Brain Death: Consensus and Controversies

Fundacio Grífols • Conferències Josep Egozcue
Barcelona • November 15, 2016

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Brain Death: Overview

• Areas of consensus
  – Medical acceptance with variations among test batteries
  – Legal acceptance growing internationally
  – Successful organ donation system using brain dead donor

• Areas of controversy
  – Soundness of the biophilosophical justification for the equivalency of brain death to human death
  – Sensitivity and specificity of clinical and imaging tests
  – How to accommodate religious or emotional disagreement

• Future directions
LE COMA DÉPASSE
(MEMOIRE PRÉLIMINAIRE)

PAR MM.

P. MOLLARET et M. GOULON

Après quatre années de réflexion, nous croyons venu le moment d'ajouter un chapitre nouveau au domaine traditionnel des comas.

Précisons de suite que ce problème du coma dépasse a été mis, l'année dernièere, au programme de la prochaine Journée de Réanimation de l'Hôpital Claude-Bernard du 7 octobre 1959, en vue d'une mise au point intégrale.

La présente communication, qui n'a ainsi qu'une valeur préliminaire, peut être offerte, peut-être, en hommage à la XXIIIe Réunion Neurologique Internationale, qui a accepté de tenir une de ses séances dans le Centre de Réanimation où fut élaboré ce travail. Précisons également que le coma dépasse a déjà conquis droit de cité dans l'important volume qui vient de paraître de H. Fischgold et P. Mathis (Obnubilations, comas et dupeurs, Masson édit., Paris, 1959, p. 5 et pp. 51-52) ; nous remercions ces auteurs d'être venus se faire présenter les premiers malades et d'avoir donné place à quelques-uns de nos documents.
A Definition of Irreversible Coma

Report of the Ad Hoc Committee of the Harvard Medical School to Examine the Definition of Brain Death

Our primary purpose is to define irreversible coma as a new criterion for death. There are two reasons why there is need for a definition: (1) Improvements in resuscitative and supportive measures have led to increased efforts to save those who are desperately injured. Sometimes these efforts have only partial success so that the result is an individual whose heart continues to beat but whose brain is irreversibly damaged. The burden is great on patients who suffer permanent loss of intellect, on their families, on the hospitals, and on those in need of hospital beds already occupied by these comatose patients. (2) Obsolete criteria for the definition of death can lead to controversy in obtaining organs for transplantation.

Characteristics of Irreversible Coma

An organ, brain or other, that no longer functions and has no possibility of functioning again is for all practical purposes dead. Our first problem is to determine the characteristics of a permanently nonfunctioning brain.

A patient in this state appears to be in deep coma. The condition can be satisfactorily diagnosed by points 1, 2, and 3 to follow. The electroencephalogram (point 4) provides confirmatory data, and when available it should be utilized. In situations where for one reason or another electroencephalographic monitoring is not available, the absence of cerebral function has to be determined by purely

Henry K. Beecher, M.D

JAMA 1968;205: 337-340
“Brain Death”

- Irreversible cessation of all brain clinical function constitutes human death
- Misleading but standard term
- Accepted by physicians and society though persisting confusion about definitions
- Accepted better by physicians than families; opposite of circulatory death which is accepted better by families than physicians

Bernat JL. *Nat Rev Neurology* 2013;9:164-173
Legal Definition of Death in USA

**Uniform Determination of Death Act (UDDA):**

An individual who has sustained either:

1. Irreversible cessation of circulatory and respiratory functions, or
2. Irreversible cessation of all functions of the entire brain, including the brain stem, is dead

A determination of death must be made in accordance with accepted medical standards

President’s Commission. *Defining Death*, 1981
Brain-Circulation Relationship

• The neurological criterion is the fundamental criterion of death: “brain death”
• The circulatory-respiratory criterion of death is valid because, in the absence of CPR, it leads to fulfilling the brain criterion
• Only in the presence of respiratory-circulatory support is the brain criterion tested

“Brain Death” Internationally

• Law in all states in the USA and throughout the developed and developing world
• Practiced in more than 80 countries with varying legality and test requirements
• Critiques for over 40 years have not gained traction with the public:
  – No laws abandoned in any jurisdiction
  – No practices changed by medical societies

Wahlster S et al. *Neurology* 2015;84:1870-1879
“Brain Death” in Europe

• 28 European countries surveyed
• Strong consensus that:
  – Brain death equals human death
  – American Academy of Neurology criteria valid
• Differences among countries on:
  – Prerequisites for determination
  – Number of examinations and interval between
  – Use of ancillary tests
• Desirability of international consensus

Citerio G et al. Neurocrit Care 2014;21:376-382
Citerio G et al. Neurocrit Care 2014;21:376-382
Fig. 3 Number of countries in which the specialists allowed to confirm the diagnosis of brain death is defined by law.
Fig. 2 Minimum observation time between clinical examinations for brain death (hours). Minimum (0 h) and maximum (12 h) are shown. Q1 lower quartile (1 h); M median (3 h); Q2 upper quartile (6 h). The interquartile range for the distribution is 5 h.
Fig. 4 Specialists involved in brain death diagnosis. Professional background of physicians who usually confirm the brain death diagnosis. *Other refers to specialist (8) and non-specialist (8) doctors. Other specialists are: pediatrician in case of brain death determination in children (4), cardiologist (1), medico legal doctor (1), radiologist (1). In some countries, law states minimum experience criteria for non-specialists involved or independence of the transplantation team (7).
“Brain Death” in Spain

- Medical and legal acceptance as death
- Ancillary tests not required
- Two examinations separated by at least 6 hours
- Apnea test defines arterial PCO$_2$ level required
- Three physicians involved in death determination
- Robust program of organ donation with increase in donation following publication of guidelines

Citerio G et al. *Neurocrit Care* 2014;21:376-382
Figure: Monthly evolution of interannual absolute number of deceased organ donors in Spain after implementation of good practice guidelines

Interannual absolute number of deceased organ donors = number of deceased organ donors within past 12 months at a given date.¹

Knowledge of “Brain Death” in Spain

• Among 3,547 surveyed adolescents
  • 38% knew about the concept; said the person was dead
  • 54% were unaware of the concept
  • 8% said the person was not dead

• Among 288 surveyed secondary school teachers
  • 64% knew about the concept; said the person was dead
  • 34% were unaware of the concept
  • 3% said the person was not dead

Febrero B et al. Transplant Proc 2013;45:3586-3588
Rios A et al. Transplant Proc 2012;44:1486-1488
“Brain Death” Intuitive Acceptance

- Surveys show widespread misunderstanding of definitions but conceptual acceptance
- Academic disputes persist but critics for over 40 years have not succeeded in changing laws anywhere or practices recommended by medical societies
- Recent survey: medical professionals say it is more reliable than circulatory death

“Brain Death” in Print Media

- Reviewed 940 articles in leading USA and Canadian newspapers from 2005-2009
- “Brain death” was used colloquially in 39% but defined in only 3.6% (Canada) and 2.7% (USA) articles
- That brain death was a determination of death was noted in < 10% of articles
- Organ donation mentioned in 33.5% (Canada) and 21.2% (USA)

Daoust A, Racine E. J Med Ethics 2014;40:253-259
“Brain Death” in Film and Television

- Two authors reviewed 24 productions of 160,000 in Paley Center for Media and 3.7 million in Internet Movie Database (IMDB)
- None demonstrated complete examination
- Only 2 depicted an apnea test
- Only 13% provided an accurate understanding
- Organ donation was mentioned in 71% but done professionally in 9% and 27%

Figure 2: Authors’ responses to the statement, “After watching this production, I believe the public would have a complete and accurate understanding of brain death.”

“Brain Death” Religious Acceptance

- Roman Catholicism acceptance:
  - Death determination historically a medical issue: Pope Pius XII statement in 1957
  - Statement of acceptance of brain death from Pope John Paul II in August 2000
  - Re-examination in 2006 by Vatican Pontifical Academy of Sciences led to repeat endorsement

Furton EJ. *National Catholic Bioethics Quarterly* 2002;2:455-470
Pontificia Academia Pro Vita 1997-1998

Vatican Casa Santa Marta  November 1997
ADDRESS OF JOHN PAUL II 
TO THE 18th INTERNATIONAL CONGRESS 
OF THE TRANSPLANTATION SOCIETY

Tuesday 29 August 2000

Distinguished Ladies and Gentlemen,

1. I am happy to greet all of you at this International Congress, which has brought you together for a reflection on the complex and delicate theme of transplants. I thank Professor Raffaello Cortesini and Professor Oscar Salvatierra for their kind words, and I extend a special greeting to the Italian Authorities present.

To all of you I express my gratitude for your kind invitation to take part in this meeting and I very much appreciate the serious consideration you are giving to the moral teaching of the Church. With respect for science and being attentive above all to the law of God, the Church has no other aim but the integral good of the human person.

Transplants are a great step forward in science's service of man, and not a few people today owe their lives to an organ transplant. Increasingly, the technique of transplants has proven to be a valid means of attaining the primary goal of all medicine - the service of human life. That is why in the Encyclical Letter Evangelium Vitae I suggested that one way of nurturing a genuine culture of life "is the donation of organs, performed in an ethically acceptable manner, with a view to offering a chance of health and even of life itself to the sick who sometimes have no other hope" (No. 86).
Thus, when the functions of the brain which are, so to speak, at the service of the soul, cease completely because of some defect or perturbation - since the messengers of the sensations and the agents of movement no longer act -, it is as if the soul was no longer present and was not [in the body], and it has gone away.

Denique, dum haece eius tamquam ministeria vitio quolibet seu perturbatione omni modo deficient desistentibus suntitis sentiendi et ministris movendii, tamquam non habens cur addit abscedit [anima].

Saint Augustine, De Gen. ad lit., L. VII, chap. 19; PL 34, 365
Attacks Leading to Refinements

- Choice of the definition of death
- Imprecise correspondence between the definition and criterion of death
- Perceived inadequacies of the advocated whole-brain criterion of death
- The impossibility of stating any uniform definition of death

“Brain Death” Critiques

- Shewmon: not what we mean by death; integration occurs outside the brain;
- Veatch: “higher brain formulation”
- Truog: an unnecessary anachronism
- Taylor: a legal fiction to permit organ donation
- McMahan, Lizza: more than one kind of death
- Chiong: no uniform definition of death

Bernat JL. Nat Rev Neurology 2013;3:164-173
The inadequacy of the integration rationale for the whole-brain criterion was endorsed by the US President’s Council on Bioethics (2008).

Shewmon criticized the Council’s alternative rationale “the inability of the organism to conduct its self-preserving work” has having the same flaw as that which they replaced.

We need greater refinement of “the organism as a whole” to defend the whole-brain criterion.

Shewmon DA. *J Med Philos* 2010;35:256-298
Analysis of Death

• Sequential analysis: proceeds from the conceptual to the measureable
  – **Paradigm**: preconditions that frame analysis
  – **Definition**: make explicit ordinary meaning when we use the word *death*
  – **Criterion**: general measureable standard
  – **Tests**: physicians devise and perform
• Even opponents concur with analysis format

Death: Definition & Criterion

• **Definition**: irreversible cessation of the critical functions of the organism as a whole

• **Criterion**: irreversible cessation of function of a critical number of neurons of the cerebral hemispheres and brain stem ("whole-brain formulation")

• **Tests**: adults: AAN 2010; children: multisociety task force, 2011; others

Bernat JL. *Nat Rev Neurology* 2013;9:164-173
Whole-Brain Criterion of Death

• Determination requires the irreversible cessation of whole-brain function
• Higher brain formulation is popular in academic circles but is not accepted anywhere in the world
• Brain stem criterion accepted in UK
• Requires cessation of clinical functions, not all neuronal activities

Bernat JL. *Am J Bioethics* 2014;14(8): 3-8
Whole-Brain Criterion Features

- Increased intracranial pressure:
  - Transtentorial brain herniation
  - Loss of intracranial blood flow
  - Secondary diffuse neuronal death
- Fail-safe mechanism to assure loss of all brain clinical functions
- Ancillary tests: no intracranial blood flow

Bernat JL. *J Law Med Ethics* 2006;34:35-43
Organism as a Whole

• Not whole organism
• Greater than the sum of component parts
• Organism’s unity, wholeness, integrity
• Life of cells, tissues, organs or other component parts differ from life of organism (as a whole)
• “Brain dead” patient is dead but components remain alive with technological support
• Emergent functions of whole organism

Loeb J. The Organism as a Whole. G.P. Putnam’s Sons, 1916
Emergent Functions

• Function of a whole entity that is not present in any of its component parts
• Derive from ensembles of cells, tissues, and organs; hierarchies of emergent functions
• Cannot be predicted or understood by studying component subunits
• Human conscious awareness is the most exquisite example: an ineffable emergent function of the ensemble of distributed parallel hierarchical networks of brain neurons

Criteria of Life Forms

- **Dynamics** (signs of life): metabolism, regeneration, growth, propagation
- **Integration**: life derives from mutual interaction of its component parts
- **Coordination**: integration of parts is conducted within a certain order
- **Immanency**: characteristics originate from and are intrinsic to the life form

Criteria of an Organism

• **Completion**: the organism is not a component of part of another living entity but is itself an intrinsically independent and completed whole

• **Indivisibility**: no organism can be divided into more than one living organism; if divided, the completed organism resides in one part

Criteria of an Organism

• **Self Reference:** life processes serve the self-preservation of the whole at the expense of component parts

• **Identity:** despite incremental changes in form or gain/loss of component parts, the living being remains one and the same throughout life

Death of an Organism

- **Loss of Immanency**: life processes no longer spring from itself
- **Loss of Self-Reference**: function of parts no longer supports whole
- **Loss of completeness and indivisibility**: components no longer comprise a whole
- These conditions are satisfied by the brain dead human organism

Tests of Death

• Cardiopulmonary tests are adequate in cases without ventilatory support
• Brain death tests must be used when ventilatory support is used or planned
• Tests must have no false-positive determinations and as few false-negatives as possible
Antoine Wiertz (1806-1865)  L’inhumation précipitée  Wiertz Museum, Brussels
A device patented by Count Karnice-Karnicki to assure that, if prematurely buried, a person could make known his or her living state.
**Brain Death: Examination**

- Known structural lesion that accounts for clinical findings
- Exclude all reversible causes
- Unresponsiveness to all stimuli
- Cranial nerve areflexia
- Apnea, tested properly (respiratory therapy protocol)

Wijdicks EFM et al. *Neurology* 2010;74:1911-1918
Brain Death: Medical Controversies

- One or two examinations?
- Value of ancillary ("confirmatory") tests
- Need for standardization
- Therapeutic hypothermia protocols
- Failure to accept by family members
- Religious opposition
- Organ transplantation issues

“Brain Death” Future Directions

- Better education of medical personnel and the public
- Rigorous biophilosophical justification of equivalence of “brain death” and human death: clarify which emergent functions define the organism as a whole
- Greater consensus on societally acceptable accommodations for those who do not accept it
- International standardization of practice criteria
- Determination of the role of ancillary tests

Bernat JL. *Am J Bioethics* 2014;14(8): 3-8