POLICY FORUM: PEER-REVIEWED ARTICLE
What Should We Do About the Mismatch Between the Legal Criteria for Death and How Brain Death Is Diagnosed?
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Abstract
Mismatch between whole-brain death criteria embedded in statutes and accepted tests physicians use to diagnose brain death have clinical and ethical implications that could undermine public trust in death pronouncements. We consider merits and drawbacks of 4 ways to address this problem.

Legal and Clinical Mismatch
In 1980, the Uniform Determination of Death Act (UDDA) defined death (“brain death”) as “irreversible cessation of all functions of the entire brain, including the brain stem … in accordance with accepted medical standards.”¹,² Whole-brain criteria of death have since been adopted in all 50 states.³ Although the American Academy of Neurology (AAN) and other organizations have outlined “accepted medical standards” for determining brain death (BD) by neurological criteria,⁴,⁵,⁶ controversy is ongoing because testing pursuant to these standards can only approximate BD as codified in law.⁷,⁸

Several recent high-profile cases have highlighted this mismatch,⁷ although they are not unique.⁹ This mismatch has reignited controversy among BD experts,¹⁰ spawned lay misunderstanding,¹¹ and could threaten public trust in physicians, their BD diagnoses, or BD as a concept. Addressing conceptual, ethical, and practical implications of this mismatch requires that physicians recognize BD as currently defined and the difficulties of assessing function loss “irreversibility” in the “entire brain.”¹,² After discussing these difficulties, we offer 4 solutions for reconciling the mismatch: loosening the whole-brain criterion of death, requiring more stringent testing for diagnosing brain death, acknowledging the incongruence between the concept of death and its bedside determination, and the first 2 solutions in combination.

Irreversible Cessation
One reason for the mismatch between medical and legal standards for determining BD is that accepted medical standards cannot determine irreversible cessation. Function
Loss irreversibility was recently reaffirmed as a legal requirement for death when a prisoner who was resuscitated after circulatory arrest argued (unsuccessfully and in court) that his life sentence already had been served. Although broad religious, ethical, clinical, and legal consensus exists that death is irreversible and final, in practice, recognizing exactly when life transitions to death is not so easy. Circulatory death (CD) is currently diagnosed operationally, based on permanence; the function loss irreversibility criterion is fulfilled and fulfillable only when resuscitation is abandoned or life-sustaining measures are withdrawn. Physicians have always relied on permanent cessation of circulation and respiration to determine death without needing to prove function loss irreversibility—and, as we discuss in relation to BD, proving irreversibility is a problem, because prevailing tests rely on permanent cessation.

Hypoxic brain tissue invariably becomes functionally quiescent before it is irreversibly destroyed. BD examination cross-sectionally evaluates function but cannot distinguish between a “stunned,” quiescent brain and an irreversibly damaged brain. The clinical term ischemic penumbra refers to a brain that is hypoperfused (ie, deprived of sufficient oxygenated blood) and nonfunctional but potentially salvageable; hypoperfusion is a well-recognized state of perilesional neurons in patients with acute ischemic stroke, one that can confound BD diagnosis. Technological advances further blur the line between quiescent and dead brain. For example, it was recently demonstrated that some cellular activity in pig brains can be restored several hours postmortem. Although metabolically active brain cells do not necessarily mean that a brain is living and “proof of demise of every neuron is not required to demonstrate irreversible loss of whole brain function,” cellular restoration is one reason function loss irreversibility is hard to confirm clinically.

The AAN recently defended clinical standards for diagnosing BD in prognostic rather than in conceptual terms, stating that it was “unaware of any cases in which compliant application of the Brain Death Guidelines led to inaccurate determination of death with return of any brain function.” Yet confidence in this assertion is limited because accepted standards for diagnosing BD have not been rigorously tested. Patients who meet BD criteria are almost always withdrawn from cardiopulmonary support, which ensures function loss irreversibility. Cardiopulmonary support was continued in Jahi McMath’s case, however. Independent physicians appropriately declared her to be BD by accepted medical standards, but months later she reportedly demonstrated some preserved brain functions. If some of her brain functions really were preserved, her case seems to illustrate the limited specificity of BD diagnostic tests. Despite being controversial, the McMath case is important since opportunities to longitudinally follow a patient after a BD diagnosis are few.

Whole Brain Function
In states that have adopted the UDDA, BD determination mandates the “irreversible cessation of all functions of the entire brain, including the brain stem … in accordance with accepted medical standards.” However, accepted diagnostic tests only enable a physician to examine a patient’s motoric responses, which are controlled by the brain stem. Clinical examination must demonstrate apnea, cranial nerve areflexia, and unresponsiveness caused by an irreversible pathology, excluding mimicking and potentially reversible conditions. But “super locked-in patients” with completely destroyed brain stem efferent pathways could appear brain dead, despite preserved consciousness or afferent olfactory and visual pathways, analogous to vegetative patients who demonstrate subclinical awareness when carefully interrogated.
Although brain stem destruction damages the reticular activating system, presumably causing unconsciousness, this effect is not currently empirically verifiable.29,30

Other examples illustrating the mismatch between accepted medical standards for diagnosing BD and the whole-brain criterion of BD codified in law are patients diagnosed as brain dead per accepted medical standards but who retain neurohormonal functions, such as vasopressin release, which requires an intact neurosecretory hypothalamus.7,31,32 McMath, for example, reportedly underwent menarche and pubertal development7 and showed signs of autonomic environmental reactivity.8,33 Even patients who otherwise meet criteria for BD can have cerebral activity revealed on an electroencephalogram (EEG),34,35 and though EEG activity does not necessarily indicate “meaningful” brain function, it probably reflects subclinical cognition.36,37

Early BD proponents assumed that brain tissue disintegration invariably followed BD diagnosis.2,9,38,39 Liquefaction can follow total brain infarction eventually, but patients diagnosed as brain dead by current tests often have grossly intact brain tissue at autopsy.40,41 McMath’s magnetic resonance image reportedly showed some areas of preserved brain tissue 9 months after the initial insult.8,17,33 Other authors note frequent persistence of patients’ cerebral electrical activity and blood flow despite a BD diagnosis, particularly following infratentorial injuries.42 Although preserved brain structure and blood flow do not necessarily imply preserved function, it seems clear that (1) many nonmotoric brain functions, including higher-order and afferent functions, are difficult to interrogate without an intact brain stem; (2) many young brain-dead patients have sustained blood circulation for long periods after a BD diagnosis; and (3) persistent hormonal and autonomic functions seem to contradict a BD diagnosis according to the UDDA’s requirement, even when diagnosed appropriately per accepted medical standards.

Saying What We Mean, Meaning What We Say

We and others have argued that “all functions of the entire brain”1,2 is best interpreted as the functioning of the brain-as-a-whole or the core function of the brain, rather than as the persistence of a single or even each individual brain function.38,43 Defenders of the functioning of the brain-as-a-whole concept argue that the apparent mismatch posed by persistent hypothalamic or autonomic activity, for example, stems from misinterpreting “all functions of the entire brain.” But persistence of a single noncritical brain function does not indicate that the function of the brain-as-a-whole has irreversibly ceased.

Despite being widely accepted for decades, the brain-as-a-whole concept remains vague and challenging to defend.43,44 Conceptions of the brain’s role as a control center or “somatic integrator” have been criticized because many vital body functions operate independently or in parallel with the brain.45,46 Other authors, including us, have emphasized that critical functions, such as cardiorespiratory circulation or consciousness, define the brain-as-a-whole.43 The President’s Council on Bioethics’ 2008 report suggests that “the work of self-preservation” performed by the brain should be regarded as central.45

Yet none of these brain-as-a-whole refinements seem to adequately rebut important criticisms or clarify responses to key clinical and ethical questions: Which specific functions are essential for life? Why are critical functions found in the spinal cord or elsewhere regarded as less important?14,44 Why should autonomic and hormonal
functions not be regarded as key parts of “the work of self-preservation”? Proposed brain-as-a-whole definitions seem superficially reasonable but, to date, no necessary and sufficient criteria have been formulated to define life or death of an organism as a whole.

Reconciliation

Although the UDDA requires “irreversible cessation of all functions of the entire brain” to diagnose BD, as just discussed, accepted medical standards are only achievable through physicians’ use of currently available diagnostic tests, which do not assess function loss irreversibility or brain functions other than motor responses and respiration. This mismatch between legal criteria and what’s achievable via currently available tests for diagnosing BD means that false-positive diagnoses of BD are possible in cases of low but not absent brain perfusion or brain stem destruction. How should this mismatch be reconciled?

We propose 3 options: improving testing, amending the UDDA, or accepting the inevitability of mismatch.

Improving testing. To preserve the UDDA, testing standards must be tightened. Mandating repeat examinations after a minimal-interval waiting period might help. Many experts recommend this strategy in certain cases (eg, primary brain stem injuries), and this strategy would apply when hypoperfusion mimics function loss irreversibility. One limitation of this strategy is that the duration of an interval that would sufficiently ensure brain function cessation irreversibility remains unknown. Prolonged waiting is not feasible or desirable for many reasons, including fewer patients qualifying as organ donors.

Another strategy for improving tests would be to mandate ancillary testing to assess whole-brain function more comprehensively. A drawback of this strategy, however, is that ancillary tests are expensive, not always available, and can generate false positives and false negatives. Another method—universal perfusion scanning—also might not eliminate the mismatch between accepted standards for diagnosing BD and the whole-brain criterion of death, because viable brain tissue might survive below commonly accepted neuroimaging detection thresholds. Even future technological advances that expand our understanding of consciousness or render today’s ancillary tests obsolete might not help clearly distinguish live patients from dead ones. Thus, it seems reasonable to conclude that testing for whole-brain function will evolve and that establishing enduring standards that render tolerance for ambiguity unnecessary will be challenging, if not impossible.

Amend the UDDA. A second strategy is to amend the UDDA to align it more closely with clinical practice. Since death is difficult to define and since transitions from living, to dying, to death resemble a continuum more than they resemble the binary concept currently enshrined in law, amendment would be reasonable. One option would be to define BD in terms of cessation of function of the brain-as-a-whole, although a lack of tests for measuring functioning of the brain-as-a-whole remains. Another option would be to define BD in terms of brain stem death, as in the UK. This definition would address the mismatch, but practical and philosophical problems would remain for patients who retain consciousness or a quiescent, potentially revivable brain, despite absence of evidence of brain stem function.
Accept mismatch. A third strategy involves preserving BD as defined in the UDDA, while accepting that tests for BD offer only approximations of BD. Death is irreversible by definition, but physicians have always relied on permanent cessation of circulation and respiration to determine death without needing to prove function loss irreversibility.\textsuperscript{15} Death can be viewed as a process on a continuum that has important clinical and ethical dimensions, but legally BD is a discrete event.\textsuperscript{13,14,50}

Since it might be impossible to conclusively demonstrate irreversibility and loss of all brain functions, acknowledging the limitations of accepted standards is more intellectually honest and might help overcome public misperceptions and mistrust.\textsuperscript{11,50} A risk is that accepting the mismatch means accepting that some patients’ BD diagnoses will probably be wrong.\textsuperscript{10,14,15,52,53} However, it comports with current declarations of CD, which is routinely diagnosed based on permanent cessation of function (ie, resuscitation attempts either are not attempted or have failed and been aborted), not on biologic irreversibility.\textsuperscript{15}

A Fourth Strategy?
Revising both legal criteria for BD and diagnostic capacity to assess BD might be the best way to address the mismatch between the two. Doing so might help respond to current public skepticism and lack of understanding of BD\textsuperscript{54,55,56,57} and acknowledge lay tendencies to care more about prognosis than abstractions.\textsuperscript{54,57,58,59} Such a change could obfuscate determinations of a time of death and require a refinement of the dead donor rule,\textsuperscript{60} which expresses general clinical and ethical consensus that a person must be dead before their organs can be retrieved. When one acknowledges that current testing can only imperfectly approximate BD, the question of whether to abandon the dead donor rule will also need to be carefully considered.\textsuperscript{60,61,62,63}

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