon the EBM "gold standard" and substitute a new, "adaptive" clinical-trial model [30]. This "alternative model" would make it possible to proceed by screening the initial cohort for patients who respond positively to the treatment, in order to shed light on the reasons for this effectiveness and to determine device targets and tunings more precisely before beginning a new trial of the experimental treatment on the rest of the cohort. Nevertheless, this suggestion is sometimes criticized as an attempt to justify resorting to DBS to treat disorders for which it is not effective, particularly for an overly complex psychiatric disorder.

Benefit/risk balance and defining the pathologies concerned

The use of DBS to treat neurological disease elicits far fewer ethical debates than applying it to treat psychiatric illness. Indeed, the idea that the symptoms of a movement disorder could be relieved by electrical stimulation of an organic substratum does not contradict the general understanding of neurological and neurodegenerative pathologies. With pathologies categorized as belonging to the field of psychiatry, though, the situation is quite the opposite. There is controversy as to the causes of mental illness and as to the relevance of organic intervention. True, the discovery of antipsychotic drugs (and other psychopharmacological substances) was a turning point in psychiatric practice. Nevertheless, intense debate persists. For mental illnesses that do not respond to pharmacological treatment, DBS is presented as a resource likely to provide some improvement. Most arguments in favor of using DBS in psychiatry are essentially founded on "last-chance" reasoning [12,31], despite the fact that certain findings emerged incidentally, when patients were implanted for a neurological disorder, like in OCDs. The risk involved in the surgical procedure, which should lead to the application of the principle of non-malfeasance (the physician's obligation to do no harm to the patient), is offset by the absence of any other medical alternative judged to be effective, reliable, and salutary, whereas the persistent suffering of the patient and the will he or she expresses to seek a treatment to relieve the suffering justify the application of the principles of beneficence and autonomy. Nevertheless, in this case, the ethical evaluation is not unequivocal. The "last-resort" argument must be used conservatively, to avoid presenting DBS as a "wild card" treatment, to be played when all else fails. Also, it would be ethically reprehensible to take advantage of patients who are desperate and "ready to try anything." It is extremely hard to evaluate the veracity of informed consent when patients have been suffering from disabling symptoms for years or decades, have already tried a series of other treatment options, and have no reason to hope their situation will improve. Informed consent is even harder to assess in the field of psychiatry, when a patient's cognitive abilities may be altered by mental illness [19,32]. For children and adolescents suffering from psychiatric disorders, the ethical issue is even more critical as parental expectations and perceptions may diverge from the patient's preferences [33,34].

The deceptive results of the above mentioned two large-scale, randomized, sham-controlled trial of DBS for treatment-resistant depression, conducted in the USA, which found that DBS do not reduce depression symptoms better than sham stimulation, reactivated the debate on the relevance of the neurophysiological approach for psychiatric disorders [35]. However, they have also generated new research on electrical stimulation parameters, while promising results for other disorders, such as OCDs, motivate ongoing research on DBS in psychiatry [36].

Benefit/risk balance and defining the patients concerned

DBS is a complex course of treatment, necessitating specialized medical skills and equipment available only at a few highly advanced medical centers. This generates disparities in access to treatment, implying inequalities between patients and significant economic, family, and social challenges for patients who wish to live closer to those medical centers. As a result, a de facto primary patient selection occurs according to criteria with no direct relationship to the disease: depending on the patient's geographical location or his or her motivation and resources for living close to treatment centers. If a patient presents an illness for which DBS is a more routine and widespread treatment – for example, PD and neurological disorders, another concern arises, in terms of disparities in the quality of the treatment provided [37,38].

Medical selection criteria also apply, in relation to the patient's assumed aptness to withstand the brain surgery and benefit from DBS. Patients' age and mental capacity are official or officious criteria. While the application of DBS in adults continues to expand, paediatric indications for DBS are still very limited [39,40], despite some interesting results to treat dystonia in children [41,42]. Several explanations may be found. First, children are more (physically and mentally) vulnerable. Second, a robust risk assessment cannot be obtained solely by extrapolating from data collected on adults. For instance, surgical and infectious risks are different [3,43]. One other important explanation may be found in the fact, stated by Cif & Coubes, that "validated selection criteria for DBS procedures such as response to medication in Parkinson's disease and quantified severity criteria are lacking

in pediatric dystonia" [42]. For adults, in addition to patient response to pharmacological molecules (an L-Dopa test), patients are screened on the basis of age (which must not be too advanced), the absence of severe cognitive disorders (dementia), and, overall, a "pure" disease profile. In the case of PD, this means that patients with severe psychiatric disorders are supposed to be eliminated. As a result, it is estimated that only 5 to 10% of PD patients can benefit from DBS treatment. Such a screening for "pure" disease profiles raises questions. A variety of incidental discoveries (regarding OCD treatment, for example) occurred thanks to a flexible interpretation of guidelines for the selection of patients for neuromodulation. These discoveries are evidence that screening out a patient because he or she presents a psychiatric disorder in conjunction with neurological disease is not necessarily a sound principle, because the patient might ultimately have benefited from DBS treatment for both disorders. Once again, the most convincing ethical approach seems to be to allow the healthcare team to evaluate candidates for the procedure on a circumstantial, case-by-case basis. Until recently, DBS was designed solely as a "last-chance" or "late-stage treatment", when less burdensome treatments had failed or stopped being effective. Even in the treatment of PD, for which DBS has been demonstrated to be effective for over twenty years, implantation is still a backup or second-tier treatment, used when drug therapy no longer produces enough positive effects, or when it causes more harmful than beneficial effects. Yet the effectiveness of DBS has led doctors to consider the advantage of performing the procedure earlier, before the patient reaches such an advanced state of the disease that he or she has to stop working or engaging in social activities. Despite the positive results, these studies have elicited varied reactions [44,45]. In this regard, it is necessary to differentiate between studies which proceeded very cautiously, loosening the criteria of the progression of the disease without anticipating a decline in efficacy of the medication [46,47], and other studies, opting for the implant procedure at an earlier stage of the disease, anticipating the appearance of motor fluctuations that medication could not control [48,49]. This last is ethically debatable: why should patients who can still benefit from drug treatment, which is easier to withstand and less limiting socially, be exposed to the risk of neurosurgery [50]? Research currently underway in France on infrared stimulation for preventive purposes (notably, studies carried out at Clinatec under AL Benabid supervision) are an offshoot of the will to intervene as early as possible. In this case, the point is no longer to treat, even at a very early stage. Instead, researchers hope to prevent the degeneration of brain cells by treating individuals who are still asymptomatic, but in whom latent PD has been detected by brain imagery (PET scan). As Benabid himself notes, "Is it appropriate to perform surgery on persons who, in another event, might have lived very well and for a long time with drug therapy? Should people who are not yet really ill undergo surgery to prevent them from becoming ill? Furthermore, it is easy to see when L-Dopa is working or not: there is a clear and evident difference between a patient who is slowed or blocked by the disease and a patient who can move around normally. […] But when you have a patient whose handwriting is beginning to deteriorate or […] who begins to be weary, which is highly subjective and difficult to quantify, it is not easy to determine whether these symptoms, which are barely present, have improved" [51].There is clearly a strong concern regarding ethical implications of intervening in the brain prior to any symptomatic expression of the disease.

A renewal of disciplinary approaches and the promotion of interdisciplinarity

DBS is sometimes perceived as the symbol of the renewed interest in physical action (electrical) over chemical action (pharmacological), after a period of relative disregard for neurosurgery (or even doubt in the relevance of the scientific approach). The field, associated with psychosurgery, suffered from a bad reputation for treatments that were considered archaic and sometimes an affront to human dignity. In the late 1980s, when Alim-Louis Benabid published his findings on PD [52], he effectively revived an approach that seemed to be obsolete, but this moment was just a step in the zigzagging course of knowledge and inquiry in neuroscience [53]. Physical action has not replaced chemical treatment, because DBS is used as a backup treatment when medication is no longer enough. A short term analysis might indicate that DBS was invented for the treatment of neurological disease and later introduced to the field of psychiatry (for the treatment of OCD, resistant depression, etc.), but a longer-term view of it as part of a range of electrotherapy techniques makes it clear that

medical and technological innovation occurred equally in both psychiatry and neurology [27,54]. DBS is not the Trojan horse of neurology, conquering the land of psychiatry. In fact, it could be said to be rebuilding bridges, as a treatment resource. The bridges between the two fields go beyond simply sharing the same tool. Even though the causal mechanism of DBS is still not entirely clear, even for neurological diseases, its efficacy is based on a physical, organic action that challenges certain paradigms in psychiatry [55,56]. Inversely, in neurology, physical treatment of movement disorders may be accompanied by behavioral disorders, and lead to the observation that psychological dissatisfactions exist [57]. Hence, far from being reducible to a "neurologization" of psychiatry, the development of DBS produces an osmosis between practices and knowledge, setting various investigations and inquiries in motion, creating a need for a multi-disciplinary approach. This may generate disturbances when disciplinary strategies are opposed to each other. Nevertheless, in medical practices, multi-disciplinary teams have been set up, implementing interdisciplinary procedures in order to meet patient needs. Healthcare teams bring together neurologists, neurosurgeons, and psychiatrists, as well as psychologists, undeniably improving the quality of care [58]. For pediatric neuromodulation, interdisciplinary clinical team structures have also been promoted as a part of a necessary "broad clinical gaze" [27].The resources needed by the healthcare team in order to implement this innovative, technical treatment have promoted the creation of settings in which patients receive a more comprehensive and individualized care.

EFFECTS OF THE TECHNIQUE

DBS' effects, whether positive or negative, are likely to generate difficulties for patients and their families and friends. First of all, hospitals, clinics, doctors, and manufacturers of medical devices are by law held to be liable for any damage that may result from any one of the following: failure to provide the patient with sufficient information; organizational flaws in the hospital department or in patient follow-up; errors in performing the surgery; or a design or manufacturing defect in the device (the electrode, wires, neurostimulator unit, battery, recharging system) [59]. Besides these well-known legal resources of medical law and liability, DBS raises specific questions.

Informing the patient, adapting the treatment, and involving the family

Before and after the surgery, it is of crucial importance to make sure the patient and home caregivers are fully informed. This information must be as comprehensive as possible, covering not only the risks of the procedure and the risk of infection due to the implant, but also the risk of behavioral disorders that may occur in the short and medium term. In the short term, post-operative inflammation may cause serious difficulties for the patient, ranging as far as aggressive behaviors and suicidal tendencies. In the short and medium term, once the inflammation has subsided, difficulties may arise while the stimulation is being adjusted. On all of these subjects, the information provided must be as precise and thorough as possible (in France: articles L. 1111-2 & R. 4127-35 Public Health Code; Cour de cassation (1re civ) 6 Feb. 2013 n°12-17423; Conseil d'Etat 10 May 2017 n°397840). If the hospital can organize it, an educational patient training about the treatment is recommended. A full informed consent is also required by medical ethics, because it is the bedrock of the principle of personal autonomy for the patient. In addition to meeting requirements in terms of the liability of the doctors and the healthcare facility, and over and above the necessary respect for the patient's individual choices, pre-procedure counseling optimizes the chances that the treatment will be well accepted and that all kind of difficulties will be identified. It has become clear that attention to the patient's first-person experience is a key element for a successful treatment because each person reacts to DBS differently, and because the device requires individualized tuning. Input from the family and home caregivers, especially watchful in the post-operative months, can be crucial. Certain behavioral changes that have a negative effect on the patient's quality of life (irritability, exasperation, impatience, etc.) are easier for daily home spouses and children to detect. Certain healthcare teams have made these discussions part of the pre-op routine, scheduling a counseling session for the patient alone and another with patient and caregivers. Including family members in the discussion between patients and healthcare staff increases the chances that a problem will be solved. However, it also raises

significant legal and ethical challenges. Medical privacy does not oppose a patient's decision to share personal medical information with a family member or primary home caregiver, but sharing this information without the patient's explicit consent is against the law. However, so far, no suitable legal status has been defined for these third parties associated with DBS treatment. In the majority of cases, including for psychiatric illness, the patient is an adult and remains legally capable and competent for making decisions alone. Therefore, the caregivers are not patient representatives. Other legal status, designed to solve crisis situations (such as urgent decision in the context of a surgical procedure), are note adequate either (like the "personne de confiance" in French law: article L. 1111-6 Public Health Code). A delicate balance must here be found, between family implication (in order to optimize the treatment), respect for patient autonomy (in order to protect him or her from outside pressure) and the preservation of a trust-based healthcare relationship. The broad range of individual situations calls for case-by-case assessment (shared within the healthcare team), centered on respect for patient autonomy and medical privacy. For children, parental consent is crucial but the child's understanding and acceptance is to be sought (depending on his or her mental maturity). Parental authority is a legal setting, allowing to make decision for the minor in difficult situations, supposedly following his or her best interest. However, it should not turn into a bad "protectionism", forgetful of the rights and interests of the child instead of searching for a shared decision [33]. Legal orders often consider the need to take the child's opinion into consideration (in France: article 371-1 Civil Code; articles L. 1111-2 Public Health Code). Furthermore, for children and for adults, patient-centred clinical assessment tools are becoming more and more important in medical practice, leading to the idea that the patient's experience may help to capture other improvements that impairment based measures are insensitive to [27,41].

Treatment efficacy and social adjustment

DBS is a treatment for chronic illnesses that disable the patient (physically and/or psychologically and socially). Patients have been forced to learn to live with the disease. By informing patients and their close relatives and by developing patient education as much as possible, certain difficulties with "the return to normal life" [22] might be lessened. For patients, support in the environment at home is crucial [60], and the disease leads to adjustments in the family (see the 2001 COMPAS study, "L'impact de la maladie de Parkinson sur la vie du conjoint" on how the disease affects the patient's spouse). After DBS, these home routines may change abruptly. For certain diseases, especially PD, DBS may produce a spectacular improvement in motor skills. The patient may quickly regain his or her independence, whereas the home had been reorganized to deal with his or her needs and disabilities. To optimize the medical benefit and relieve it of the burden of family difficulties and dissatisfaction [54,61], it seems to be necessary to inform and prepare the patient and his or her caregivers. When DBS provides relief for their disability, they must then learn to live with the device. This implies various adjustments: on the one hand, adjustments between their expectations and reality; and on the other hand, adjustments between their fears and their possibilities. The former are the result of DBS efficacy, combined with its potential effect on emotions and motivation. The patient may experience a feeling of euphoria, and an appetite for activity that is difficult to match up with his or her actual possibilities, both physical and social. The latter are related to the technical limitations of the implanted medical device. The patient may fear that the device will fail without warning, due to any one of several factors: sensitivity to electromagnetic radiation, device dysfunction, or dead battery. For implanted patients, the "burden of normality" [62] can be measured by this double standard: don't overdo it, but don't limit yourself too much; do not deceive yourself into thinking the disease is cured, because it continues to progress; but do take full advantage of the opportunities provided by relief of the symptoms. In this context, an ethical reflection on the "agentivity" and empowerment of patients is entirely appropriate. Decisional autonomy does not end once the surgical procedure is over and the initial adjustments have been made; it should also be expressed in the control over the technical devices. The right to decide to have the stimulation turned off is a minima option. Providing patients with possibilities like switching the power unit between different pre-programmed modes, or having a rechargeable system or not, are other ways of ensuring that the treatment is centered on the patient. From this perspective, certain regulatory limitations actually seem to contradict the

ethical concern for the autonomy to which the patient is entitled. For example, in France some conditions are required for access to devices with a rechargeable battery: besides the patient's cognitive abilities, the requirement that the patient have "family supervision compatible with recharging the device" [63].Such a requirement could discriminate against certain patients. Moreover, it seems implicitly to create a form of moral duty for the family. How could such a duty be interpreted legally, in case of family disputes (a divorce, for example)? What consequences may result, in terms of patient follow-up (removal of the device)? Here, concerns for patient safety conflict with the ethical principle of autonomy.

Behavioral disorders, impact on identity, and legal repercussions

DBS has been associated with a range of behavioral disorders, including impulse control disorder, pathological gambling, hyper sexuality, compulsive shopping, and pathological crying [64-70], suicidal tendencies [71] or hypomania [56]. However, the studies do not always converge: for PD, certain studies report disorders while others demonstrate an improvement after neuromodulation [72]. Moreover, assessment must account for behavioral effects induced by medication with dopamine receptor agonists, which may continue to be administered, although dosage can be reduced thanks to stimulation. The behavioral modifications that may result from DBS have elicited intensive ethical discussions in relation to their consequences. The debate has taken shape most notably around the question of personal identity. Because every individual is positioned in a personal narrative that combines the memory of his or her personal history, self-perception, and interpreting feedback from other people's gaze, sudden change may have serious consequences. Not all behavioral modifications jeopardize the continuity of the subject's perception of his or her personal identity: only the most intense or the most abrupt seem to cause serious damage. However, the immediacy and strength of the effects produced by DBS – already pointed out in relation to motor functions –prove to be of some concern in this respect [73,74]. Care must be taken not to make an artificial opposition between a "true personality" which would be that of the individual prior to treatment and a personality altered by the treatment: according to Paul Foley, identity is forged throughout the patient's lifetime by his or her personal biography as it was affected by the disease and by the treatment [11]. Although Foley's position deserves to be reconsidered carefully, to avoid denying the existence of detrimental modifications, it does have the merit of emphasizing the primordial role of personal autonomy. Even when a behavioral change is perceived, it may be accepted or even appreciated by the patient. The patient is the first person entitled to evaluate the negative or positive impact of the change, and, if he or she wishes, to request that a remedy be attempted by adjusting the device or stopping the stimulation. Although, as it has already been pointed out, the role of the family and caregivers is very important, it appears to be ethically unacceptable for a third party's opinion to be decisive. In addition, studies have demonstrated that the family's evaluation of DBS effects could sometimes be quite different from that of the patient [43,75]. The amplitude of the disorders may sometimes lead to especially sensitive decisions, if modifying the tuning of the device does not solve the problems. One of the cases that was most often cited in these discussions involved a patient who was severely disabled by PD, in whom DBS caused such an intense manic state that commitment to a psychiatric institution was necessary [76]. When, in order to restore a more coherent state of consciousness and behavior to the patient, the device was readjusted or the stimulation was stopped, severe, painful motor symptoms of PD returned. Confronted by this dilemma, the patient chose stimulation. This choice shows the implementation of the principle of personal autonomy in stark light: regardless of how hard it is for the healthcare team or the patient's family to understand a patient's decision, it must be respected. Even when the dysfunctions appear to be milder, they may have serious social consequences, severely impacting the patient's family, finances, and career, perhaps even resulting in legal problems. When these disorders cause detrimental behavior, the patient may be tempted to file a lawsuit for reparations or, in some other cases, if he or she has caused damage to a second party, he or she may be named in a lawsuit. This last situation raises the question of the causal link between the damage and the person responsible for doing the damage, since the latter suffers from impulse control disorder, summed up as follows: "Did My Brain Implant Make Me Do It?" [77]. By extrapolating from lawsuits over dopamine agonist

medication in France, it can be observed that judicial opinion relies largely upon assessments provided by appointed medical experts, and that fairly often, it is based on whether difficulties were absent prior to the treatment. The courts hold the lack of incidents prior to treatment as a reliable clue to the causal role of the treatment in the emergence of the disorder, especially if the problems encountered by the patient are resolved after treatment is stopped or changed. Inversely, the existence of disorders prior to treatment is noted as an element likely to rule out any causality between the treatment and the patient's detrimental behavior. If the disorders have proved to be truly detrimental to the patient's private life, family and social relationships, and career, financial compensation may be considered.

Controlling the device

Currently, innovation of the DBS device involves the development of a closed-loop system [14,78-81]. The goal is to overcome the inadequacies of a pre-set unit (which may periodically over- or under-stimulate the patient's brain). The closed-loop system would generate stimulation tailored to the patient's needs as the day goes on. Information about the patient's brain function would continuously be transmitted online to a remote processor, which would apply an algorithm adapting stimulation to need in real time. From an ethical and legal viewpoint, this innovation raises new questions. Some are related to the protection of personal privacy, because so much is revealed by this data. Fears center not so much on the disclosure of thoughts to a third party, which is unlikely, but on misappropriation of the data by the health insurance provider, public or private. However, the privacy issue is not specific to the DBS device. On the one hand, it is related to the overall question of access to and security of systems that collect, process, and host personal health data, and on the other, to legislation guaranteeing the protection of rights granted by healthcare coverage (French Social Security Code) and laws prohibiting discriminatory treatment (French Insurance Code). The problem that does relate specifically to closed-loop DBS devices involves questions about patient autonomy, insofar as the treatment is regulated by automatic adjustment, rather than by a decision reached after conferring with the neurologist. True, it is possible to compare this situation to that of other patients who are fitted with automatic implantable devices (like the AICD, or automatic implanted cardioverter defibrillator, for example). Nevertheless, DBS is a special case in that it potentially has an impact on behavior and impulses. As a result, any dysfunction (not to mention an improbable but still fearsome takeover by a computer-hacking effort) would raise specific problems. Would the patient be able to detect a dysfunction? Would he or she succeed in proving it?

Going beyond the impact of the innovation making it possible to adjust the DBS device using online data transfer, the question of non-medical uses must also be considered. Indeed, the effect of DBS on memory or on impulses arouses interests that have very little to do with the goal of providing relief to people suffering from brain diseases [30]. Some are eager to apply the neurological technique to the purposes of "neuro-improvement" (memory optimization) or social control (controlling criminals, for example). The fact that DBS requires invasive and risky surgery minimizes the danger of seeing the treatment deviate from its original purpose. Nevertheless, the fear of such a slide deserves to be taken seriously. As a result, the French Comité Consultatif National d'Ethique listed DBS among the "biomedical techniques that could be applied to 'neuro-improvement' of a person in good health" that might be considered in a society "obsessed with brain efficiency" [82]. True, the case of a human augmented by DBS seems less likely to occur than that of a convicted criminal controlled by DBS. As an extension of the use of medication for social control, and in view of its reversibility, DBS sometimes might be perceived as a solution to limit the risk of a repeat offense. According to a survey of the 299 North American neurosurgeons who belong to the World Society for Stereotactic and Functional Neurosurgery, 54% were convinced that, in the future, SCP will be used for neuro-improvement. Only 48.6 % judged it would be unethical to perform DBS to improve memory; 56.8 % found it was ethically justified to apply the treatment to reduce the sex drive of sex offenders who request such an operation [83]. According to another study, neurosurgeons would be willing to apply DBS for individuals who display violent or anti-social behavior [84]. Regardless of the reservations some may have in relation to these tendencies, they should alert legal thinkers. Here, social pressure is decisive [85].

CONCLUSION

This brief survey shows the diversity and complexity of the ethical and legal questions raised by DBS. Although some of them can be answered by existing medical ethics and law resources, others demand further reflection. This article did not differentiate between neurological and psychiatric applications for DBS applications. Covering the two together respects a current trend in technique to dissolve barriers between practices and knowledge. However, doing so could also involuntarily conceal issues that are specific to the psychiatric (or neurological) field. Despite this possible bias, it seems possible to point out certain key points. The characteristics of DBS shed light on certain fundamental questions. The permeability of the boundary between research and treatment comes into much clearer focus. Difficulties in determining the role and status of family and home caregivers stand out in sharp relief. The striking contrast between "on" and "off" states, and the issues raised by potential behavioral effects reveal the weaknesses in our conceptions of identity and personality: perception of the self as the result of a form of continuity and of an independent will.

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