"Not only is she really dead, she's really most sincerely dead."
(Munchkin Coroner in the Wizard of Oz, after examining the Wicked Witch of the East)

The Problem of "Near-Complete" Brain Death: How Current Brain Death Policy is Flawed

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Introduction

Brain death is a modern clinical concept that is central to the practicalities of organ transplantation in that most transplanted organs come from patients who have been declared to be brain dead. In a typical clinical scenario, a patient receives a massive injury to his or her brain (for example, from a burst cerebral aneurysm) and ends up in an intensive care unit on a ventilator, as well as possibly receiving other life-support interventions such as drug infusions for blood pressure support or dialysis. While in the intensive care unit, the patient's neurological status is periodically assessed and if there is suspicion that the patient is brain dead, a formal brain death evaluation is carried out according to local protocol. If the patient is found to be brain dead, the patient's relatives are approached regarding possible organ donation.

This paper is concerned with the problem of what should be done if the formal brain death criteria are met only imperfectly, such as where all the criteria for brain death are met save one. An example of this scenario is the patient who meets all the criteria for brain death except he or she still has an intact gag reflex. We make the case that, while the notion of brain death appears to be well accepted in the Western world, there are a number of difficulties with the actual diagnosis of brain death as it is currently carried out clinically. This paper also discusses these issues, identifying inconsistencies and confusion that has developed in the diagnosis of brain death.

It is concluded that the notion of brain death in widespread clinical use may be fundamentally flawed.

Diagnosing Brain Death

Traditionally, death has been defined as the permanent cessation of the heartbeat and respiration (classical death). Modern developments in resuscitation, however, have forced a reappraisal of the concept. Technical advances have also changed the landscape. Ventilators, dialysis equipment and drug infusions which artificially support the circulation often permit the bodies of critically ill patients to be supported despite severe physiological insults, including death of the brain itself. Critical care practitioners all have tragic stories of individuals harboring dead brains in technically living bodies. When this occurs, difficult issues must often be addressed. When brain death is established, cessation of life support measures (sometimes after organ harvesting for transplantation) is usually carried out; cardiopulmonary collapse and classical death follows promptly.

The advent of transplantation surgery provided a strong clinical motivation to define death in terms of loss of brain function rather than as the cessation of cardiorespiratory activity. This is because the success of transplantation surgery depends on the use of viable organs uncompromised by circulatory failure. With time, the concept of brain death as synonymous with death of the person has gained worldwide recognition.

A key pathophysiological event in brain death is a severe elevation of intracranial pressure (ICP) from causes such as hemorrhage or edema. When the ICP rises to approach arterial blood pressure, cerebral perfusion pressure (CPP) approaches zero (remember: mean CPP = mean BP - mean ICP), cerebral perfusion stops and brain death ensues. Autopsy findings of the brain depend on the precipitating event but may include total liquefaction in cases of prolonged artificial life support (what's known as "respirator brain"). With primary hemispheric lesions (e.g., large unilateral tumors), transtentorial or tonsillar herniation are often present. A careful neurological examination centering on the assessment of brain-stem reflexes is the basis for the determination of brain death. The diagnosis of brain death is determined primarily on the basis of clinical findings, and depends on investigations such as electroencephalography and cerebral angiography only in special cases.

Associated with the concept of brain death is the need for a reliable, structured method of diagnosis. A variety of such criteria have been published. Of these, the original Harvard Criteria [1] are perhaps the best known. They include the following: (a) unresponsivity to intensely noxious stimuli (unresponsive coma), (b) total absence of spontaneous breathing, (c) absence of brainstem and spinal reflexes, (d) absence of postural activity such as decerebration, and (e) a flat electroencephalogram (EEG). Hypothermia and the presence of CNS depressants such as barbiturates must also be excluded. Finally, the clinical and EEG findings should be unchanged in a second evaluation at least 24 hours later. More relaxed criteria such as the Minnesota Criteria [2] were later proposed: Notably absent from this criteria list are absent spinal reflexes and EEG activity (electroencephalography being viewed as an optional confirmatory investigation). The key elements of the Minnesota criteria are**:** (a) absence of spontaneous movement, (b) absence of spontaneous respiration over a four minute test period, (c) absence of brain reflexes as evidenced by: fixed dilated pupils; absent gag, corneal and ciliospinal reflexes; absent doll's eye movements; absent response to caloric stimulation, and absent tonic neck reflex, (d) unchanged status for at least twelve hours and (e) responsible pathological process deemed irreparable.

With the worldwide spread of transplantation surgery, numerous studies, reviews, and regional guidelines regarding brain death were published. Publications from the Inter-Agency Committee on Irreversible Coma and Brain Death [3], the American Neurological Association [4], the Conference of Royal Colleges and Faculties of the United Kingdom [5], the President's Commission for the Study of Ethical Problems in Medicine and Behavioral Research [6] and other sources [7- 17, 20, 21] provide a maze of criteria, cautions, exceptions, and ancillary investigations. That such a variety of guidelines should sometimes be a source of confusion to clinicians should be no surprise. Even more confusing was the airing of a highly publicized BBC television program entitled: "Transplants: Are the Donors Really Dead?" which stimulated considerable correspondence in the medical literature [e.g. 18,19].

Although the diagnosis of brain death is a clinical one, from time to time the clinician may seek guidance from a variety of ancillary tests. Perhaps the most common such test is electroencephalography, the expected finding being a "flat" or "isoelectric" EEG [24]. As well, confirmation of brainstem death can be facilitated by observing a flat auditory brainstem response (ABR). [25] Absence of cerebral circulation can be demonstrated by four-vessel angiography and radionuclide methods [26]. More recently, absent flow signals on transcranial Doppler ultrasonography has also been suggested as a method to demonstrate the absence of cerebral circulation in brain death [27,28]. All these methods suffer from potential technical problems that require skilled technical support to make the techniques meaningful and reliable in the ICU environment.

Incomplete Brain Death

As suggested by the above commentary, much has been written about criteria for the diagnosis of brain death. However, one important clinical situation that appears to be rather ignored in the medical literature (despite being clinically common) concerns the patient with a massive brain injury who meets the criteria for brain death only imperfectly, perhaps because one small patch of neurons in a brain-stem nucleus are still operating intermittently. In real-world clinical practice such patients have zero chance of survival and as a result difficult issues must be faced. We call this the problem of incomplete (or near-complete) brain death [29-31].

One approach is to continue to intervene medically, using all available resources, hoping against hope that some miraculous recovery might occur. This approach suffers from a number of drawbacks. First, in the real clinical world miraculous recoveries simply do not occur following massive structural brain damage involving the entire brain stem. Secondly, in a setting of limited resources this approach is very wasteful; these patients end up getting very expensive and complex care that serves them or their loved ones little or no benefit. A third drawback of this approach is that it merely prolongs the patient's death. In essence, medical interventions in this setting are futile with respect to patient recovery.

As a consequence, once the hopelessness of the situation is established, in the actual clinical world such patients are usually withdrawn from life support, and cardiorespiratory arrest follows inevitably some time later. Tragically, in this setting the organs can almost never be used for transplantation, as they must usually be harvested prior to collapse of the circulation. Thus the organs "go to waste," even when the patient has signed his or her organ donor card and even when the family is enthusiastically in favor of organ donation.

The impediment against organ harvesting in this setting is simply that the patient has not met the required (local) criteria for brain death. Yet the criteria for brain death are in some respects arbitrary. For instance, while the original Harvard criteria for brain death require the loss of all spinal reflexes, more recent criteria do not. Similarly, the various national guidelines are not all exactly identical, so it is likely that there are some patients who meet some existing national criteria for brain death yet do not meet others.

Since the waste of transplantable organs in this setting appears to be tragic, there are individuals who argue that a different philosophical approach to brain death is necessary if one is to allow organ retrieval to be performed in such a setting. In this context, the philosophical principles advocated by Peter Singer and others avoid some of the philosophical difficulties that would otherwise occur.

Peter Singer, professor of bioethics at Princeton University's Center for Human Values, is a well-known bioethicist with what some see as radical views. In his various writings he has challenged our most closely held beliefs on infanticide, euthanasia, and the moral status of animals. He also challenges the conventional wisdom on brain death.

In his book *Rethinking Life and Death* [32], Singer notes that following the Harvard Brain Death Committee report published in 1968, most countries have adopted brain death as an acceptable criterion for declaring a person legally dead. He also notes that this

event transpired with virtually no opposition despite its ground-breaking nature. What is less widely known, Singer points out, is that this "redefinition" coincided historically with the advent of organ transplantation — a mere nine months before the Harvard report came out, Dr. Christiaan Barnard performed the first successful cardiac transplant. Singer rightly doubts that this is a coincidence.

Singer also points out that it is simply not true that all brain function necessarily ceases with brain death – for instance, pituitary function often continues for some time after formal criteria for brain death are met. (In fact, in a large number of cases in which people have been declared to be brain dead, there are clear signs that parts of the brain still function. Despite being declared "brain dead", between 22 percent and 100 percent of such people keep on secreting arginine vasopressin (DDAVP), a hormone which regulates water retention [33]. As this hormone is made only in the brain, it strongly suggests that in such cases the entire brain has not entirely stopped functioning.)

Singer takes the position that brain dead individuals are still alive, but that organ harvesting from these individuals is none the less acceptable. His position is that rather than employ artificial or contrived definitions of death, we should recognize that the only intellectually honest course is to admit that all lives are not equally valuable. Some lives are indeed in such a degraded and hopeless state that even though a person's body is technically "alive," it is still ethically acceptable to utilize their organs for transplantation.

Another prominent bioethicist, Dr Robert Truog, director of the multidisciplinary intensive care unit at Children's Hospital in Boston, takes a somewhat similar view. Truog notes that patients who fulfill the criteria for brain death frequently respond to surgical stimuli with significant increases in both heart rate and blood pressure, and makes the case that this implies that there may be some residual brain function in these individuals. He suggests that it may be time to "uncouple" the concepts of brain death and organ donation so that, if a family requests it, organs might be taken from a patient while he or she is only near death or permanently comatose. This would allow people in persistent vegetative states to be organ donors, even though taking their organs would clearly hasten their deaths. [34, 35] The details of this position are discussed in the next sections.

Still, not surprisingly, many clinicians object to this viewpoint, as does Dr. Francis Delmonico, who is the director of kidney transplantation at Massachusetts General Hospital. "It is crucial for the public trust that organs only be removed from people who are dead, not those who are comatose but still alive." [33] No doubt a great many others agree with Dr. Delmonico.

President's Bioethics Commission

In 1981 the President's Commission for the Study of Ethical problems in Medicare and Biomedical and Behavioral Research published a landmark study intended to establish a common ground for American law related to brain death [36]. The commission defined brain death conceptually (but not operationally) as the "Irreversible cessation of all functions of the entire brain, including the brain stem." Operational criteria for diagnosing this condition were not explicitly addressed is the report; this aspect was dealt with by another committee (composed of medical experts rather than bioethics experts) who published a contemporaneous report in JAMA [37]. This separation of the conceptual and the operational aspects of brain death is an appealing intellectual process but logic nevertheless requires that they be mutually consistent and philosophically compatible. This appears not to be the case.

It is interesting to note that the British have taken a rather different approach to the concept of brain death, advocating a view based on the permanent absence of brainstem function [38-40] rather than loss of function of the entire brain. They argue that death of the brainstem necessarily entails the death of the reticular activating system, which in turn necessarily results in permanent loss of consciousness.

However, there are some potential problems with the British approach. For one thing, critics argue, it has not been proven rigorously that reticular activating system function always parallels brainstem function. As noted earlier, the American approach is more conservative, requiring that all brain function, not just brain stem function, be absent.

Irreversible Loss of Function?

While the President's Commission defined brain death in terms of "irreversible cessation of ALL functions of the ENTIRE brain," in the years since this definition was offered it has become eminently clear that many (indeed, perhaps most) patients diagnosed with brain death do NOT actually meet this requirement. The evidence that this is the case has been meticulously documented by Troug and Fackler [35]. In summary, the evidence is as follows:

> (1) Many patients diagnosed with brain death often still synthesize arginine vasopressin

> (which regulates serum osmolality), implying the present of residual function in the brains hypothalamus.
>
> (2) Many patients diagnosed with brain death maintain some degree of cerebral electrical activity, as evidenced by a detectable ongoing electroencephalogram (EEG).
>
> (3) Environmental responsiveness (such as increase in heart rate and blood pressure in responses to a surgical incision) is present in almost all brain death patients brought to the operating room for organ harvesting.
>
> (4) Since the spinal cord is considered to be a part of the central nervous system, and since the brain is defined as identical to the central nervous system, it follows, Truog and Fackler argue, that the presence of intact spinal reflexes (very commonly encountered in brain dead patients) is inconsistent with complete brain death.

Space limitations prevent a detailed discussion on this issue; suffice it to say, however that much has been written on the various aspects of these inconsistencies in recent years, there is indeed an enormous gap between the concept of brain death as developed by the Presidential Commission and the actual operational criteria used clinically in transplant centers across the USA and elsewhere.

What to do?

The gap between what is required to declare brain death and what is actually done in the real clinical world is a problem of considerable importance.

What should be done? Troug and Fackler [35] discuss several options. The first option they discuss involves simply ignoring the problem. This approach is simple to implement and would be unlikely to jeopardize the ongoing availability or organs (as might, for example, occur if the operational criteria for declaring brain death were made tighter). However, not everyone is prepared to ignore the inconsistencies, and occasionally these inconsistencies are brought to the attention of the mass media who, while always well-intended, often lack the time, space or motivation to inform the public as fully as they might, resulting in public confusion and a decrease in organ donors.

A second approach is to tighten up the operational criteria for the diagnosis of brain death. For instance, one could carry out tests of EEG studies to establish that no electrical activity remains, do cerebral flow studies and so on. While this approach appears to be logical and appealing, it suffers from a number of serious drawbacks.

First, the criteria for diagnosing brain death are currently primarily clinical rather than technical. Adding a number of technical procedures to the mix will both add enormous cost to the process and reduce the number of available organs. Secondly, the diagnosis of brain death would be delayed; such delays are known to have a negative impact on the quality of the organs obtained since many brain dead patients rapidly become hemodynamically unstable as time progresses. This appears to be especially true when diabetes insipidus sets in (personal observation). Finally, these tests are themselves imperfect. Each diagnostic test has an associated sensitivity and specificity that must be considered, even if not known exactly [30].

In fact, if we wished to modify the operational criteria to truly ensure the irreversible cessation of all functions of the entire brain it would be necessary to secure pathological evidence of fatal brain destruction, a point made by Bryne et al. [41].

Even cerebral blood flow studies can be misleading. While it is intuitively compelling that the sustained cessation of cerebral blood flow throughout the brain will inevitably lead to brain death, the absence of detectable cerebral blood flow on testing is neither necessary nor sufficient to establish brain death in that there are known to exist situations where there is cerebral blood flow despite clinical brain death and vice versa.

A final approach to deal with the gap between the conceptual definition of brain death and the operational criteria actually used is to alter the conceptual definition from that originally proposed by the Presidential Commission. Given the difficulty associated with the other approaches discussed, this would appear to be only sensible measure. Truog and Fackler [35] comment on this approach:

> This option may seem like trying to redefine the laws of nature, unless it is realized that death is a process consisting of the disintegration of the body as a whole manifesting as the sequential death of organ systems, individual organs, and ultimately separate cells. The moment in this process at which death is said to have occurred is a point that cannot be discovered by any empirical

process, but rather must be chosen by societal consent.

One approach, then, would be is simply discard the notion of brain death and go back to the traditional cardiorespiratory definition of death that served for thousands of years. Although the impact on organ transplantation would be catastrophic, a minority of individuals have advocated exactly this approach [41-43]. However this approach is both impractical as a matter of public policy and philosophically distasteful, in that it abandons both the needs of those patients in need of organ transplantation and the view of the brain and consciousness as defining the central element of personhood.

Consciousness - Based Approach

A number of philosophers and bioethicists, aware of the numerous problems and inconsistencies discussed above, have sought to develop an alternative understanding of death based on the concepts of "loss of personhood" and the notion of "permanent loss of consciousness". While the current concept of brain death focuses on brain stem testing and emphasizes the loss of vegetative functions of the brain, the new formulation focuses on those brain components that contribute to consciousness (the cerebral cortex or neocortex); this approach is sometimes referred to as the neocortical or "higher-brain" criterion for death.

Truog and Fackler [35] offer two types of argument to support this consciousness-based higher-brain approach to defining death. First, they offer moral argument where "one asserts that it is ethically permissible (and even obligatory) to regard patients who have lost higher-brain functioning as dead; that it is repugnant to our moral sensibilities to artificially maintain vegetative functioning in a human being after the irreversible loss of personhood". Truog and Fackler's [35] second argument "is an ontological formulation that asserts that the continuing presence of personal identity is conceptually necessary for human life". These two arguments lead to the view that it is consciousness more than anything else that is the essential and central condition for being alive, regardless of the definition of death as being the irreversible loss of the capacity for consciousness [44].

Implications of the New Definition

Consciousness may be defined as being self-aware and being aware of one's environment. But if the irreversible and permanent loss of the capacity for consciousness were accepted as the conceptual basis for defining death, what criteria would be used to establish the diagnosis?

Truog and Fackler [35] note that while such criteria have not yet been universally agreed on, nevertheless "unlike the choice of conceptual definition, identification of the neurologic substrate of consciousness and the criteria for establishing its "irreversible loss" is a scientifically and empirically answerable question. They also note that "current whole-brain criteria mandate the presence of coma, already requiring physicians to accurately diagnose the absence of consciousness." Furthermore, it is of interest that a number of judges have tackled this very issue, presuming that consciousness is permanently lost in individuals in a persistent vegetative state for a sufficiently prolonged period of time. Finally, new technologies that measure cerebral glucose metabolic rate throughout the brain (based on positron emission tomography) may make this task easier in the future.

Objections to the Consciousness Approach

A number of objections can be raised against the "higher-brain" criteria for defining death. First, there is little in the way of societal agreement that this approach is desirable, and given that the definition of death is established by societal consent, this is necessarily a problem. Furthermore, it is unlikely that society would be willing to consider to be dead anyone who, despite being permanently unconscious, was able to breath unassisted. (Almost everyone would expect a person to be apneic and pulseless before being brought to a morgue or a funeral home). Still, societal views can and do change, especially in the highly educated sectors of society.

A second concern with the higher-brain approach concerns the nature of consciousness itself. Since consciousness is necessarily subjective, how can we be certain that it is present or absent based on objective tests? Although such a question may be philosophically unanswerable, it should be clear that where the required physical substrate has been destroyed, so too has the consciousness associated with the substrate.

Discussion

The problem of incomplete brain death is complicated by the fact that the degree of incompleteness may depend on the criteria for brain death that is used. For instance, the original Harvard criteria for brain death required that spinal reflexes be absent, but this requirement is lacking in contemporary criteria. Thus a patient who meets the usual criteria for brain death but

still has intact spinal reflexes would have incomplete brain death by the Harvard criteria but would still meet more modern criteria. In this instance both cases the higher-brain criteria would also be met

However, consider the case of a patient with a massive head injury who still has a gag reflex but no other evidence of brain stem function despite prolonged care in the ICU. In this case the usual brain death criteria are not met but the higher-brain criteria for death would be met, so that organ harvesting would be appropriate should that criteria for death be used. Is this case (where the gag reflex is intact) substantially different from the not uncommon situation where brainstem function is lost but neuroendocrine function (with production of arginine vasopressin) appears to be intact? The main difference between these two scenarios is that in the former the gag reflex is tested while in the latter case it is rare to test neuroendocrine function.

Conclusion

The current clinical approach to the patient with incomplete brain death who has no chance of survival is usually to withdraw life support, the result inevitably being eventual cardiopulmonary collapse and the loss of an opportunity to harvest organs for transplantation. This is because the criteria for brain death are not met in such instances. Yet the criteria for brain death have varied over time and vary between nations. Furthermore, there is considerable evidence that the whole brain is often not completely dead; when brain death criteria are met neuroendocrine function may be intact.

A controversial ethical approach advocated by Singer, Truog and others eliminates the worry associated with these problems. They argue that organ harvesting from permanently unconscious patients who have no chance of survival if removed from life support is indeed ethical, provided that family consent is obtained and the prior wishes of the patient are honored. This approach not only eliminates a number of philosophical concerns related to the problem of brain death, but may have positive practical implications for patients in need of transplantable organs.

Analysis of the problem of managing the patient with near-complete brain death identifies a number of inconsistencies regarding how brain death is established clinically. Simply put, the clinical testing usually carried out very often does not establish that the whole (entire) brain has died. Since these patients cannot recover and will die, honoring their prior wishes to be organ donors becomes feasible if a consciousness based criteria for declaring death is used.

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