



OPINION ARTICLE

REVISED Brain death debates: from bioethics to philosophy of science [version 2; peer review: 2 approved]

Previously titled: Brain death debates: from bioethics to epistemology

Alberto Molina Pérez

Institute for Advanced Social Studies, Spanish National Research Council (IESA-CSIC), Cordoba, 14004, Spain

V2 First published: 16 Feb 2022, 11:195
<https://doi.org/10.12688/f1000research.109184.1>
 Latest published: 20 Jun 2022, 11:195
<https://doi.org/10.12688/f1000research.109184.2>

Abstract

50 years after its introduction, brain death remains controversial among scholars. The debates focus on one question: is brain death a good criterion for determining death? This question has been answered from various perspectives: medical, metaphysical, ethical, and legal or political. Most authors either defend the criterion as it is, propose some minor or major revisions, or advocate abandoning it and finding better solutions to the problems that brain death was intended to solve when it was introduced. Here I plead for a different approach that has been overlooked in the literature: the philosophy of science approach. Some scholars claim that human death is a matter of fact, a biological phenomenon whose occurrence can be determined empirically, based on science. We should take this claim seriously, whether we agree with it or not. The question is: how do we know that human death is a scientific matter of fact? Taking the philosophy of science approach means, among other things, examining how the determination of human death became an object of scientific inquiry, exploring the nature of the brain death criterion itself, and analysing the meaning of its core concepts such as “irreversibility” and “functions”.

Keywords

Death criteria, Brain death, Bioethics, Epistemology, Philosophy of Science, Functions, Irreversibility, Uniform Death Determination Act



This article is included in the [Sociology of Health gateway](#).

Open Peer Review

Approval Status

	1	2
version 2 (revision) 20 Jun 2022	 view	 view
version 1 16 Feb 2022	 view	 view

1. **Michael Nair-Collins** , Florida State University College of Medicine, Tallahassee, USA
2. **Milena Maglio** , Greater Paris University Hospitals (Assistance Publique-Hôpitaux de Paris), Paris, France
 Université Paris Cite, Paris, France
Vivien García, Université de Lorraine, Nancy, France

Any reports and responses or comments on the article can be found at the end of the article.

Corresponding author: Alberto Molina Pérez (amolina@iesa.csic.es)

Author roles: Molina Pérez A: Conceptualization, Investigation, Writing – Original Draft Preparation

Competing interests: No competing interests were disclosed.

Grant information: The author(s) declared that no grants were involved in supporting this work.

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How to cite this article: Molina Pérez A. **Brain death debates: from bioethics to philosophy of science [version 2; peer review: 2 approved]** F1000Research 2022, **11**:195 <https://doi.org/10.12688/f1000research.109184.2>

First published: 16 Feb 2022, **11**:195 <https://doi.org/10.12688/f1000research.109184.1>

REVISED Amendments from Version 1

In this version, the terms partisanship and epistemology have been removed. Several paragraphs have been rephrased to improve clarity, especially the distinction between absolute irreversibility, relative irreversibility, and permanence (in the last paragraph of the article). A few references have been added.

Any further responses from the reviewers can be found at the end of the article

Introduction

More than 50 years after the neurological determination of death—also known as “brain death”—was admitted as a new criterion of death (Beecher *et al.*, 1968), and despite its broad acceptance in medical practice (Wahlster *et al.*, 2015; Lewis *et al.*, 2020b; Greer *et al.*, 2020), brain death continues to raise confusion (Dalle Ave & Bernat, 2018; Rodríguez-Arias *et al.*, 2020), disagreement among scholars (Joffe *et al.*, 2007, 2012; Youngner *et al.*, 1989), and opposition among the general public (Skowronski *et al.*, 2021; Shah *et al.*, 2015). Brain death has been and still remains debated. In 2018, the Harvard School of Medicine organised a three-day conference on current controversies related to determining death (Hastings Center Report, 2018). In 2020, the World Brain Death Project published consensus recommendations on determination of brain death (Greer *et al.*, 2020). The same year, the US Uniform Law Commission (ULC) appointed a Study Committee on updating the 1981 Uniform Determination of Death Act (UDDA), which is the legal statute adopted in more than 40 states in the United States of America and which has had a significant influence in the laws throughout the world. In 2021, more than 100 scholars endorsed the Statement in Support of Revising the UDDA and in Opposition to a Proposed Revision (Shewmon, 2021).

According to the current neurological criterion, as defined in the UDDA and other laws around the world, death is determined by the “irreversible cessation of all functions of the entire brain, including the brainstem”. Recent proposals to revise this criterion focus on the cessation of a limited number of functions, especially consciousness and some brainstem functions, including spontaneous respiration, and require the permanent (*i.e. will not reverse*)—but not necessarily irreversible (*i.e. cannot reverse*)—cessation of these functions (Gardiner *et al.*, 2020; Lewis *et al.*, 2020a).

Foreseeable advances in medicine and neurosciences may completely challenge our current concept of human death by opening yet unknown possibilities to restore or reactivate consciousness, cognition, and other brain functions. Current and future technology, such as brain–computer interfaces (Kübler, 2019; Abdalmalak *et al.*, 2020) linked to brain-stimulation technology (Xia *et al.*, 2019; Fox *et al.*, 2020; Hakon *et al.*, 2020) and machine learning (Iturrate *et al.*, 2020), may allow us to detect brain activity and function unnoticed today (Owen, 2019), and to artificially restore some brain functions, for example through neural stem cell transplantation therapy (Otsuki & Brand, 2018; Zhang *et al.*, 2019) or other therapeutic interventions (Thibaut *et al.*, 2019), thus challenging the irreversibility of death (Brummitt, 2018).

In 2019, researchers recirculated pigs’ brains, through a device called BrainEx, four hours after their decapitation (Vrselja *et al.*, 2019). Glial cells were still able to maintain their inflammatory responses and neurons were responding to depolarizing current stimulation. Would such a device be able to restore human brain activities in similar conditions, stretching our knowledge on irreversibility of seemingly lost brain function? If so, would these patients be considered alive? It depends on whether those neural activities are mere activities or if they exert specific functions, like cognition or perception. Indeed, human death is usually determined by the irreversible cessation of either respiratory and circulatory functions, or all brain functions (President’s Commission, 1981), while simple neuronal activities are ignored. However, the notions of activity and function are not clearly defined in the literature, and these notions are often used interchangeably, while their distinction may be key to define death (Shemie *et al.*, 2014; Greer *et al.*, 2020).

In transplantation medicine, a clear and unambiguous determination of death is mandatory. Indeed, one of the main ethical norms in transplantation is the dead donor rule (Dalle Ave *et al.*, 2020), which states that an individual should be declared dead before the procurement of any vital organs. This norm ensures that individuals will not be killed for transplantation purposes, and that they won’t suffer during organ recovery. What would happen if there were no clear criteria for determining death? Are certainty and universality required for the determination of death or could some degree of uncertainty and diversity be acceptable?

Advances in medical technology may enable perception, motricity, cognition, or communication, to be artificially prolonged beyond a state in which they would normally be irreversibly destroyed. What would that mean for our understanding of what it is to be a human person? What kind of quality of life would such technology offer? Would that life be worth living? How would it impact social justice and equality? How would it affect personal identity and human

rights? What would be the future of humankind if, in our quest to surmount mortality, we could eliminate the very concept of death through technology and neurosciences (Sandberg *et al.*, 2008; Bamford & Danaher, 2017; Harari, 2018)?

These questions are of a philosophical nature and belong, in particular, to the domain of moral philosophy. To this day, most academic debates around brain death have been and are bioethical. However, I believe that a different philosophical approach can shed light on old controversies and help either settle open disputes or, on the contrary, raise new questions. I am talking about the philosophy of science. Death criteria are supposed to have an epistemic or scientific value. Some scholars claim, and most physicians certainly agree, that human death is a matter of fact, a biological phenomenon whose occurrence can be determined empirically, based on scientific knowledge and methods, and that medicine has epistemic authority over it. We should take this claim seriously, whether we agree with it or not, and analyse it from the perspective of the philosophy of science.

50 years of bioethical controversies around death determination

Since it was introduced in 1968, the brain criterion of death is at the centre of a heated debate that has produced a vast and complex literature. The debate among bioethicists has had some key recurring features (Belkin, 2018): first and foremost, argument over alleged flaws in the conceptual logic and consistency of the rationale for equating brain death with human death; second, efforts to fix perceived limitations of brain death-based practices to optimize transplantation; and third, a basic unease provoked by the experience of using the criteria and managing a warm and heart-beating body in a state previously known as “irreversible coma.”

With regard to the second feature, the 2018 special Hastings Center Report illustrates the central role played by the dead donor rule in bioethical debates (see also: Arnold & Youngner, 1993; Veatch, 2004; Nair-Collins *et al.*, 2015; Rodríguez-Arias, 2018; Dalle Ave *et al.*, 2020).

With regard to the first feature, one of the first and still open controversies concerns the nature of the justification of introducing brain death as a criterion of death, some claiming it had been initially proposed to solve practical and moral problems, including the opportunity of recovering organs without violating the “dead donor rule” (Pernick, 1999; Rodríguez-Arias, 2017).

In 1981, Bernat, Culver and Gert proposed the “whole-brain” concept of death, a scientific and philosophical justification based on the idea that life requires the integration of the organism and that the brain is the organ responsible for its integration (Bernat *et al.*, 1981). Apart from the UK and a handful of nations, most developed countries soon adopted the whole-brain rationale (Wijdicks, 2002). However, Bernat and colleagues’ claim that individuals with a cessation of all brain functions are not integrated organisms but merely a group of artificially maintained subsystems has been challenged repeatedly and decisively (Youngner & Bartlett, 1983; Gervais, 1986; Halevy & Brody, 1993; Lizza, 1993; Seifert, 1993; Veatch, 1993; Taylor, 1997; Truog, 1997; Brody, 1999; Halevy, 2001; Potts *et al.*, 2001; Shewmon, 1998, 2001; Byrne & Weaver, 2004; Zamperetti *et al.*, 2004; Joffe, 2007; Shemie *et al.*, 2014; Brugger, 2016; Verheijde *et al.*, 2018). As a consequence, some advocates of the brain criterion have proposed refined versions of this rationale in terms of “organism-as-a-whole” (President’s Council, 2008; Moschella, 2019; Bernat, 2019; Huang & Bernat, 2019; Omelianchuk, 2021), whereas critics have proposed alternatives in terms of “embodied consciousness” (Veatch, 2005; Veatch & Ross, 2016), personhood (Green & Wikler, 1980; Bartlett & Youngner, 1988; Lizza, 2006), or homeostasis (Nair-Collins, 2018). Most of these propositions are compatible with a single brain-based criterion of death, although for different reasons and with varying implications for the boundary between life and death.

A different way of addressing the issue of determining death is to focus on its intrinsically legal, ethical, and political nature, by arguing that brain death is a legal fiction (Shah *et al.*, 2011), advocating for a pluralistic policy that would allow stakeholders to choose among several definitions of death (Veatch, 1976; Bagheri, 2007; Molina-Pérez *et al.*, 2008; Ross, 2018), requiring consent for brain death testing (Berkowitz & Garrett, 2020), and calling for an open public conversation on end-of-life practices (Youngner & Arnold, 2001; Rodríguez-Arias & Veliz, 2013).

Taking the philosophy of science approach to human death

Death debates focus on a single question: Are death criteria, and especially the brain criterion, *good* criteria? They may be good in a scientific or medical sense because patients declared dead according to these criteria are actually dead, although there may be false positives and false negatives (Bernat & Dalle Ave, 2019). They may be good in a moral or policy sense because, for instance, they allow practices that are ethically and socially valuable, such as organ procurement. They may be good for a combination of reasons. These reasons have their advocates and opponents, both committed to truth and quality scholarship and based on good evidence and well-considered scientific and/or philosophical arguments. Almost all authors have either defended the death criteria, proposed some minor or major revisions and improvements of the

criteria, or plead to abandon them—especially the brain criterion—and promoted better solutions to the problems these criteria were meant to solve.

Regardless of whether death criteria are true or accurate, or whether they are good policy, we should take a step back to examine the issue of “determining death” as an object of scientific inquiry by itself. This is the philosophy of science approach that I am advocating. Taking this approach means examining how the determination of human death became a scientific issue and why medicine claims epistemic authority over it. It means asking, for example, whether death criteria are heuristics or definitions, and whether the determination of the patient’s death is the conclusion of a syllogism. To adopt this approach is also to analyse the meaning of the core concepts of death criteria, such as “irreversibility” and “functions”. Ideally, the answers to these questions could be shared by most scholars, regardless of their position on the issue of brain death.

Analyses of death definitions and criteria that take science seriously are scarce (Nair-Collins, 2015). In addition to the question of whether the main justification for brain death is rather scientific/epistemic or moral/practical, debates with a more philosophy of science orientation have revolved around two central questions: the nature of death as an event or a process (Morison, 1971; Pallis, 1983), and the requirement of irreversibility (as opposed to permanence) for the loss of functions (Bernat, 2010; Dalle Ave & Bernat, 2016; Gardiner & McGee, 2017). To my knowledge, few other publications have adopted what I consider a philosophy of science approach, with some notable exceptions (e.g.: Walton, 1981; Chiong, 2005; Nair-Collins, 2015; Meier, 2020).

Taking this approach may help settle old debates and also bring novel insights. For example, death is characterised in medicine and described or defined in most legislations as the irreversible cessation of specific functions: either circulatory and respiratory functions or all brain functions. However, the meaning of the concepts used, especially the concept of function, requires clarification. These concepts are rarely defined in the medical literature and their interpretation varies between professionals. Hence, the consistent interpretation of the death criteria that rely on these concepts is not warranted, which may cause a lack of uniformity in death determination.

By applying to the criteria of death an analysis similar to the one used in the philosophy of biology to define biological functions (Molina-Pérez, 2017), Anne Dalle Ave, James Bernat and I revealed that the current US law is conceptually inconsistent (Molina-Pérez *et al.*, forthcoming). Indeed, the UDDA uses the phrase “cessation of functions” with two different and conflicting meanings for its two criteria. On the one hand, it means the cessation of spontaneous functions, i.e. the cessation of the organ’s spontaneous functioning. On the other hand, it means the cessation of either spontaneous or artificially supported functions. We also showed that this inconsistency in the UDDA—and other laws throughout the world that acknowledge both criteria—derives from the conceptual assumptions underlying James Bernat’s 1981 “Whole-Brain” rationale for equating brain death with death. By conducting a logical deconstruction of the rationale, we showed that its premises are false and that, therefore, its conclusions cannot be drawn.

This type of analysis leads to policy recommendations and ethical considerations. After exploring possible ways to address the inconsistency, we found only two viable options: one is to keep the law as it is while admitting that death is a legal fiction, and the other is to pick a single criterion of death, either a circulatory-respiratory criterion, which would imply that “brain dead” patients maintained in the ICU are not dead, thus disrupting organ procurement (DBD) programmes, or a single brain criterion, which may affect medical practice and hinder programmes of organ recovery after circulatory death (DCDD) (see Rodríguez-Arias *et al.*, 2013; Dalle Ave *et al.*, 2016; Ortega-Deballon & Rodríguez-Arias, 2018).

In order to better assess death determination criteria, further analyses of the concept of function are needed. On the one hand, brain functions are at the intersection of three different but related scientific fields: biology, psychology, and neurology. While functions in general have been very much discussed in philosophy of biology (Garson, 2016; Molina-Pérez, 2017) and to some extent in philosophy of psychology (Ariew *et al.*, 2002; Parot, 2008), they have received much less attention from either physicians or philosophers of medicine (Roux, 2014; Shewmon & Verheijde, 2020). A distinction needs to be made between the brain’s functions, as considered by physiology, and the brain’s functionality, as considered by neuroscience (Northoff & Tumati, 2019). In the context of neurophilosophy and brain-computer interfaces, brain’s functionality requires visible and coordinated behavioural responses in reference to specific environmental contexts. In other words, brain functions are not merely considered as physiological mechanisms, but also viewed in terms of whether they serve their “intended behavioural purpose”.

On the other hand, as critical care medicine keeps pushing forward its resuscitation capabilities, we still do not know where to find—and whether there are—absolute limits to the reversibility of functional losses. The cessation of brainstem

functions, such as the initiation of respiration, can now be reversed with life-support technologies such as mechanical ventilation. This means that, although the spontaneous control of these functions by the brain is lost, the functions themselves can still be executed and controlled by artificial means (Meier, 2020; Molina-Pérez *et al.*, forthcoming). Future advances, including BCIs, might help support, restore or replace not only brainstem functions, but also those necessary for cognition, and may, consequently, alter the threshold of irreversibility. This raises the question of the limits and meaning of irreversibility in the determination of death.

The cessation of functions can be interpreted in at least three different ways: as absolutely irreversible, relatively irreversible, or permanent (Tomlinson, 1993; Bernat, 2010). Absolute irreversibility means that the cessation of functions cannot be reversed under any circumstances, regardless of any present or future medical and technological interventions. It could be understood in the sense of a physical or biological impossibility to, past some point, reverse the dying process. Relative irreversibility means that the cessation of functions cannot be reversed in some context, but might be reversed in a different one. It could be understood as an incapacity to reverse the loss of functions because of a lack of human competence, technical means, resources, etc. Most circulatory and respiratory arrests were irreversible in the 19th century, before the development of resuscitation techniques, but can now be reversed because these means now exist. Relative irreversibility thus depends on when and where the capacity to reverse the loss of functions is available and feasible, which in turn depends on other considerations, including the ethical, social, economic, and political framework. However, it is not always clear which of these two interpretations of the notion of irreversibility (absolute or relative) is used in current definitions and criteria of death. Finally, permanence means that the loss of functions will not reverse spontaneously and that, although we would be capable of reversing it, we will not do so. This may occur for instance to respect the patient's living will.

Data availability

No data are associated with this article.

Acknowledgments

This article is inspired and partly derives from the introduction of a research project application, coordinated by Anne Dalle Ave, with contributions by Anne Dalle Ave, Ralf Jox, Andrea Kübler, Georg Northoff, Bernabé Robles del Olmo, Fernando Vidal, and myself. This article was written as part of the project PID2020-119717GA-100 funded by Spain's Ministry of Science and Innovation.

References

- Abdalmalak A, Milej D, Yip LCM, *et al.*: **Assessing Time-Resolved fNIRS for Brain-Computer Interface Applications of Mental Communication.** *Front. Neurosci.* 2020; **14**.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Ariew A, Cummins R, Perlman M: *Functions: New essays in the philosophy of psychology and biology.* Oxford University Press; 2002.
- Arnold RM, Youngner SJ: **The Dead Donor Rule: Should We Stretch It, Bend It, or Abandon It?** *Kennedy Inst. Ethics J.* 1993; **3**: 263–278.
[Publisher Full Text](#)
- Bagheri A: **Individual choice in the definition of death.** *J. Med. Ethics.* 2007; **33**(3): 146–149.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Bamford S, Danaher J: **Transfer of personality to a synthetic human ('mind uploading') and the social construction of identity.** *J. Conscious. Stud.* 2017; **24**(11-12): 6–30.
- Bartlett ET, Youngner SJ: **Human Death and the Destruction of the Neocortex.** Zaner RM, editor. *Death: Beyond Whole-Brain Criteria.* Netherlands: Springer; 1988; (pp. 199–216).
[Publisher Full Text](#)
- Beecher HA, *et al.*: **A definition of irreversible coma: Report of the Ad Hoc Committee of the Harvard Medical School to examine the definition of brain death.** *JAMA.* 1968; **205**: 337–340.
[Publisher Full Text](#)
- Belkin G: **A Path Not Taken: Beecher, Brain Death, and the Aims of Medicine.** *Hastings Cent. Rep.* 2018; **48**: S10–S13.
[Publisher Full Text](#)
- Berkowitz I, Garrett JR: **Legal and Ethical Considerations for Requiring Consent for Apnea Testing in Brain Death Determination.** *Am. J. Bioeth.* 2020; **20**(6): 4–16.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Bernat JL: **How the distinction between 'irreversible' and 'permanent' illuminates circulatory-respiratory death determination.** *J. Med. Philos.* 2010; **35**(3): 242–255.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Bernat JL: **Refinements in the Organism as a Whole Rationale for Brain Death.** *Linacre Q.* 2019; **86**(4): 347–358.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Bernat JL, Culver CM, Gert B: **On the Definition and Criterion of Death.** *Ann. Intern. Med.* 1981; **94**: 389–394.
[Publisher Full Text](#)
- Bernat JL, Dalle Ave AL: **Aligning the Criterion and Tests for Brain Death.** *Cambridge Quarterly of Healthcare Ethics: CQ: The International Journal of Healthcare Ethics Committees.* 2019; **28**(4): 635–641.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Brody BA: **How much of the brain must be dead?** Youngner A, Schapiro, editors. *The Definition of Death: Contemporary Controversies.* Johns Hopkins University Press; 1999.
- Brugger EC: **Are Brain Dead Individuals Dead? Grounds for Reasonable Doubt.** *J. Med. Philos.* 2016; **41**(3): 329–350.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Brummitt JL: **The Frontiers of Immortality.** Bess M, Pasulka DW, editors. *Posthumanism: an Introductory Handbook.* Farmington Hills: Cengage Gale; 2018.
- Byrne PA, Weaver WF: **'Brain death' is not death.** *Adv. Exp. Med. Biol.* 2004; **550**: 43–49.
[Publisher Full Text](#)
- Chiong W: **Brain Death without Definitions.** *The Hastings Center Report.* 2005; **35**: 20.
- Dalle Ave AL, Bernat JL: **Using the brain criterion in organ donation after the circulatory determination of death.** *J. Crit. Care.* 2016; **33**:

- 114–118.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Dalle Ave AL, Bernat JL: **Inconsistencies Between the Criterion and Tests for Brain Death.** *J. Intensive Care Med.* 2018; **35**: 772–780.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Dalle Ave AL, Shaw D, Bernat JL: **An analysis of heart donation after circulatory determination of death.** *J. Med. Ethics.* 2016; **42**(5): 312–317.
[Publisher Full Text](#)
- Dalle Ave AL, Sulmasy DP, Bernat JL: **The ethical obligation of the dead donor rule.** *Med. Health Care Philos.* 2020; **23**(1): 43–50.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Fox KCR, et al.: **Intrinsic network architecture predicts the effects elicited by intracranial electrical stimulation of the human brain.** *Nat. Hum. Behav.* 2020; **1**(14).
- Gardiner D, McGee A: **Death, permanence and current practice in donation after circulatory death.** *QJM: Monthly Journal of the Association of Physicians.* 2017; **110**(4): 199–201.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Gardiner D, McGee A, Bernat JL: **Permanent brain arrest as the sole criterion of death in systemic circulatory arrest.** *Anaesthesia.* 2020; **75**: 1223–1228.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Garson J: *A Critical Overview of Biological Functions.* Springer; 2016.
- Gervais KG: *Redefining Death.* Yale University Press; 1986.
- Green MB, Wikler D: **Brain Death and Personal Identity.** *Philos. Public Aff.* 1980; **9**: 105–133.
[PubMed Abstract](#)
- Greer DM, et al.: **Determination of Brain Death/Death by Neurologic Criteria: The World Brain Death Project.** *JAMA.* 2020; **324**: 1078.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Hakon J, et al.: **Transcutaneous Vagus Nerve Stimulation in Patients With Severe Traumatic Brain Injury: A Feasibility Trial.** *Neuromodulation.* 2020; **23**: 859–864.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Halevy A: **Beyond Brain Death?** *J. Med. Philos.* 2001; **26**(5): 493–501.
[Publisher Full Text](#)
- Halevy A, Brody BA: **Brain Death: Reconciling Definitions, Criteria, and Tests.** *Ann. Intern. Med.* 1993; **119**(6): 519–525.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Harari YN: *21 lessons for the 21st century.* London: Jonathan Cape; 2018.
- Hastings Center Report: **Defining Death: Organ Transplantation and the Fifty-Year Legacy of the Harvard Report on Brain Death.** 2018; **48**(S4).
- Huang AP, Bernat JL: **The Organism as a Whole in an Analysis of Death.** *J. Med. Philos.* 2019; **44**: 712–731.
[Publisher Full Text](#)
- Iturrate I, Chavarriga R, Millán JDR: **General principles of machine learning for brain-computer interfacing.** *Handb. Clin. Neurol.* 2020; **168**: 311–328.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Joffe AR: **The Neurological Determination of Death: What Does it Really Mean?** *Issues in Law & Medicine; Terre Haute.* 2007; **23**(2): 119–140.
- Joffe AR, Anton N, Mehta V: **A survey to determine the understanding of the conceptual basis and diagnostic tests used for brain death by neurosurgeons in Canada.** *Neurosurgery.* 2007; **61**: 1039–1047; discussion 1046–1047.
[Publisher Full Text](#)
- Joffe AR, Anton NR, Duff JP, et al.: **A survey of American neurologists about brain death: understanding the conceptual basis and diagnostic tests for brain death.** *Ann. Intensive Care.* 2012; **2**: 4.
[Publisher Full Text](#)
- Kübler A: **The history of BCI: From a vision for the future to real support for personhood in people with locked-in syndrome.** *Neuroethics.* 2019; **13**: 163–180.
[Publisher Full Text](#)
- Lewis A, Bonnie RJ, Pope T: **It's Time to Revise the Uniform Determination of Death Act.** *Ann. Intern. Med.* 2020a; **172**: 143–144.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Lewis A, et al.: **Determination of death by neurologic criteria around the world.** *Neurology.* 2020b; **95**: e299–e309.
[Publisher Full Text](#)
- Lizza JP: **Persons and death: What's metaphysically wrong with our current statutory definition of death?** *J. Med. Philos.* 1993; **18**(4): 351–374.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Lizza JP: *Persons, Humanity, and the Definition of Death.* Johns Hopkins University Press; 2006.
- Meier LJ: **The Demise of Brain Death.** *Br. J. Philos. Sci.* 2020; **000**.
[Publisher Full Text](#)
- Molina-Pérez A, Rodríguez-Arias D, Youngner SJ: **Should individuals choose their definition of death?** *J. Med. Ethics.* 2008; **34**(9): 688–689.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Molina-Pérez A: **Téléologie et fonctions en biologie. Une approche non causale des explications téléo-fonctionnelles.** PhD dissertation. Universidad Autónoma de Madrid, Spain. 2017.
[Publisher Full Text](#)
- Molina-Pérez A, Dalle Ave A, Bernat JL: **Inconsistency between the circulatory and the brain death criteria of death in the Uniform Determination of Death Act.** *J. Med. Philos.* forthcoming; Preprint:
[Publisher Full Text](#)
- Morison RS: **Death: Process or event?** *Science.* 1971; **173**(3998): 694–698.
[Publisher Full Text](#)
- Moschella M: **The human organism is not a conductorless orchestra: A defense of brain death as true biological death.** *Theor. Med. Bioeth.* 2019; **40**(5): 437–453.
[Publisher Full Text](#)
- Nair-Collins M, Green SR, Sutin AR: **Abandoning the dead donor rule? A national survey of public views on death and organ donation.** *J. Med. Ethics.* 2015; **41**(4): 297–302.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Nair-Collins M: **Taking Science Seriously in the Debate on Death and Organ Transplantation.** *Hastings Cent. Rep.* 2015; **45**(6): 38–48.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Nair-Collins M: **A Biological Theory of Death: Characterization, Justification, and Implications.** *Diametros.* 2018; **55**: 27–43.
[Publisher Full Text](#)
- Northoff G, Tumati S: **"Average is good, extremes are bad" – Non-linear inverted U-shaped relationship between neural mechanisms and functionality of mental features.** *Neurosci. Biobehav. Rev.* 2019; **104**: 11–25.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Omelianchuk A: **Brain Death as the End of a Human Organism as a Self-moving Whole.** *The Journal of Medicine and Philosophy: A Forum for Bioethics and Philosophy of Medicine.* 2021; **46**(5): 530–560.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Ortega-Deballon I, Rodríguez-Arias D: **Uncontrolled DCD: When Should We Stop Trying to Save the Patient and Focus on Saving the Organs?** *Hast. Cent. Rep.* 2018; **48**: S33–S35.
[Publisher Full Text](#)
- Otsuki L, Brand AH: **Cell cycle heterogeneity directs the timing of neural stem cell activation from quiescence.** *Science.* 2018; **360**(6384): 99–102.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Owen AM: **The Search for Consciousness.** *Neurology.* 2019; **102**(3): 526–528.
- Pallis C: **Whole-brain death reconsidered—Physiological facts and philosophy.** *J. Med. Ethics.* 1983; **9**(1): 32–37.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Parot F: *Les fonctions en psychologie.* Paris: Mardaga; 2008.
- Pernick MS: **Brain Death in a Cultural context.** Youngner SJ, Arnold R, Schapiro R, editors. *The definition of death: contemporary controversies.* Johns Hopkins UP; 1999; pp. 3–33.
- Potts M, Byrne PA, Nilges RG, et al.: *Beyond Brain Death: The Case Against Brain Based Criteria for Human Death.* Springer Science & Business Media; 2001.
- President's Commission: **Defining Death: A Report on the Medical, Legal, and Ethical Issues in the Determination of Death.** President's Commission for the Study of Ethical Problem in Medicine and Biomedical and Behavioral Research. Washington, DC. 1981.
- The President's Council on Bioethics: **Controversies in the Determination of Death: A White Paper of the President's Council on Bioethics.** 2008. (p. 168).
- Rodríguez-Arias D, Ortega-Deballon I, Smith MJ, et al.: **Casting light and doubt on uncontrolled DCD protocols.** *Hast. Cent. Rep.* 2013; **43**(1): 27–30.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Rodríguez-Arias D, Véliz C: **The death debates: A call for public deliberation.** *Hast. Cent. Rep.* 2013; **43**(6): 34–35.
[Publisher Full Text](#)
- Rodríguez-Arias D: **Juntas y revueltas. La muerte cerebral fue concebida para facilitar la donación de órganos.** *Dilemata.* 2017; **23**: 57–87.
- Rodríguez-Arias D: **The Dead Donor Rule as Policy Indoctrination.** *Hast. Cent. Rep.* 2018; **48**: S39–S42.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Rodríguez-Arias D, Molina-Pérez A, Díaz-Cobacho G: **Death Determination and Clinicians' Epistemic Authority.** *Am. J. Bioeth.* 2020; **20**: 44–47.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Ross LF: **Respecting Choice in Definitions of Death.** *Hast. Cent. Rep.* 2018; **48**(S4): S53–S55.
[PubMed Abstract](#) | [Publisher Full Text](#)

- Roux E: **The concept of function in modern physiology.** *J. Physiol.* 2014; **592**(11): 2245–2249.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Sandberg A, Bostrom N: *Whole brain emulation: A roadmap. Technical report #2008-3.* Future of Humanity Institute, Oxford University; 2008.
- Seifert J: **Is Brain Death' Actually Death?** *Monist.* 1993; **76**: 175–202.
[Publisher Full Text](#)
- Shah SK, Truog RD, Miller FG: **Death and legal fictions.** *J. Med. Ethics.* 2011; **37**: 719–722.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Shah SK, Kasper K, Miller FG: **A narrative review of the empirical evidence on public attitudes on brain death and vital organ transplantation.** *J. Med. Ethics.* 2015; **41**(4): 291–296.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Shemie SD, et al.: **International guideline development for the determination of death.** *Intensive Care Med.* 2014; **40**(6): 788–797.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Shewmon A: **Chronic 'brain death': Meta-analysis and conceptual consequences.** *Neurology.* 1998; **51**(6): 1538–1545.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Shewmon A: **The Brain and Somatic Integration: Insights Into the Standard Biological Rationale for Equating "Brain Death" With Death.** *J. Med. Philos.* 2001; **26**(5): 457–478.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Shewmon DA, Verheijde JL: **Evidence-based guideline update for determining brain death in adults.** 2020.
[Reference Source](#)
- Shewmon DA: **Statement in Support of Revising the Uniform Determination of Death Act and in Opposition to a Proposed Revision.** *J. Med. Philos.* 2021.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Skowronski G, O'Leary MJ, Critchley C, et al.: **Death, dying and donation: Community perceptions of brain death and their relationship to decisions regarding withdrawal of vital organ support and organ donation.** *Intern. Med. J.* 2020; **50**(10): 1192–1201.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Taylor RM: **Reexamining the definition and criteria of death.** *Semin. Neurol.* 1997; **17**(3): 265–270.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Thibaut A, Schiff N, Giacino J, et al.: **Therapeutic interventions in patients with prolonged disorders of consciousness.** *Lancet Neurol.* 2019; **18**: 600–614.
[Publisher Full Text](#)
- Tomlinson T: **The Irreversibility of Death: Reply to Cole.** *Kennedy Inst. Ethics J.* 1993; **3**(2): 157–165.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Truog RD: **Is It Time to Abandon Brain Death?** *Hast. Cent. Rep.* 1997; **27**(1): 29–37.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Veatch RM: *Death, Dying, and the Biological Revolution.* Yale University Press; 1976.
- Veatch RM: **The Impending Collapse of the Whole-Brain Definition of Death.** *Hast. Cent. Rep.* 1993; **23**(4): 18–24.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Veatch RM: **Abandon the Dead Donor Rule or Change the Definition of Death?** *Kennedy Inst. Ethics J.* 2004; **14**(3): 261–276.
[Publisher Full Text](#)
- Veatch RM: **The Death of Whole-Brain Death: The Plague of the Disaggregators, Somaticists, and Mentalists.** *J. Med. Philos.* 2005; **30**(4): 353–378.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Veatch RM, Ross LF: *Defining death: The case for choice.* Georgetown UP; 2016.
- Verheijde JL, Rady MY, Potts M: **Neuroscience and Brain Death Controversies: The Elephant in the Room.** *J. Relig. Health.* 2018; **57**(5): 1745–1763.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Vrselja Z, et al.: **Restoration of brain circulation and cellular functions hours post-mortem.** *Nature.* 2019; **568**: 336–343.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Wahlster S, et al.: **Brain death declaration: practices and perceptions worldwide.** *Neurology.* 2015; **84**(18): 1870–1879.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Walton DN: **Epistemology of Brain Death Determination.** *Metamedicine.* 1981; **2**: 259–274.
[Publisher Full Text](#)
- Wijdicks EFM: **Brain death worldwide: Accepted fact but no global consensus in diagnostic criteria.** *Neurology.* 2002; **58**: 20–25.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Xia X, Wang Y, Li C, et al.: **Transcranial magnetic stimulation-evoked connectivity ... with disorders of consciousness.** *Neuroreport.* 2019; **30**(18): 1307–1315.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Youngner SJ, Bartlett ET: **Human death and high technology: The failure of the whole-brain formulations.** *Ann. Intern. Med.* 1983; **99**(2): 252–258.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Youngner SJ, et al.: **'Brain death' and organ retrieval. A cross-sectional survey of knowledge and concepts among health professionals.** *JAMA.* 1989; **261**: 2205–2210.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Youngner SJ, Arnold RM: **Philosophical debates about the definition of death: Who cares?** *J. Med. Philos.* 2001; **26**(5): 527–537.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Zamperetti N, Bellomo R, Defanti CA, et al.: **Irreversible apnoeic coma 35 years later. Towards a more rigorous definition of brain death?** *Intensive Care Med.* 2004; **30**(9): 1715–1722.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Zhang GL, Zhu ZH, Wang YZ: **Neural stem cell transplantation therapy for brain ischemic stroke: Review and perspectives.** *World J. Stem Cells.* 2019; **11**(10): 817–830.
[PubMed Abstract](#) | [Publisher Full Text](#)

Open Peer Review

Current Peer Review Status:  

Version 2

Reviewer Report 04 July 2022

<https://doi.org/10.5256/f1000research.126017.r141312>

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Michael Nair-Collins 

Department of Behavioral Sciences and Social Medicine, Florida State University College of Medicine, Tallahassee, FL, USA

No further comments. I congratulate the author on a thoughtful and well-informed manuscript.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Bioethics, philosophy, brain death

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 27 June 2022

<https://doi.org/10.5256/f1000research.126017.r141313>

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Milena Maglio 

¹ Clinical Ethics Center, Greater Paris University Hospitals (Assistance Publique-Hôpitaux de Paris), Paris, France

² SPHERE, Université Paris Cite, Paris, France

Vivien García

École de Santé Publique de Nancy, Université de Lorraine, Nancy, France

No further comments

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Milena Maglio: moral philosophy, bioethics and clinical ethics. Vivien García: moral and political philosophy, ethics and philosophy of technology.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 31 March 2022

<https://doi.org/10.5256/f1000research.120659.r123955>

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Milena Maglio 

¹ Clinical Ethics Center, Greater Paris University Hospitals (Assistance Publique-Hôpitaux de Paris), Paris, France

² SPHERE, Université Paris Cite, Paris, France

Vivien García

École de Santé Publique de Nancy, Université de Lorraine, Nancy, France

In “Brain death debates: from bioethics to epistemology”, Alberto Molina Pérez recalls the still controversial character of the neurological determination of death. He also maintains that “to this day, most academic debates around brain death have been and are bioethical”. To support this claim, he draws on extensive literature on the topic; this is undoubtedly one of the great qualities of his contribution. But the main thesis of this opinion article goes further, Molina Pérez argues for a shift of the debate toward “epistemology or, to be more accurate, ... philosophy of science”. More exactly, he suggests examining “the determination of death as an object of scientific inquiry”. Aiming at illustrating the relevance of the change of approach he pleads for, Molina Pérez briefly analyses two core concepts of death criteria — “irreversibility” and “functions” — and shows that each of them bear meaning which are different and possibly conflicting.

The main strength of the paper lies in this demonstration, in particular, in the analysis of the concept of “functions”. The distinction between “brain functions” and “brain functionality” is quite convincing and original. Although promising, the analysis of the concept of “irreversibility” is not so clear. Here come the first suggested revision. On page 3 (§2), the author refers to a distinction between “permanent” and “irreversible” cessation of “functions”. In the first case, he says, the cessation “will not reverse” but it is “not necessarily irreversible”. In the second case, the cessation “cannot reverse”. However, on page 5 (last §). Molina Pérez presents 3 possible interpretations of “irreversibility”: “as either absolute, relative, or permanent”. Presented this way, the permanent cessation of a functions seems to be one type of irreversibility. Moreover, only 2 of the 3 terms are

explained, so it is not clear if relative and permanent “irreversibility” can be taken as synonyms. We suggest that the author clarify the formulations of these two paragraphs.

Another possible criticism (which leads to the suggestion of a second minor revision) could be that the author raises many interesting questions without addressing them, i.e: “What a death criterion is: is it a heuristic or a definition? Is it descriptive, stipulative or performative? Is it a rule of inference, and if so, what is its logical structure? For example, is the determination of the death of an individual the conclusion of a syllogism?”

This is problematic because:

1. these questions are clearly related to the main goal of this paper: “examining how the determination of human death became a scientific issue and why medicine claims epistemic authority over it”;
2. according to the author, here lies all the interest of his “epistemological or philosophy of science approach”.

If the author has already addressed these questions elsewhere, or plans to do so, he should at least provide references. If not, he could reduce the number of questions and focus on the relevant ones for the present article.

As pointed out in Michael Nair-Collins' review, Molina Pérez should make clear what he means by “epistemology” and “philosophy of science”. As non-native English speakers, and academics trained in continental philosophy, our understanding of how Molina Pérez uses these words is probably different from Nair-Collins' one. To prevent misunderstandings (and this is the third revision suggested), the author should definitely clarify his take on the matter.

Beyond these terminological concerns, and without suggesting any revision this time, we would like to stress that the core thesis of the paper — the need for a shift “from bioethics to epistemology” — is not self-evident. As a matter of fact, after reporting the outcomes of a forthcoming study, Molina Pérez argues that the “type of analysis [he supports] leads to policy recommendations and ethical considerations”. In a provocative way, one could say that the author finally moves from “epistemology” to bioethics, or assert that this epistemological “digression” fundamentally serves (normative) ethical purposes.

The brain death debates could certainly benefit from taking more seriously the “epistemological” approach. But the latter will hardly eliminate, in particular in the medical field, a haunting ethical question: why do we value human life? This is not a mere theoretical problem. In some medical practices, in end-of-life decisions, before the determination of death comes into play (and whatever criteria we choose for this purpose) this question frequently reappears, either implicitly or explicitly. For example, in Controlled Donation After Cardiac Arrest — even if the Dead Donor Rule remains a fundamental moral norm for organ retrieval — the issues related to futile treatments and the decision to withdraw life-sustaining treatments can be far more relevant than the definition of death.

Is the topic of the opinion article discussed accurately in the context of the current literature?

Yes

Are all factual statements correct and adequately supported by citations?

Yes

Are arguments sufficiently supported by evidence from the published literature?

Yes

Are the conclusions drawn balanced and justified on the basis of the presented arguments?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Milena Maglio: moral philosophy, bioethics and clinical ethics. Vivien García: moral and political philosophy, ethics and philosophy of technology.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

Author Response 07 Apr 2022

Alberto Molina Pérez, Institute for Advanced Social Studies, Spanish National Research Council (IESA-CSIC), Cordoba, Spain

Comment: *“the analysis of the concept of ‘irreversibility’ is not so clear”*

Response: I appreciate your comment on the lack of clarity of the term “irreversibility”. In the first paragraph you mention, the focus is on the requisite of permanence (i.e. will not reverse) as opposed to irreversibility (i.e. cannot reverse). Although briefly explicated, both terms remain quite vague but I would prefer not to enter into further details there. In the second paragraph you mention, further clarification is indeed necessary. I have made a series of changes to better explain absolute irreversibility, relative irreversibility, and permanence.

C: *“Another possible criticism...”*

R: With regard to your comment on unaddressed questions, my objective was to show a sample of the questions that can be asked from a philosophy of science perspective and for which, as far as I know, no one has yet proposed an answer, neither have I. This article is a way to draw the attention of researchers like you to a field of research that is still underexplored and to lay the foundations for future work; a work that will require the collaboration of many.

To avoid the accumulation, I have rephrased the passage as follows: “It means asking, for example, whether death criteria are heuristics or definitions, and whether the determination of the patient’s death is the conclusion of a syllogism.”

C: *“Molina Pérez should make clear what he means by ‘epistemology’ and ‘philosophy of*

science'..."

R: To avoid any confusion, I have removed the term "epistemology".

C: *"Beyond these terminological concerns..."*

R: It is true that after conducting a conceptual and logical analysis of death criteria from a philosophy of science perspective, my colleagues and I moved back to bioethics. I sincerely hope that this back and forth may prove useful to address normative questions. However, I would not say that the epistemological approach is a digression at the service of ethical purposes. In my opinion, these are two autonomous and complementary ways to approach and address some of the issues raised by the determination of human death.

C: *"The brain death debates could certainly benefit from taking more seriously the "epistemological" approach. But..."*

R: I agree that some end-of-life ethical issues, such as the dead donor rule and the decision to withdraw life-sustaining treatments, are independent from the epistemic issues raised by the definition and determination of death. I believe it is important to distinguish, as much as possible, facts from values, 'is' from 'ought'. One of the criticisms formulated against brain death is that it is a way of disguising normative questions under the appearance of a factual question. If we are not careful, the same strategy could be used for other end-of-life issues.

Competing Interests: No competing interests were disclosed.

Reviewer Report 21 March 2022

<https://doi.org/10.5256/f1000research.120659.r123954>

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Michael Nair-Collins

Department of Behavioral Sciences and Social Medicine, Florida State University College of Medicine, Tallahassee, FL, USA

In "Brain death debates: from bioethics to epistemology," Alberto Molina Pérez argues that the debates on brain death have been characterized by a partisan nature: authors are, roughly, either for or against brain death as an appropriate criterion for death. In place of partisanship, Molina Pérez suggests a non-partisan, epistemological or philosophy of science-based approach to the topic, which would involve examining how the nature of death became an object of scientific inquiry, exploring the brain death criterion, and analyzing the core concepts of "irreversibility" and "function".

Overall, I think the article has the potential to contribute something of value to the brain death literature. Its key point – that the brain death literature can benefit from an examination rooted in philosophy of science – is well-taken. Is death something that can be studied empirically, is it a matter of physiology? Can there be an objective, rationally defensible answer to the question of what is human death, as a matter of physiology? Alternatively, is the nature of death necessarily a “social construction” or fundamentally a matter of agreement rather than discovery? Are all biological categories necessarily vague? Are pluralistic concepts always appropriate, such as how, some argue, the species concept is appropriately pluralistic and different species concepts can be marshalled for different scientific purposes – and so too for the concept of function, irreversibility, and death? And so on... These are all fundamentally situated in theories from the philosophy of science and philosophy of biology, and as such, these areas of research have much to offer the bioethical debates about brain death.

My main suggestions for revision involve the concept of partisanship and the terminology of “epistemology” vs. “philosophy of science”.

To suggest partisanship is to suggest a strong commitment to a cause (or political party), which is grounded in noncognitive reasons of affiliation with one’s “team”, rather than a commitment to truth and quality scholarship. This rendering of the debate seems to suggest that there aren’t any standards by which we might say that one view has better evidence and reasons in support of it; it also suggests that it is not the case that at least one side is, in fact, correct.

Of course, brain death is a very longstanding debate, and it is very complex, drawing on metaphysics, philosophy of science, physiology, ethics, and much else besides, and it may well be true that we are unable to determine – as an epistemic matter – which side, if any, is actually right. But those considerations demand epistemic and moral humility. They do not lead quite so far as to suggest that this is a partisan issue of affiliation and persuasion, and that there aren’t any standards we could appeal to in evaluating distinct views. One could attempt to defend the view that all debates in scientific domains are characterized by something like incommensurability and as such, adherents are, in fact, partisan, and reason and evidence would not arbitrate such disputes. However I don’t think that broader thesis is being made here.

Second, the notion that taking a bioethical approach leads to partisanship, while taking a philosophy of science approach is non-partisan, doesn’t make sense to me. Why would simply approaching the issues from one perspective render one partisan, but approaching them from a different perspective render one non-partisan? Furthermore, any conclusions drawn from a philosophy of science approach are going to have implications for questions regarding brain death anyway, which would seem to lead back to partisanship on this view anyway.

Overall I don’t get the sense that the concept of partisanship does a lot of work in the paper. My recommendation is to remove it entirely, or if not, clarify its use in light of the above comments.

Regarding the terms “epistemology” and “philosophy of science”, I am a little uncertain about how they are used here. My understanding is that epistemology is the study of knowledge, while philosophy of science is a field that studies many aspects of science and its practice, drawing on epistemology, metaphysics, formal logic, philosophy of language, and so on. I am certain that I would not be alone in this interpretation of these terms, so I would suggest just rephrasing in terms of “philosophy of science” throughout and removing “epistemology” to avoid creating

unnecessary confusion for readers.

What follows are a number of comments; this should be read simply as having a conversation, rather than any particular requests for revisions based on the text below. The author should make any changes they think important or interesting enough, but need not reply to every point.

Some comments on the term “function”: It is stated in the paper that “the notions of activity and function are not clearly defined in the literature” (p. 3). Perhaps their definitions are motivated, and bad definitions, but they are defined in the literature. The World Brain Death Project (Greer et al. 2020) and the International Guidelines for Determination of Death group (Shemie et al 2014) both explicitly define these terms, where “function” means something like “measurable on bedside neurological examination” and “activity” means “cellular phenomena recordable by technology”.

Granted, I think that their definitions are bizarre, and clearly motivated by the goal of pretending that clinical practices in the diagnosis of brain death are consistent with the UDDA and the whole-brain criterion of death, when they are certainly not, since some brain function in the form of osmoregulation can continue in patients declared brain dead, and hence it is not true that “all functions of the entire brain” have ceased.

It is interesting to ask about the field within which we should address the question of function (cf. p. 5 discussion of biology, psychology, neurology definitions of function). Quite obviously, in this context the field is clinical medicine. And in clinical medicine, physicians assess cardiac, renal, hepatic (etc.) function using laboratory tests and imaging technology. It would be absolutely bizarre to suggest that a physician cannot assess their patient’s kidney function by evaluating lab measurements of urine and blood, because this only shows “activity and not function”. It would be similarly bizarre to suggest that a physician cannot assess their patient’s heart function with an EKG because this reflects the electrical activity of cells “recordable by technology”. This is what Greer et al 2020 and Shemie et al 2014 are saying with their definitions. The purpose is to be able to claim is that osmoregulation is not a function because it cannot be assessed at the bedside (which isn’t true anyway – normal urine output signals osmoregulation and hypothalamic function).

In any case, on any reasonable understanding of how physicians can and do assess the function of organs, there must be a variety of ways to do that, including bedside assessment, questionnaires, laboratory tests, imaging, and so on.

Finally, the notion that “brain functions are not merely considered as physiological mechanisms, but also viewed in terms of whether they serve their intended behavioral purpose” (p. 5) seems incorrect, or to build in illicit assumptions, even within the context of neurophilosophy and brain-computer interface. First, any theory of function that makes it come out that all brain functions must have an overt, 3rd-person observable, behavioral manifestation does not seem right. There are many functions the brain is involved in that involve managing the homeostatic environment of the physiochemical milieu, even as simple as shunting blood from the periphery to the core, or causing blood vessels to constrict or dilate, and so on. In locked-in syndrome, the entire suite of normal cognitive functions are maintained, and occur without behavioral manifestation. Some of these cognitive functions become apparent through blinking, for sure, but not all. To assume that brain functions must have an overt behavioral manifestation seems to take an unjustified behaviorist approach to mentation.

And then second, a function as understood within the context of natural selection would not have any “intended” purpose, behaviorally manifested or not. A function is something that had some advantage in an environment of evolutionary origin, and was reproduced, and that is it, at least on this view. For example, the intrinsic automaticity of the sinoatrial node manifests a clear function in preserving the heartbeat, but it does not “intend” anything, nor does it have an “intended purpose”. Who could have intended such a purpose?

On the dead donor rule: The manuscript states [death criteria] “may be good in a moral or policy sense because ... they allow ... organ procurement” (p. 4). This is a common thing to say, but I think it is confused. The criteria for death neither allow nor prohibit any policy or practice. In the case of organ procurement, it is the dead donor rule that prohibits organ procurement, not death criteria. If we as a society agree that donors should be dead first – we support the dead donor rule – then they should be dead. The criteria for what constitutes being dead cannot then be derived in such a way that it bypasses the entire point of the dead donor rule, which is to restrict organ procurement. If the dead donor rule matters, then the criteria for death must be independent of the dead donor rule itself, otherwise it becomes trivial, and is not a genuine constraint on behavior at all. On the other hand, if it’s ok to take organs from patients in state X, AND it turns out that patients in state X are still living, then it follows that the dead donor rule need not be adhered to. Either way, death criteria do not prohibit or allow anything.

Nair-Collins does not defend the brain criterion (p. 4): “As a consequence, some advocates of the brain criterion ..., or homeostasis (Nair-Collins 2018)”.

Is the topic of the opinion article discussed accurately in the context of the current literature?

Yes

Are all factual statements correct and adequately supported by citations?

Yes

Are arguments sufficiently supported by evidence from the published literature?

Yes

Are the conclusions drawn balanced and justified on the basis of the presented arguments?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Bioethics, philosophy, brain death

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 07 Apr 2022

Alberto Molina Pérez, Institute for Advanced Social Studies, Spanish National Research Council (IESA-CSIC), Cordoba, Spain

Comment: *"To suggest partisanship is to suggest a strong commitment to a cause..."*

Response: With regard to the use of the term "partisanship", I really appreciate your comment because I was not aware that this term could be interpreted in this context as it is in the political sphere. This was not the intention. As you say, this rendering of the debate would suggest "that there aren't any standards by which we might say that one view has better evidence and reasons in support of it" and "that it is not the case that at least one side is, in fact, correct". However, this is not the way I see the debate; quite the contrary. On the one hand, I think that all parties involved are strongly committed to truth and quality scholarship, and that their views are based on good evidence and well-considered reasons. On the other hand, I also believe that it is possible to critically assess the distinct views and show that some of them are based on flawed, inconsistent or unsatisfying arguments from a scientific and/or philosophical perspective. To do so in a useful way, we need to agree on the standards of evaluation and on the meaning of the concepts used. Some disagreements may be based on the fact that the different parties do not speak the same language, although they think they do. Other disagreements may stem from the fact that the parties have different objectives or different interpretations of what a "good" criterion means to them, although they are not necessarily aware that this is the root of their disagreement. This is why I think a "neutral" approach is needed to be on the same page. This would not solve all disagreements, but it would enable more fruitful debates based on more solid ground.

C: *"Second, the notion that taking a bioethical approach..."*

R: I agree with you. However, (bio)ethics refers to well-founded standards of right and wrong that prescribe what we ought to do. In this case, the question is whether or not we should keep using brain death (as it is or some modified version of it) to determine human death. Some support using brain death because they consider it is a good/right criterion for varying reasons (scientifically, ethically, as a policy, etc.) while others oppose it because they consider it is a bad/wrong criterion (scientifically, ethically, as a policy, etc.).

The approach I am advocating for in this article means taking a step back, setting aside the question of whether brain death is good/right or bad/wrong, and asking more general questions to understand the very nature of a (any) death criterion.

This is similar to your own proposition: *"An objective and unbiased investigation of the biology of death is independent of, and should be undertaken prior to, an analysis of the normative questions engendered by debate about determination of death."* (Nair-Collins 2015)

Perhaps the main difference is that you emphasize the scientific questions about the biology of death and dying, which I totally agree with, whereas I emphasize the (more general?) philosophical questions about the science of death determination. In some cases, both approaches coincide. For example, with regard to the distinction between activities

and functions, you show how the definition of “function” in terms of clinical observability by the IGDD group is an ad hoc strategy to rule out neuroendocrine functions (op. cit.). This is real philosophy of science and it's beautifully done. However, a more general question remains unanswered: how does/should medicine define functions and distinguish them from mere activities? I think it is (ideally) possible to come to an agreement on this issue regardless of where everyone stands on brain death. But it is true (hopefully) that the conclusions drawn from this—objective and unbiased, to use your words—approach of functions in medicine can have implications for the debates on brain death and the question of whether we should keep using it as is, revise it, or abandon it.

C: *“Overall I don't get the sense that the concept of partisanship does a lot of work in the paper.”*

R: I have removed any reference to partisanship from the abstract and the text. I have also tried to emphasize that discrepancies between scholars are not based on mere opinions or ideological affiliations:

“They [death criteria] may be good for a combination of reasons. These reasons have their advocates and opponents, both committed to truth and quality scholarship and based on good evidence and well-considered scientific and/or philosophical arguments.” (p.3)

“Ideally, the answers to these questions could be shared by most scholars, regardless of their position on the issue of brain death.” (p.3)

C: *“Regarding the terms ‘epistemology’ and ‘philosophy of science’...”*

R: I understand your confusion with regard to the use of the term “epistemology”. In France and in Spain, where I trained as a philosopher, “epistemology” and “history and philosophy of science” are used as synonyms. This is not the case elsewhere. In the first draft of the manuscript, I used “epistemology” alone because it felt more natural to me, then I added “or philosophy of science” to try to convey this equivalent meaning. Following your advice, to avoid any confusion for readers, I removed the term “epistemology”.

C: *“Some comments on the term ‘function’...”*

R: Definitions of activity and function are scarce and, when available, suboptimal (to say the least). I have included in the manuscript the two references you mention so that the reader can make their own opinion.

C: *“Granted, I think that their definitions are bizarre...”*

R: I agree. Still, I think it should be possible to find a more charitable interpretation. I am increasingly convinced that some disagreements, especially between philosophers and clinicians, are just misunderstandings based on different mental frameworks—not only with different ways of approaching the same questions but also different views on what it means to give these questions a satisfactory answer. This does not necessarily mean that these particular definitions are correct or even justifiable, but it means that we should (also) assess their validity/justification against the internal logic of functional attributions in

medicine. What is this internal logic? That's the question I ask myself.

C: *"It is interesting to ask about the field within which we should address the question of function..."*

R: Your comment prompted me to adopt the role of the devil's advocate and seek alternative interpretations. First, the distinction between "measurable on bedside" vs. "recordable by technology" reminded me of debates about theory and observation in science and whether the use of instruments to augment the human senses counts as an observation. Second, we could reverse the reasoning. Let's suppose that Greer, Shemie, and colleagues make the following implicit assumption: only living organisms have functions. Based in it, we could argue that if brain dead patients are dead (and I am sure they truly believe it) and if, despite being dead, there is still osmoregulation and other hypothalamic activity, then these activities are not functional. These lines of argumentation are just two sketchy examples that could be further developed and improved. Personally, I find them unconvincing, but at least they make sense (kind of).

C: *"Finally, the notion that "brain functions are not merely considered as physiological mechanisms..."*

I don't have a clear idea on this yet. I would need to think about it more.

C: *"And then second, a function as understood within the context of natural selection would not have any "intended" purpose, behaviorally manifested or not..."*

Obviously, functions (and biological traits in general) don't have intentions. The notions of intention, purpose, design, etc., are controversial in biology and are usually considered as informal ways of talking. The intended purpose of a biological trait (organ, structure, process, etc.), in the context of natural selection, is what this trait (an occurrence of it) is supposed to do according to the type it belongs to, and this type is constituted by its etiology. In other words, the sinoatrial node of a particular heart in a particular individual is supposed to preserve the heartbeat (and thus contribute to the circulation of blood) because it belongs to a type of cells (or group of cells) who, because they have had in the past (previous generations) the consequence of preserving the heartbeat, have contributed to the reproductive success of their ancestor organisms. In simpler words, the function of a trait is what this trait has been selected for. This is what, in the context of an etiological conception of functions (e.g. Larry Wright, Karen Neander, Ruth Garrett Millikan), we can consider as being the "intended purpose" of a trait, although there is nobody or nothing to actually intend it nor any actual purpose into it, but it is an easier way of talking.

I have now put the expression "intended behavioural purpose" between quotation marks to indicate that it must not be taken literally.

C: *"On the dead donor rule..."*

R: Indeed, it is the dead donor rule that prohibits organ procurement, not the criterion itself, and I agree that both things must be independent. However, we can consider death

criteria from at least two different perspectives. One is medical, the other is legal. Medical criteria are supposed to determine whether the patient is dead or not as a matter of fact in the biological realm (I am not sure whether this characterisation is accurate and, if so, whether I would agree with it, but let's assume it), whereas legal criteria determine whether the patient is dead or not as a matter of law in the social and legal realms. Legal death allows social and legal practices beyond organ donation: autopsies, burial, mourning, inheritance, payment of life insurances, etc. Legal death and biological death do not necessarily coincide. For instance, an individual who has been missing for many years can be declared dead *in absentia*, without any actual proof of their death. This is a good policy because families and society as a whole need such a mechanism (although there may be false positives). Similarly, we could consider the UDDA (i.e. the current legal criteria of death, including the brain criterion) as good policy regardless of the issue of organ procurement.

C: *"Nair-Collins does not defend the brain criterion..."*

R: Indeed. I corrected the wording of the sentence to avoid any confusion: "As a consequence, some advocates of the brain criterion..., whereas critics..., or homeostasis (Nair-Collins 2018)".

Competing Interests: No competing interests were disclosed.

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