Preserved Hypothalamic Function is Not Consistent with the Whole-Brain Criterion for Death

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Abstract

The whole-brain criterion for death requires the absence of all functions of the entire brain. It follows logically that the preservation of any function of any part of the brain is not consistent with the whole-brain criterion for death. The hypothalamus is a part of the brain and has been shown to continue functioning in up to 50% of patients declared dead by neurologic criteria. Therefore, up to 50% of patients declared dead under the whole-brain criterion for death are false positive misdiagnoses. Numerous responses have been offered to explain why preserved hypothalamic function is consistent with the whole-brain criterion for death. All these responses fail.

Keywords

Brain death; hypothalamus; diabetes insipidus; false positive; determination of death by neurologic criteria

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The whole-brain criterion for death requires the absence of all functions of the entire brain. This criterion is enshrined in the Uniform Determination of Death Act (UDDA) of the United States, which states that an individual with "irreversible cessation of all functions of the entire brain, including the brainstem" is dead [1].

This criterion should be distinguished from the brainstem criterion, which requires only the cessation of brainstem functions, but not all brain functions [2], as well as the higher-brain criterion, which requires the absence of brain functions necessary for conscious awareness [3-5]. The whole-brain criterion should also be distinguished from the "brain-as-a-whole" criterion, which requires the cessation of *critical* functions of the brain, explicitly allowing some continued brain functions if they are deemed "non-critical" [6-7]. The brainstem criterion is used in a few nations, while the whole-brain criterion forms the basis for law in most of the world, including the United States; neither the higher-brain nor brain-as-a-whole criteria have been officially enacted in any jurisdiction.

This chapter exclusively addresses the whole-brain criterion, specifically as characterized by the UDDA: "irreversible cessation of all functions of the entire brain, including the brainstem" [1]. Given this concept, it is a matter of valid deductive logic that the preservation of any function of any part of the brain is not consistent with the absence of all functions of the entire brain. The hypothalamus is a part of the brain, and some functions of the hypothalamus, particularly osmoregulation, can continue in some patients declared dead under the whole-brain criterion of death, rendering those declarations of death false positive misdiagnoses.

In this chapter, I review the literature on this debate, defending the claim – which, one would think, needs no defense – that some brain function is not consistent with absence of all brain function. While there are several related concerns surrounding the reliability and validity

of the determination of death by neurologic criteria (as discussed elsewhere in this book) [8], I maintain a narrow focus on hypothalamic function. Examination of the medical literature on this specific issue reveals broader concerns regarding the role of logic, scientific evidence, and transparency in the determination of death by neurologic criteria.

A note on terminology. The term "death by neurologic criteria" is used elsewhere in the book as a noun in place of "brain death", following language recommended by the World Brain Death Project [9]. In this chapter I retain "brain death" to refer to the condition in which all functions of the entire brain have ceased irreversibly. The neologism "death by neurologic criteria" incorporates substantive claims that are matters of scholarly dispute, which should not be defined away by stipulation. For example, it is insensible to claim "death by neurologic criteria is not death;" but *whether* brain death is death is a matter of scholarly disagreement. The definition of "death by neurologic criteria" offered by the World Brain Death Project is problematic in additional ways that will be explored in this chapter, in the penultimate section "Demoting the Hypothalamus in the Brain Death Literature".

Brain Death Pathophysiology and Diagnostic Tests

Brain death can have a variety of etiologies, but a general pattern in the form of a positive feedback cycle characterizes its basic pathophysiology. As intracranial pressure (ICP) rises, cerebral perfusion decreases, causing damage to neural cells leading to edema, further increase in ICP, further decrease in cerebral perfusion, and so on, until ICP rises above mean arterial pressure (MAP), eventuating in an assumed global loss of brain circulation and hence global cerebral anoxia. This process runs in a rostral-to-caudal direction, with the lower brainstem

being the last area to become infarcted and is often accompanied by herniation of the unci of the temporal lobes or the tonsils of the cerebellum.

The accepted diagnostic tests for brain death – also referred to as "medical standards" – are tied to this pathophysiological picture [9, 10]. First, the cause of coma must be known and believed to be severe enough to result in irreversible pathology. This requires the use of neuroimaging, such as a CT scan. Second, potential confounders to further testing must be ruled out, including hypothermia, sedative intoxication, acid-base disturbances, and others, along with a general assessment of patient health, including evaluation of electrolytes and kidney and liver function. These require laboratory tests.

Third, the patient is evaluated for responsiveness to auditory stimuli and pain and must be unresponsive to all such stimuli. Fourth, a variety of brainstem reflexes are tested, including pupillary response to light, deep cough response to suction, gag reflex, blink response to touching a wisp of cotton to the cornea, and vestibular (eye movement) responses to cold water placed in the ear canals and to brisk movement of the head.

If these findings are all consistent with brain death, then the final evaluation is the apnea test. The patient is hyperoxygenated prior to the test. Oxygen is passively delivered, while the ventilator is disconnected from the patient for a period of 8-10 minutes as clinicians observe for signs of spontaneous breathing. Arterial carbon dioxide partial pressure is measured before and after the test, and must rise 20mm Hg from baseline or reach 60mm Hg, for the apnea test to be considered valid. This test requires arterial blood gas analysis.

Ancillary tests, such as neuroimaging for blood flow or an electroencephalogram (EEG), are not considered required, but are often used at the physician's discretion, though they are

mandatory in some jurisdictions. These accepted diagnostic tests are essentially the same for both the whole-brain criterion of death [9, 10] and the brainstem criterion [2], though there is also variability in practice both internationally and intranationally as discussed elsewhere in this book [9].

In the medical literature, the determination of death by neurologic criteria is uniformly said to be a "clinical diagnosis", meaning that only functions that are observable at the bedside are part of the diagnostic evaluation [e.g. 9, 11]. This is false, as can be seen from the description of the diagnostic tests, which require imaging and laboratory analyses. One might respond that the "core" tests for brain death only include evaluation for unresponsiveness, brainstem areflexia, and apnea. This distinction arbitrarily ignores mandatory aspects of the evaluation, including identifying the cause of coma and ruling out confounders, along with ancillary tests which are often used and can finalize the determination if other parts of the evaluation are equivocal or cannot be performed.

Nonetheless, even granting this arbitrary rejoinder for the sake of the argument, the apnea test – one of the cardinal features of the diagnostic tests for brain death – requires laboratory analysis of arterial blood gases. Brain death is thus just as much of a technological diagnosis as any other in the ICU. It requires a thorough history, many laboratory analyses, neuroimaging, and bedside physical evaluation, combined with ongoing ICU-level monitoring of many physiologic variables; in some cases, the determination also relies on direct measurement of ICP (requiring surgical implantation of the measuring device), along with additional, more advanced imaging, or electrophysiologic analysis. Therefore, it is not a "clinical diagnosis" [9, E5]. This claim is a motivated misdescription of how brain death is in fact diagnosed. The relevance of this point will shortly become apparent.

Hypothalamic Functions in Patients Declared Dead by Neurologic Criteria

The hypothalamus is a small region at the base and center of the brain and is a component of the diencephalon. Its borders are somewhat indistinct, but is generally considered to be bordered rostrally by the lamina terminalis; caudally by the edge of the mamillary bodies, behind which is found the midbrain; dorsally by the hypothalamic sulcus and above that the thalami; ventrally by the infundibulum, pituitary stalk and below that the pituitary glands; and laterally by the basal nucleus of Meynert, nucleus accumbens, amygdala, posterior limb of the internal capsule and basis pedunculi, and caudodorsally the subthalamic nucleus [12].

The hypothalamus has been described as "the homeostatic head ganglion" [13, p. 738], for its critical role in multiple homeostatic functions, including osmoregulation (the regulation of osmolarity: the concentration of solutes, of which sodium is the most common, in extracellular fluid), hunger, thirst, sleep-wake cycles, blood pressure control, temperature control, limbic mechanisms, and neuroendocrine and autonomic regulation. The hypothalamus directly controls the posterior pituitary gland through release of vasopressin and oxytocin, and indirectly controls the anterior pituitary gland via hypophysiotropic factors passed through a local blood supply known as the hypophyseal portal system, thereby regulating secretion of adrenocorticotropic hormone, thyroid-stimulating hormone, growth hormone, prolactin, luteinizing hormone, and follicle-stimulating hormone [13].

If all functions of the brain cease, as the whole-brain criterion requires, then the functions of the hypothalamus must cease. As the magnocellular neurons of the supraoptic and paraventricular nuclei in the anterior (supraoptic) region of the hypothalamus become infarcted

or damaged, they should stop secreting vasopressin (or anti-diuretic hormone), resulting in central diabetes insipidus, which would be easily apparent by the onset of massive hypo-osmotic polyuria with hypernatremia. (There are confounders to this, which are mentioned below) [14].

Yet, central diabetes insipidus does not manifest in a large percentage of patients declared dead by neurologic criteria, entailing that hypothalamic osmoregulation remains intact. The largest review of central diabetes insipidus in patients declared dead by neurologic criteria evaluated data from 37 studies and found that 1265/2546 patients (50%, 95% CI [0.478-0.516]) manifested diabetes insipidus [15]. Therefore, the critical brain function of osmoregulation continues in up to half of patients declared dead by neurologic criteria.

Furthermore, the half-life of vasopressin is 15-18 minutes, and the neural-renal osmoregulatory system is sensitive and rapid, maintaining osmolarity within a narrow, 3% window. The magnocellular neurons are osmoreceptors, directly responsive to their extracellular osmotic environment, regulating the secretion of vasopressin on a minute-to-minute basis [16]. Clearly, they must be receiving ongoing arterial flow as well as venous drainage to perform this function.

It is also worth noting that changes in osmotic pressure local to the magnocellular neurons of the hypothalamus are often insufficient for the cells to reach threshold potential and thus fire an action potential down the axons that traverse the pituitary stalk and terminate in the posterior pituitary gland. There is a secondary osmoreceptive system located in circumventricular areas, including the organum vasculosum of the lamina terminalis and the subfornical organ. These neurons are also osmoreceptors, which supply excitatory, glutamatergic input to the primary osmoreceptors in the hypothalamus [17]. Normal osmoregulation is thus a function of the additive effect of both the primary system located in the

hypothalamus and the secondary system located in circumventricular areas, rostrally adjacent to the hypothalamus.

In addition to osmoregulation, neuroendocrine control of anterior pituitary hormones is often not lost either. In a review of 12 studies that included 386 patients, up to 84% did not show central thyroid failure, and in 2 studies that included 24 patients, up to 71% did not show central adrenal failure [14, 16].

The whole-brain criterion for death states that all brain functions must be lost. Since osmoregulation, a brain function, continues in potentially half of patients declared dead by neurologic criteria under the whole-brain criterion for death, it follows that up to half of these declarations of death are false positive misdiagnoses. Considering the limited data on central thyroid and central adrenal failure, this number of false positive misdiagnoses potentially rises even further.

Demoting the Hypothalamus in the Brain Death Literature: Efforts to Deny the Relevance of Preserved Hypothalamic Function

It has been well known for decades that some patients declared dead by neurologic criteria may have preserved hypothalamic function [e.g., 18]. More recent studies cited above simply attempt to clarify how common this is; but the basic point is (or should be) common knowledge.

However, rather than recommending changes to medical practice based on scientific evidence, in the brain death literature, clinical practice has driven what counts as evidence. Specifically, there have been many attempts to ignore, deny, or minimize the indisputable fact

that in some patients declared dead using the whole-brain criterion for death, some brain function continues.

As the UDDA and all extant concepts of brain death rely on the concept of neurologic *function*, a natural target for denying the relevance of hypothalamic functions is to deny that they are functions at all: they are relegated to being described as mere "activities", and therefore their preservation does not run afoul of the whole-brain criterion. For example, the International Guidelines for Determination of Death group allege that "examples of brain function such as the capacity for consciousness … should be distinguished from examples of brain activity such as posterior pituitary antidiuretic hormone release" [11, p. 791]. More recently, the World Brain Death Project has repeated this "function vs. activity" distinction, asserting that "*brain function* refers to the more macro phenomena that are measurable on bedside neurological examination… *brain activity* refers to neuronal cellular micro phenomena recordable by technology" [9, p. E3].

This is an ad hoc definition motivated by the desire to render osmoregulation (and potentially other evidence of brain function) consistent with the determination of death by neurologic criteria. It flies in the face of clinical practice: Physicians assess renal, hepatic, cardiac, and pancreatic function (*inter alia*) with laboratory tests and imaging; why would the function of the brain, arguably the most complex of all organs, only be assessed by simple bedside evaluation? Furthermore, this would make any findings on the EEG irrelevant to the determination (as, being technology, it can only show "activity"), thus rendering it an unacceptable component of the diagnostic algorithm. But the medical standards recommend or suggest EEG as an acceptable ancillary test [e.g. 9-10] which may be used to finalize the determination in some cases, thus creating an internal contradiction. (The World Brain Death Project has suggested moving away from its routine use in adults except for certain cases such as

skull fracture or decompressive craniectomy, thus, still accepting its validity in some cases.) [9, pp. E8-E9]

The apnea test requires laboratory analysis of arterial blood gases as an essential component of the test. If carbon dioxide partial pressure does not sufficiently rise, as measured by laboratory analysis, then the test is not valid. Therefore, one of the core aspects of the diagnostic tests requires laboratory analysis of brain function – specifically, of the medulla's capacity to respond to *a stimulus sufficient to challenge the medulla* – which can only be measured by laboratory analysis of carbon dioxide partial pressure. The "function vs. activity" distinction should thus rule out the apnea test as a valid component of the diagnostic tests as well.

Furthermore, the World Brain Death Project's definitions of "clinical" and "clinical test" are inconsistent. "Clinical" is defined as "Based on direct … observation or examination of the patient," [9, E3] while "clinical test" is "A bedside test [which] may include the use of … vital signs monitors." [9, E3]

Vital sign monitoring in a modern ICU consists of, at minimum, continuous electrocardiography, continuous photoplethysmography, and an electronic sphygmomanometer, along with a variety of physiologic measurements produced by the mechanical ventilator. These technologies provide information on aspects of patient physiology that are *not directly observable* (such as electrical activity of the heart or peripheral oxygen saturation). This non-directly observable information is detected by technological sensors of various kinds, converted into a signal, and then is altered in accordance with a variety of mathematical and electronic transformations by complex biomedical engineering devices, to finally produce *representations* of that physiologic information, in a form that is interpretable by human observers. The actual

physiologic variables measured by these devices are themselves no more "directly clinically observable" than sodium levels in the blood, or cortical activity measured by an EEG – which, notably, is based on the same physical principles as the bedside continuous monitoring electrocardiogram.

Regardless of the motivated definitions discussed above, osmoregulation – the regulation of sodium and free water in the extracellular fluid – is a vital biological function, a function of the brain, necessary for maintenance of homeostasis and the life of the organism [13-14,17]. To use the World Brain Death Project's notion of "neurologic function", osmoregulation involves the delivery of "a stimulus to provoke central processing and an efferent response" [9, Supplement 5, p. 20]; or in the words of the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research (henceforth "President's Commission"), this is cellular activity that "is organized and directed" in maintaining osmolarity, in conjunction with the kidneys, thus rendering it a function and not a mere activity [1, p. 75]. Ad hoc definitions constructed to avoid facts which do not fit professional interests in preserving the status quo in determination of death by neurologic criteria, which create internal inconsistencies in the logic of the tests, and are inconsistent with the actual practice of medicine, do not change those disfavored facts.

A related rejoinder is to assert that only "clinical functions", assessable at the bedside, count. This relies on the false claim that determination of death by neurologic criteria is a clinical diagnosis, which it is not, as reviewed above, and on the additional false claim that normal osmoregulation cannot be observed at the bedside, which it can, through normal urine output. (There are confounders, including severe acute kidney injury which would cause oliguria, or administration of vasopressin for systemic blood pressure control. But in a patient

without severe acute kidney injury and for whom vasopressin was not administered, normal urine output is a clear sign of brain function. [14])

Another point that has been made since the very early days of the construction of the concept of ”brain death” is that not every cell in the brain must die to make the determination [1, 19]. This claim has also been marshalled to avoid acknowledging hypothalamic function in brain death. However, I have not argued that all cells of the brain must die. I have focused specifically on brain *functions*, in accordance with the UDDA and all extant concepts of death. Osmoregulation, subserved by magnocellular nuclei in the hypothalamus with additive input from the circumventricular region, is an organized and directed brain *function* requiring both arterial supply and venous drainage into systemic circulation, participating in a negative feedback system with the kidneys, to maintain a vital physiologic variable within limits necessary for organismic functioning. It is not a mere “cluster of cells” randomly doing nothing of physiological significance.

Arterial supply of the posterior pituitary gland is partially provided by the inferior hypophyseal artery, which branches off the meningohypophyseal trunk of the internal carotid artery. These arteries remain outside the dura until the inferior hypophyseal pierces the dura at the inferior portion of the posterior pituitary gland [14]. This anatomical location is relevant because the inelastic container within which ICP rises is the dura, in addition to the cranium. Therefore, it is plausible that these arteries enjoy some protection from increased ICP, allowing preserved flow while flow to other areas, not protected in this way, would cease. This is yet another reason offered for why preserved hypothalamic function is consistent with the whole-brain criterion for death and the UDDA [20].

But this does not explain why preserved hypothalamic function is consistent with the whole-brain criterion for death. Neither the UDDA nor the whole-brain criterion make exceptions based on blood supply.

Furthermore, the inferior hypophyseal artery supplies the inferior portion of the posterior pituitary gland, which consists of axons whose cell bodies are located intradurally in the diencephalon, in areas not protected from increased ICP. And the secondary osmoreceptive system in the circumventricular areas is similarly not protected in this way [14]. Therefore, continued arterial supply and venous drainage is required, in areas not protected by the extradural location of the inferior hypophyseal artery, so this does not explain continued osmoregulation anyway.

Another response is that only "critical functions" count in the determination of death by neurologic criteria [21]. This is yet another attempt to carve out "special" brain functions that count while discounting others, in contradiction with the whole-brain criterion of death and the UDDA, thus rendering it irrelevant to the question at hand. The proposal here is to designate some brain functions as "not critical", while insisting only that critical brain functions must be lost to determine death by neurologic criteria, and thus, persistence of any brain function deemed "not critical" would not preclude the determination [6-7]. Of course, osmoregulation is at the top of the list for demotion to "noncritical" status, thus rendering its preservation allegedly consistent with an accurate diagnosis of brain death. However, this proposal amounts to changing the criterion, from the whole-brain criterion of death that is embodied in the UDDA, to something else, something less than the whole brain. But that is not what is at issue here. Furthermore, if anything counts as a critical function, either of the brain or of the organism as a whole, then regulating the chemical composition of the extracellular fluid, a necessary precondition for

essentially all cellular functions throughout the organism, surely counts as a critical function. Therefore, osmoregulation cannot be dismissed as a "noncritical function" anyway.

Another, similar move, is to directly claim authority over the criterion itself, so that, rather than law providing the legal standard that physicians are tasked with determining (using diagnostic tests, or "medical standards"), some argue that physicians themselves have the authority to define the criterion that is to be identified. Once again, this is irrelevant to the question at hand, which is whether hypothalamic function is consistent *with the whole-brain criterion*, or the UDDA, which it is not.

Wijdicks, for example, has argued that the diagnostic tests, or the medical standards, themselves define the condition that is being diagnosed, rather than being diagnostic tests for a physiologic condition defined by law [22]. If this were true, then, assuming a competently performed examination, a false-positive determination would be impossible in principle: the tests, and the condition being tested for, are one and the same, so a positive result is – by definition – a true positive. If a false-positive determination is impossible in principle then there is no empirical observation that could refute the claim that "the diagnostic tests have perfect sensitivity and specificity". Without even the possibility of any empirical evidence bearing on this claim, arguably it is not a scientific claim at all, which is inconsistent with medicine's proclaimed commitment to scientific practice [23]. In any case, this amounts to another attempt to change the criterion from the whole-brain criterion for death to something else, and thus is irrelevant.

The first sentence of the UDDA defines the condition – irreversible cessation of all functions of the entire brain – that physicians are tasked with identifying. The second sentence states "Determination of death must be made in accordance with accepted medical standards"

[1]. Some suggest that this second sentence gives medicine authority to define the condition being diagnosed. It does not. First, if it did, it would render the first sentence of the UDDA moot, by granting physicians the authority to change the criterion defined in the first sentence. Laws are not written to be self-defeating, to undermine their own authority, nor to render themselves moot. Second, the President's Commission discussed the meaning of each phrase of the UDDA sequentially [1, pp. 72-81]; as for "accepted medical standards" the intent was "to require the use of *diagnostic measures and procedures* that have passed the normal test of scrutiny and adoption by the biomedical community" [1, p. 78; emphasis added]. Thus, the second sentence refers to diagnostic tests used to identify the condition defined in the first sentence, *irreversible cessation of all functions of the entire brain*; it does not grant physicians authority to ignore the first sentence. Death is not "whatever the medical community says it is".

Finally, two more recent rejoinders have been proposed. Several scholars have questioned whether the hypothalamus is a part of the brain. Lewis, Bonnie, and Pope, in discussing recent lawsuits, wrote "this raised the question of whether the pituitary and hypothalamus are part of the 'entire brain'" [24, p. 143]. In a different article they surmised,

> the authors of the UDDA do not appear to have intended the phrase 'all functions of the entire brain' to encompass functions of the pituitary gland and hypothalamus; in their 188-page report, they mentioned 'coma' 120 times, 'brainstem' 22 times, and 'apnea' 9 times. But not once did the Commission mention any terms to describe pituitary/hypothalamic/hormonal function [25, p. 17].

There are many brain areas that the Commission did not specifically mention; indeed they did not specifically mention *most* areas of the brain. This does not imply they intended "all functions of the entire brain" to mean anything other than *all functions of the entire brain*. This is hardly a convincing argument, either legally or anatomically. Besides, it is unarguable that the hypothalamus is a part of the brain [14].

Finally, both the American Academy of Neurology (AAN) and the World Brain Death Project have simply asserted, in an impressive feat of bold unconcern for logical contradiction, that some brain function is consistent with no brain function; that is, that hypothalamic brain function is consistent with cessation of all functions of the brain. The AAN wrote,

> The AAN endorses the perspective of the UDDA that brain death has occurred when the irreversible loss of all functions of the entire brain including the brainstem has been determined. However, the AAN endorses the belief that preserved neuroendocrine function may be present … and is not inconsistent with the whole brain standard of death [20, p. 230].

Neuroendocrine function is brain function. Preservation of any brain function is inconsistent with "loss of all functions of the entire brain". To assert otherwise is a naked logical contradiction.

The World Brain Death Project made the same claim, although used the term "neuroendocrine activity". However, as repeatedly shown above, osmoregulation is a brain *function*, even under their own definition, and the President's Commission's definition, of

"function". Simply *calling* it an "activity" in this context does not change the fact that it is an organized, directed function which maintains, in coordination with the kidneys via a negative feedback process, a vital physiologic parameter within limits necessary for organismic functioning. The World Brain Death Project wrote,

> [Brain death/death by neurologic criteria] is defined as the complete and permanent loss of brain function as defined by an unresponsive coma with loss of capacity for consciousness, brainstem reflexes, and the ability to breathe independently… Persistence of … neuroendocrine activity does not preclude the determination [9, p. E3].

It is to be noted first that the World Brain Death Project has changed the criterion for death; this is not the whole-brain criterion for death, and is not equivalent to the UDDA. Leaving aside the difference between "permanent" and "irreversible", the first part of the definition closely resembles the whole-brain criterion ("complete and permanent loss of brain function"). However, the second part, which defines the first part, describes the major clinical features of the diagnostic tests (coma, brainstem areflexia, apnea), and is not equivalent to the whole-brain criterion. This definition is similar to the proposal by Wijdicks, where the diagnostic tests define the criterion. The new criterion, labeled with the neologism, "death by neurologic criteria," is a syndrome characterized by unresponsiveness, brainstem areflexia, and apnea. These three characteristics are the "cardinal features" of long-accepted medical standards, or diagnostic tests. As the AAN wrote in its 2010 "Evidence-based guideline update", "the medical standards for the determination of brain death … [consist of, at minimum] 3 clinical

findings necessary to confirm irreversible cessation of all functions of the entire brain…: coma (with a known cause), absence of brainstem reflexes, and apnea" [10, p. 1911]. The syndrome characterized by the co-occurrence of these three findings is distinct from the condition of irreversible cessation of all functions of the entire brain. As argued above, the medical community has no authority to change the physiologic condition it is entrusted to identify using diagnostic tests; and even less to do so under the guise of merely clarifying definitions "to ensure consistency" [9, p. E3].

This proposal has the same implication as Wijdicks's. It effectively renders false positive misdiagnoses impossible by definition, so long as the medical standards are followed competently. Furthermore, this stipulated definition renders hypothalamic function consistent with the determination of death by neurologic criteria merely by definition. Hypothalamic function, especially osmoregulation, is consistent with the syndrome of coma, brainstem areflexia, and apnea, and is not assessed by current medical standards, therefore, its preservation is consistent with these standards. But we already knew that. The new terminology simply hides the fact that under current practice, patients who do not satisfy the UDDA or the whole-brain criterion for death, are routinely declared dead, *specifically by appealing to the UDDA or to the whole-brain criterion for death*.

The World Brain Death Project nonetheless endorsed brain death in terms of the whole-brain criterion, albeit incoherently, by stating in the first part of the definition that brain death is the "complete and permanent loss of brain function". It went on to state that neuroendocrine *activity*, which is actually hypothalamic and circumventricular *function*, is consistent with "complete … loss of brain function" [9, p. E3]. This amounts to the same logical contradiction asserted by the AAN.

Concluding Thoughts

Preservation of hypothalamic function in patients declared dead under the UDDA and the whole-brain criterion for death is but one of many concerns surrounding the concept and diagnosis of brain death [8]. However, an in-depth examination of this narrow issue is valuable, as it reveals broader patterns in the medical literature and clinical practices relevant to death determination.

With respect to the preservation of hypothalamic brain function in patients declared dead by neurologic criteria, which explicitly contradicts the UDDA and whole-brain criterion for death, the medical profession has made no changes to its diagnostic practices considering this information since the concept of brain death was developed in the 1960s. Nor has it evinced any transparency about this fact, either with the public, media outlets, or in any of its many "updated" standards for clinicians, who may not be well-conversant with the primary brain death literature and must rely on professional society updates for accurate and scientifically informed guidance for clinical practice. Instead, professional society standards and individuals in both medicine and bioethics have repeatedly ignored, minimized, or denied facts that challenge professional interests in maintaining the status quo in determination of death by neurologic criteria, while continually repeating the false claim that the diagnosis of brain death, relative to the UDDA and the whole-brain criterion for death, is made with near-perfect accuracy [e.g., 10, 20, 22, 26].

Certainly, it is a weighty responsibility that has been entrusted to the medical profession. The determination of death is unique among all possible medical determinations, and it is

associated with profound consequences for the patient, family, and many other interested parties. It is unreasonable to expect perfection in this or any human endeavor, therefore, perfection is not expected. Nonetheless, it *is* reasonable to expect that professional societies, and individual physicians, will be competent, trustworthy, and will follow the law in carrying out such a grave duty. It is also reasonable to expect that diagnostic practices will be informed by scientific knowledge, will be logically coherent, and that, above all, there will be transparency with all stakeholders, including transparency regarding facts that are uncomfortable or that cast doubt on the reliability and validity of accepted practices.

The review of the medical literature on hypothalamic functioning in brain death reveals that these behaviors and standards rightly expected of the medical profession have not characterized its practice with respect to determination of death by neurologic criteria. Instead, the literature is characterized by decades of ad hoc, irrelevant, false, illogical, specious rejoinders, clearly designed to protect the status quo in death determination.

For the medical profession to be worthy of the special trust required to play this important role in society, professional societies and coalitions of such societies, such as the World Brain Death Project, the American Academy of Neurology, and others, must change course. They should stop closing ranks to protect narrow professional interests in maintaining the status quo over the far more important values of truthfulness, scientific credibility, and transparency. They should stop refusing to acknowledge troublesome facts that do not align with the manufactured narrative of brain death as a well-justified, accurately diagnosed medical condition; because it is neither of those things.

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