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Defining Function in Medicine: Bridging the Gap Between Biology and Clinical Practice

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The classification of preserved hypothalamic activity in brain death and brainstem death as functional or non-functional has become a subject of debate. While proponents of the neurological criterion claim that these activities lack functional significance (Shemie et al. 2014), Nair-Collins and Joffe (2023) argue for their functional physiological role. However, the interpretation of the term "function" within the medico-legal framework, where death is characterized by the irreversible cessation of all brain *functions*, remains unclear.

The concept of function permeates medical discourse, yet it lacks a precise definition. While biologists and philosophers have extensively debated function in biology in general, its specific meaning in physiology and medicine has received comparably less attention (Molina Pérez 2017; Roux 2014; 2021). Dorland's Illustrated Medical Dictionary defines function as "the special, normal, or proper physiologic activity of an organ or part." However, this definition remains inadequate and requires further elaboration. In the context of death determination, Nair-Collins (2015) initiated a discussion on the scientific meaning of the terms "activity" and "function" in death criteria, but progress in this area has been limited.

In this article, Nair-Collins and Joffe (2023) claim that hypothalamic-pituitary activities are physiologically functional. This raises two questions: whether the author's claim is correct and what conclusions can be drawn from it.

Physiology focuses on the study of functions in healthy, living individuals, i.e. in the normal case. I will assume that *in the normal case* the hypothalamus indeed has physiological functions, such as the secretion of vasopressin and other hormones. If all parties agree on this, the controversy only arises in the case of brain-dead individuals. Advocates of the brain death criterion argue that preserved hypothalamic activities in brain-dead individuals lack functional significance, while Nair-Collins and Joffe present a contrasting viewpoint. However, on the one hand, it is unclear how and why these activities would cease to be functional upon brain death. On the other hand, the fact that hypothalamic activities are functional in the normal case does not necessarily imply that they are also functional in brain death, which is not the normal case. Both parties appear to make a logical leap from one case to another without providing sufficient explanation or justification. Consequently, even if the authors are correct in asserting the physiological function of hypothalamic-pituitary activities, the implications for determining death remain unclear.

It becomes more problematic when we consider that the brain criterion of the Uniform Determination of Death Act can be read in both directions: (a) if all brain functions are lost, then the individual is dead, and (b) if the individual is dead, then all brain functions are lost. The authors' argument aligns with one reading: since all brain functions are *not* lost, then the individual is *not* dead. Brain death advocates' argument align with the other reading: since the individual is dead, then any persisting hypothalamic activity cannot be functional. While both interpretations are possible, they do not contribute significantly to the matter at hand because they rely on circular reasoning, i.e. they beg the question. In the first case, using the term "function" for preserved hypothalamic activity assumes that the organism is alive. In the second case, assuming that brain-dead individuals are dead leads to the conclusion that preserved hypothalamic activities are not functions.

To illustrate this, consider an analogous situation in organ donation after circulatory determination of death, where a donor's heart can be preserved in a near-normothermic beating state using a portable ex-vivo organ perfusion system until transplantation. The question arises: is this heart functional? In other words, does its continued beating activity qualify as a function? Some might argue that organs and cells do not immediately die or cease their activity after death but can remain active for some time, particularly when preservation measures are employed. However, these activities cease to be functional when they are no longer part of a living organism. When the donor is declared dead based on the irreversible loss of heart function, there is no longer an organism of which the heart can be part. Thus, the preserved beating of this heart is not functional but merely an activity. Assuming that there is no living organism entails that the preserved heart activity does not qualify as a function.

Alternatively, some might contend that a heart can temporarily fail to perform its function, for example when it fibrillates and the blood flow is interrupted.

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However, if medical intervention restores the heart to its normal state, it implies that the function was not irreversibly lost. Similarly, when an explanted heart is preserved in an ex-vivo (or ex-situ) perfusion system, it cannot contribute to the circulatory system of an organism until it is transplanted. Nonetheless, it retains its capacity to fulfill that function. In other words, the beating of this explanted heart is functional, even though it is not currently performing its function within a person's body. The successful transplantation of the heart and its subsequent contribution to circulation within a recipient's organism indicate that this heart had not irreversibly lost its function in the first place. Consequently, declaring the donor's death based on the irreversible loss of heart function constitutes a false positive. Assuming that preserved heart activity (or capacity) constitutes a function implies that the donor was not dead (at least according to this criterion).

In this situation, as in the case of preserved hypothalamic activity in brain death, death and loss of function are so intertwined that it seems difficult not to fall into circular reasoning. One conclusion I draw from my doctoral thesis is that, in biology, the concepts of function and life are not independent, but inextricably linked (Molina-Pérez 2017). However, clinical practice is not biology. The function of an organ in a medical setting need not mean the same as in a natural setting.

My intention here is not to engage in a debate over the validity of different viewpoints regarding the functional significance of preserved activities in the hypothalamus or the heart. Rather, I aim to highlight the critical importance of exploring and defining the concept of function in medicine, which currently lacks clarity. My point is that, whatever our position in the brain death debate, reaching a consensus on this conceptual matter would minimize misunderstandings and establish a robust foundation for further insightful analysis. This applies to other concepts, such as irreversibility and consciousness (Molina-Pérez and Ave 2022). To accomplish this, it is imperative to approach death determination not only through a bioethical lens but also through the lens of epistemology and the philosophy of science (Rodríguez-Arias, Molina-Pérez, and Díaz-Cobacho 2020; Molina Pérez 2022).

For example, this approach has revealed that the two criteria of the UDDA are inconsistent in their use of the notion of function (Molina-Pérez, Bernat, and Dalle Ave 2023). While in the first criterion the cessation of circulatory and respiratory functions refers to both *spontaneous* and *artificially supported* functions, the second criterion only refers to the cessation of *spontaneous* brain functions. According to the first criterion, a patient whose heart or lungs have irreversibly stopped functioning is not necessarily dead, as the circulatory and respiratory functions normally performed by these organs can be maintained artificially using life support technology (e.g. mechanical ventilation, extra-corporeal membrane oxygenation). However, according to the second criterion, an individual whose entire brain, including the brainstem, has irreversibly stopped functioning is declared dead, even though some of the functions that the brain typically performs, such as initiating breathing, thermoregulation, and blood pressure regulation, are also artificially supported.

In my view, the biological concept(s) of function are not directly applicable to clinical practice. In biology, the mainstream approach views function as an explanation for the presence of a biological trait in terms of its selective success in previous generations of organisms within a Darwinian framework. Another major approach views function as an explanation for the operation of a system in terms of the causal role played by its constituent parts. This appears to align more closely with how the concept of function might be understood in medicine. However, this latter approach also tends to disregard the normative aspect of function, posing challenges when accounting for dysfunction within clinical practice.

I see two fundamental differences between biology, including physiology, and medicine. Firstly, biology serves an epistemic purpose, aiming to explain the 'why' and 'how' of its object of study. In contrast, medicine is driven primarily by a practical interest in healing patients. Medicine relies on physiology to establish functional normality, but its primary focus lies in addressing dysfunction and disease, which are deviations from normal function. Secondly, biology operates as a natural science, studying living beings as they exist in their natural state. In contrast, medicine operates within the realm of material and technological culture, using artificial means to preserve, restore, enhance, support, and replace functions that are impaired in their natural state. This broad scope of medicine extends beyond the boundaries of biology. That is why I believe that the concept of function required in medicine must encompass both the natural and the artificial.

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