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«The Brain as a Whole» Concept: Facilitating Approaches to Brain Death Understanding (Short Communication)

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Summary

James Bernat claimed that «the formulation of whole-brain death provides the most congruent map for our correct understanding of death». However, the author has recently proposed the categorization of another phrase: «brain as a whole (BAAW)». This is because patients with primary brainstem lesions who otherwise meet the clinical criteria for BD may still have EEG, CBF, evoked potentials, and hypothalamic-pituitary neurosecretion.

Bernat and colleagues suggested «tightening the clinical tests for brain death or loosening the whole-brain criterion of death». They emphasize that the BAAW criterion is an intermediate standard between the whole-brain and brainstem views, tolerating the irreversible cessation of critical brain functions, whereas the BD/DNC determination does not require the cessation of all brain functions or the death of every neuron.

In this paper, we have revised the concept of BAAW, which is intuitive and facilitates a conceptual and practical approach, but requires further refinement to specify precisely which brain functions must cease at brain death and which may continue.

Keywords: brain death; clinical criteria; hypothalamus; brainstem; autonomic nervous system

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In recent decades, three main brain-oriented formulations of death have been discussed: whole-brain death, brainstem death, and higher brain standards [1, 2]. James Bernat claimed that «the formulation of whole-brain death provides the most congruent map for our proper understanding of the concept of death» [3]. He argued that «the irreversible cessation of clinical functions of the brain constitutes death because the brain is responsible for the functioning of the organism as a whole» [4–6]. Thus, tightening the clinical tests for brain death may require a neuroimaging study demonstrating the absence of CBF, but there is a notable worldwide variation in the use of adjunctive tests [3, 7, 8].

Bernat and colleagues' defense of the whole-brain formulation of death was cited by the United States President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research as the conceptual basis for BD/DNC [4–6]. The Commission recommended that all US states adopt the Uniform Determination of Death Act (UDDA) [9].

Recently, Bernat proposed another term: «brain as a whole (BAAW)». This was suggested because patients with primary brainstem lesions who otherwise meet the clinical criteria for BD may retain EEG, CBF, evoked potentials, and hypothalamic-pituitary neurosecretion. Bernat and coworkers recommended «tightening the clinical tests for brain death or loosening the whole-brain criterion for death». They emphasized that the BAAW criterion is an intermediate standard between the whole-brain and brainstem views, allowing for the irreversible cessation of critical brain functions, while stating that the BD/DNC determination does not require the cessation of all brain functions or the death of every neuron [10].

The term BAAW was also used by Mohandas and Chou, who argued that «in patients with known and irreparable intracranial lesions, irreversible damage to the brainstem is the 'point of no return'» [11]. Pallis fully developed the brainstem criteria of BD/DNC [12]. This view is flawed because it does not consider the function of the cerebral hemispheres [13].

A major argument against «whole brain» is that some brain-dead patients retain residual hypothalamic neurosecretory function [14]. Varela affirms that the requirement of residual hypothalamic neurosecretory function in the declaration of BD/DNC is meaningless [15]. Nair-Collins states that «an individual with preservation of any function of any part of the brain is not dead under the UDDA. There is no argument, and no evidence, that can escape this conclusion. To deny it is to deny logic itself» [16].

We have recently discussed that the hypothalamus plays a key role in the central control of the autonomic nervous system (ANS). The hypothalamus contains neurons that send axons to preganglionic neurons for both the sympathetic and parasympathetic nervous systems, thereby regulating autonomic outflow. If there is residual hypothalamic function in brain dead patients, it is possible to find residual autonomic function [13].

How does the hypothalamus regulate the autonomic nervous system?

In autonomic control, the hypothalamus contains neurons that send axons directly to preganglionic neurons for both the sympathetic and parasympathetic nervous systems. These autonomic control neurons are located in the paraventricular and arcuate nuclei and the lateral hypothalamic area. The dorsal longitudinal fasciculus is the major pathway from the hypothalamus for autonomic control [16].

Magnocellular neurons of the supraoptic and paraventricular nuclei of the hypothalamus secrete the hormone arginine vasopressin (AVP) via the posterior pituitary into the peripheral circulation in response to an increase in plasma osmotic pressure or hypovolemia. In the absence of AVP or the ability of the kidneys to respond to it, diabetes insipidus (DI) develops, characterized by the excretion of large amounts of dilute urine, often accompanied by hypernatremia [17–20].

In contrast, the hypothalamus indirectly controls the anterior pituitary by secreting hypophysiotropic hormones into the local portal circulation.

The functions of the anterior pituitary hormones, their target organs, and the peripheral hormones they control are complex, diffuse, and subject to multiple interrelated feedback loops that affect metabolic functions throughout the body.

Several forebrain, hypothalamus, and brainstem structures are interconnected to organize the output of the autonomic nervous system. Collectively, this is referred to as the central autonomic network, which is further organized into a hierarchy of functional loops. The body temperature regulation is an example of hypothalamic control over brainstem and spinal autonomic nuclei related to longer-term autonomic reflexes [21, 22].

Using HRV methodology, it is possible to assess the ANS objectively. The high-frequency (HF) component is considered a marker of the parasympathetic cholinergic central system, with ambiguous responses generated mainly in the nucleus. The low-frequency (LF) band is associated with vagal and sympathetic influences. The mid-frequency (MF) band has been correlated with biofeedback of baroreceptor function and Meyer blood pressure waves.

Meanwhile, the very low frequency (VLF) range has been associated with the pressor arm of the sympathetic adrenergic system, central thermoregulatory centers, and the renin-angiotensin system. The loss of all HRV power has characterized BD/DNC. I reported a brain-dead case in which the VLF oscillations were the last to disappear, possibly related to residual sympathetic vasomotor activity that progressively disappeared due to the extension of necrosis affecting the nerve centers of the lower part of the spinal cord and the first 2–3 cervical spine segments. Therefore, this patient's preservation of HRV bands this patient's preservation of HRV bands demonstrated persistent medullary autonomic activity within the vagal and other central autonomic nuclei [13].

We have reported a patient who showed residual very low-frequency waves in heart rate variability (HRV) after completing the clinical diagnosis of BD/DNC [23]. All HRV bands were preserved in Jahi, and we showed autonomic reactivity to «Mother Talks» stimulation, suggesting enduring awareness. Therefore, we described a new state of disordered consciousness and proposed that death is the «irreversible loss of both components of consciousness — arousal and awareness.» We suggested rephrasing the definition of the World Brain Death Project (WBDP) as: «the complete and permanent loss of brain function as defined by an unresponsive coma with loss of both components of consciousness — arousal and awareness — and the ability to breathe» [13].

This discussion also examines the use of ancillary tests to confirm BD/DNC. If residual autonomic function is doubtful, the ANS should be assessed, which may provide some emotional awareness.

We also agree with Bernat that the BAAW is intuitive and facilitates a conceptual and practical approach. However, «further refinement is needed to specify precisely which brain functions must cease at brain death and which may continue» [10].

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