"Brain dead" Patients: Critically Ill or Dead? A Potential Answer to the Problem

Konstantine G Karakatsanis
Hippocrateion Hospital, Medical School, Aristotelian University of Thessaloniki, Thessaloniki, Greece

Abstract
Purpose: To evaluate whether current clinical criteria and confirmatory tests for the diagnosis of "brain death" satisfy the requirements for irreversible cessation of functions of the entire brain including the brain stem.

Methods: a) Presentation of known arguments from the medical and philosophical literature as well as several novel arguments. b) Suggestion for the application of PET into the research of "brain death" concept which might shed additional light on this subject.

Results: There are self-evident inconsistencies and contradictions inherent in the concept of "brain death" according to which this concept is invalid.

Conclusion: It seems unavoidable that the "brain death" concept should be abandoned.

Keywords: Consciousness; "Brain death"; Transplantation; PET; Deep brain stimulation

Introduction
The concept of "brain death" was introduced in medical terminology for obviously utilitarian purposes, that is: a) to lessen the "burden" on patients, on the hospitals and on those in need of hospital beds, and b) to eliminate all obstacles in obtaining organs for transplantation [1].

Inconsistencies Related to the "Brain Death" Concept
The entity of "whole brain death" (or "whole brain failure") is impossible to be diagnosed by the clinician who examines the comatose patient for any signs of brain stem function. It is obvious that one cannot test for any cerebral function by clinical bedside examination because the tracts of passage to and from cerebrum through the brain stem are invariably destroyed or nonfunctional in "brain dead" patients [2].

According to Professor Adams (member of the Ad hoc Committee of the University of Harvard Medical School), the criteria for "brain death" determination included "a permanent state of complete unreceptivity and complete unresponsively, the latter including all responses, whether brain stem, spinal or cerebral in origin" [3]. As a consequence, all spontaneous movements and elicitable reflexes must be absent in the state of "brain death". Therefore, it is obvious that the current guidelines for the diagnosis of "brain death" -according to which the maintenance of spinal reflexes and other complex (supposedly) spinal responses or automatisms (e.g. Lazarus' sign) elicited in "brain dead" patients are not incompatible with the diagnosis of "brain death" [4] - are not in agreement with the criterion established by the above mentioned Committee. It is noteworthy that the above Committee acknowledged that the "brain dead" patients are not really dead but individuals who were in irreversible coma who had "no discernible central nervous system activity" [1].

"Insofar as the neuropathology of BD (brain death) includes infarction down to the foramen magnum, the somatic pathophysiology of BD should resemble that of cervico-medullary junction transection.."; [5] in these patients with complete high cervical transection, all skeletal muscle reflexes integrated in spinal cord are completely blocked in the early phase of the "spinal shock"; thus, these patients are generally flaccid for 1-4 days after the transection of spinal cord [6]. If the brain stem had been dead, - as it (supposedly) always happens in "brain dead" patients- all impulses, including the facilitatory impulses to the spinal neurons, would have been completely interrupted; as a consequence, all skeletal muscle reflexes integrated in the spinal
cord would have been completely blocked during the initial stage of the "spinal shock"; [7] in this case, it would be impossible for the spinal reflexes to emerge in a few hours as it happens in some "brain dead" patients [8]. Therefore, the presence of these "complex spinal automatisms" in "brain dead" patients during the phase of "spinal shock" is indisputable evidence that the brain stem is, at least partially, functioning [2]. Thus, one might conclude that in many "brain dead" patients the descending neural pathways are not completely interrupted and consequently the brain stem is not dead, invalidating in turn the clinical diagnosis of "brain death" [2].

Furthermore, we argue that these complex reflexes and automatisms [9-11] which are elicited in some "brain dead" patients are very similar to some stereotyped movements mediated by the brain stem; e.g. the rotational movements of the head -controlled by the interstitial nucleus- and the raising and flexing movements of the body, controlled by the prestitital and precommissural nuclei, respectively [12]. "These stereotyped movements are feasible only when the above nuclei of the mesencephalon and lower diencephalon are functioning; this means that the brain stem is, at least, partially functioning and therefore viable, in these patients who were otherwise diagnosed as "brain dead" [2].

The multiple definition-criteria and criteria-tests inconsistencies and contradictions, eloquently shown by Shewmon [13-18] and Truog [19-20] in many patients, who meet the current clinical criteria for the diagnosis of "brain death", also invalidate this diagnosis.

In addition, a "compelling argument against even the notion of absence of cerebral functions is that in the context of brain stem infarction /destruction -which is always part of "brain death"- it is impossible to test for any cerebral function by clinical bedside exam, because the tracts of passage to and from the cerebrum through the brain stem are destroyed or non-functional" [2].

We consider that it is worthwhile to investigate, using the Positron Emission Tomography scan [21] in hemodynamically stable "brain dead" patients, [22] the potential stimulation of the cerebral cortex after application of various strong stimuli (e.g. auditory); the stimulation of the relevant part of the cerebral cortex in this case would be a compelling argument that the cortex is viable and therefore that the patient is alive.

"Brain Death" and the Content of Consciousness

The content of consciousness includes cognitive and affective mental functions. Most researchers believe that in "brain dead" patients all cerebral functions -including the two dimensions of consciousness, arousal and content- are lost because all parts of the brain are destroyed; nevertheless, none of the tests required to document "brain death" tests for the destruction of the cerebral hemispheres. Concerning the loss of content of consciousness (awareness) in "brain dead" patients, there are no criteria for the diagnosis of this loss since consciousness is, by nature, a subjective experience [23].

The author of this paper believes that the application of either diagnostic or research test in "brain dead" patients, which can be of no possible therapeutic benefit to the individual patient so tested, is not permitted if there is possibility of causing any further harm to these apneic comatose patients; for this reason, he also opposes even to using the apnea testing which may induce severe hypotension, collapse of the intracranial circulation, aggravation of brain swelling and irreversible brain damage [24]. Nevertheless, most neurologists, intensivists and neurosurgeons apply the apnea testing in spite of its potential detrimental side effects. Furthermore, others consider that it would be possible to conduct whatever research on "brain dead" patients -whom they consider (according to their own reasoning) in any case as dead and consequently they are not in danger of further damage-[25,26] under certain presuppositions.

The deep brain stimulation (DPS) -probably not more harmful compared to the apnea testing- has been applied in stereotactic operations without general anesthesia in PVS patients with spectacular effects ("raising of the level of consciousness to such a degree that the patients opened their eyes, looked around...and seemed to recognize their relatives...") [27]. The application of DPS technique -given a prior informed consent at an unsuspected time- in an initial cross section of "brain dead" patients (not in all cases thereafter) without massive brain edema could perhaps be characterized as reasonable given the value of information (status of the consciousness in "brain dead" patients) to be obtained; this information could obviously be of tremendous importance for the policy concerning the treatment of the "brain dead" patients by society in case it was demonstrated that these patients are inwardly conscious -since it is finally the criterion of life (inward consciousness) in these comatose apneic patients .

Brain Death and the Confirmatory Tests

Not one of the "confirmatory" tests has the necessary -100%-positive predictive value (the chance of having a disease given a positive test result) for the pronouncement of human death [2]. Truog and Robinson comment that "in the absence of a gold standard about what constitutes brain death, we do not know what condition or state these ancillary tests are designed to confirm"; for this reason they wonder "whether this entire literature on confirmatory testing for brain death is incoherent" [28].

The Application of Guidelines for "Brain Death" Determination

Since the concept of "brain death" was introduced in the medical literature in 1968 and twenty years after the explicit guidelines for this diagnosis that were drawn up by the AAN, [4] major "disturbing discrepancies were present among the leading neurologic clinics in the United States" [29]. It is also worthwhile to mention that one of the main theoretical defenders of the concept of "brain death", Professor Bernat, commenting on the issue of irreversibility (an indispensable requirement for "brain death") writes: "Two recent factors prompt me to reassess my previous position that irreversibility could be proved solely by clinical factors and to suggest that a laboratory test showing cessation of all intracranial blood flow should become mandatory in brain death determination" [30].
Unexpected Findings in Transplanted "Cadaveric" Kidneys

According to our (over thirty years) experience in the University Department of Nuclear Medicine (Thessaloniki, Greece), in all cases of "cadaveric" kidney transplantation from "brain dead" heart-beating donors, there is an initial damage of the kidney function - of several severity- lasting for days, weeks or, rarely, for a few months. This clinical situation "is related to ischemic damage that occurs before the donor's death and/or during the preservation period prior to transplantation" [31].

Nevertheless, the last years, one may find out that in several cases the function of the "cadaveric" transplant kidney (from "brain dead" heart-beating donors) is normal from the first post-transplantation hours; this early normal function of the transplanted "cadaveric" kidney is not concordant with ischemic damage of the transplanted kidney; the problem in this context is that, according to our extended experience, ischemic damage (as it is indirectly diagnosed using radionuclide techniques) happens in every case -but in different severity- in kidney transplantation as a result of the unavoidable ischemia. Therefore, the early normal function of the transplanted "cadaveric" kidney poses additional questions whether the conceptual definition of death ("permanent cessation of the critical functions of the organism as a whole" [32] and the operational criteria and tests for the "brain death" determination [33-34] are internally consistent and mutually compatible; furthermore, it poses the question whether these kidneys were harvested from "cadavers" and whether the "dead-donor rule" has been violated. Finally, one wonders whether the current guidelines for "brain death" determination are infallible and, furthermore, whether these "brain dead" heart-beating donors are really "cadavers".

Epilogue

The main question addressed in this article was whether the concept of "brain death" is still valid. We consider it is more than clear that, according to the above arguments, the concept of "brain death", as a synonymous term with the human death, is obviously invalid and should be abandoned.

Acknowledgement

I deeply thank Professor D.A.Shewmon for his invaluable assistance in the preparation of this manuscript.
References

1. A definition of irreversible coma (1968) Report of the Ad Hoc Committee of the Harvard Medical School to examine the definition of death. J Am Med Assoc 205: 337-40.

2. Karakatsanis KG (2008) "Brain Death": Should it be reconsidered? Spinal Cord 46: 396-401.

3. Adams RD (2001) Foreword. In: Widjicks EFM (Edr) Brain Death. Lippincott Williams & Wilkins, Philadelphia.

4. Widjicks EFM (1995) Determining brain death in adults. Neurology 45: 1003-1011.

5. Shewmon DA (1999) Spinal shock and "brain death": Somatic pathophysiological equivalence and implication for the integrative-unity rationale. Spinal Cord 37: 313-324.

6. Diamantopoulos E, Olsen PZ (1967) Excitability of motor neurons in spinal shock in man. J Neurol Neurosurg Psychiatry 30: 427-431.

7. Guyton, Hall (1996) Textbook of Medical Physiology. WB Saunders Co., USA.

8. Crenna P, Conci F, Boselli F (1989) Changes in spinal reflex excitability in brain dead humans. Electroencephalogr Clin Neurophysiol 73: 206-214.

9. Mandel S, Arena A, Scasta D (1982) Spinal automatism in cerebral death, Letter to the Editor. N Engl J Med 307: 501.

10. Ropper AH (1984) Unusual spontaneous movements in brain dead patients. Neurology (Cleveland) 34: 1089-1092.

11. Bueri JA, Sapoznik G, Maurino G, Saizar R, Garretto NS (2000) Lazarus' sign in brain death. Mov Disord 15: 583-585.

12. Guyton and Hall (2006) Ibid. WB Saunders, Philadelphia.

13. Shewmon DA (1997) Recovery from "brain death". A neurologist's apologia. Linacre Q 64: 31-96.

14. Shewmon DA (1998) "Brainstem Death", "Brain Death" and Death. A critical re-evaluation of the purported equivalence. Issues Law Med 14: 125-145.

15. Shewmon DA (1998) Chronic "brain death". Neurology 51: 1538-1545.

16. Shewmon DA (1999) Letter to the Editor. Neurology 53: 1371-1372.

17. Shewmon DA (2009) Brain Death: Can it be resuscitated? Hastings Cent Rep 39: 18-34.

18. Shewmon DA (2010) Constructing the death elephant: A synthetic paradigm shift for the definition, criteria, and tests for death. J Med Philos 35: 256-298.

19. Truog RD, Fackler JC (1992) Rethinking brain death. Crit Care Med 20: 1705-1713.

20. Truog RD (1997) Is it time to abandon brain death? Hastings Cent Rep (United States) 27: 29-37.

21. Cabeza R, Nyberg L (2000) Imaging cognition II. An empirical review of 275 PET and fMRI studies. J Cogn Neurosci 12: 1-47.

22. Widjicks EFM, Rochester MN, Bernat JL, Lebanon NH (1999) Letter to the Editor. Neurology, 53: 1369-1370.

23. Giacino JT (1997) Disorders of consciousness: Differential diagnosis and pathologic features. Semin Neurol 17: 105-111.

24. Coimbra CG (1999) Implications of ischemic penumbra for the diagnosis of brain death. Braz J Med Biol Res 32: 1479-1488.

25. DeVita MA, Wicclair M, Swanson D, Valenta C, Schold C (2003) Research involving the brain dead: An institutional response. Crit Care Med 31: S385-S390.

26. Schold C, DeVita MA, Swanson D, Wicclair M, Valenta C, et al. (2003) Policy for research involving dead. Crit Care Med 31: S391-S393.

27. Hassler R (1997) Basal ganglia systems regulating mental activity. Int J Neurol 12: 53-72.

28. Truog RD, Robinson WM (2003) Role of the brain death and dead donor rule in the ethics of organ transplantation. Crit Care Med 31: 2391-2396.

29. Greer DM, Varelas PN, Hacke S, Widjicks EFM (2008) Variability in brain death determination guidelines in leading US neurologic institutions. Neurology 70: 284-289.

30. Bernat JL (2006) The whole-brain concept of death remains optimum public policy. J Law Med Ethics 34: 35-43.

31. Taylor AT (2007) Kidney. In: Clinical Nuclear Medicine. Biersack HJ, Freeman LM (Edr), Springer-Verlag, Berlin Heidelberg.

32. Bernat JL (2001) Philosophical and ethical aspects of brain death. In: Brain Death. Widjicks EFM (Edr), Lippincott Williams & Wilkins, Philadelphia.

33. Pallis C (1976) Diagnosis of Brain Death. THE LANCET 1069-1070.

34. Pallis C (1982) From Brain Death to Brain Stem Death. Br Med J 285: 1487-1490.