

The Neurometabolic Condition of Consciousness: Mitochondrial Regulation of Neural Criticality and Brain Dynamics

Roberto Garcia Sanchez*

Abstract

Consciousness is increasingly linked to large-scale neural dynamics characterized by integration, differentiation, recurrence and criticality. However, the cellular bioenergetic mechanisms that constrain these dynamics remain underexplored. In this review, we propose a neurometabolic criticality framework in which mitochondrial function acts as a regulatory interface between cellular metabolism and network-level brain dynamics. We synthesize evidence from contemporary theories of consciousness, the energetic demands of neuronal signaling, and emerging work showing that mitochondria regulate ATP production, calcium homeostasis, redox signaling, synaptic function and mitochondrial positioning. We argue that these mechanisms can shape the physiological conditions required for critical neural dynamics associated with conscious states. We further consider astrocytic metabolism and microtubule-dependent mitochondrial transport as complementary components of a multiscale neurometabolic system. The resulting model does not identify mitochondria with conscious experience; rather, it proposes that mitochondrial regulation constrains the dynamical regime in which consciousness-related neural activity can emerge and persist. Finally, we outline testable predictions for anesthesia, sleep and disorders of consciousness, emphasizing that selective mitochondrial manipulations should alter network complexity and perturbational responsiveness before generalized neuronal failure occurs if the hypothesis is correct.

Key Words: Consciousness, Mitochondria, Neural criticality, Brain bioenergetics, Network dynamics

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1. Introduction

Consciousness is associated with a distinctive organization of brain activity rather than with a simple increase in neuronal firing. Conscious states support integration across distributed regions while

Corresponding author: Roberto Garcia Sanchez

Address: Universidad Europea de Canarias, Calle Inocencio Garcia, 1, 38300 La Orotava, Santa Cruz de Tenerife, Spain

e-mail ✉ robertogs.ull@gmail.com

preserving differentiated activity patterns, recurrent interactions, metastability, long-range coordination, and flexible responses to perturbation. These properties allow a neural system to combine information without collapsing into either independent local events or globally synchronized activity. Unconscious states may retain substantial neuronal activity while exhibiting reduced complexity, impaired integration, excessive synchronization, or diminished responsiveness to perturbation. The central biological problem is therefore to explain how a living neural system enters and maintains the dynamical regime in which conscious processing is possible.

Neural activity is metabolically embodied. Action potentials, synaptic transmission, restoration of Na^+ and K^+ gradients, calcium extrusion, neurotransmitter cycling, and recurrent signaling impose continuous energetic demands. The cerebral energy budget is dominated by processes that preserve communication, including ionic-gradient maintenance and the consequences of excitatory synaptic activity (Attwell and Laughlin, 2001). Energy availability is consequently not merely a background condition for computation. It helps determine whether neurons remain excitable, responsive, and capable of sustaining repeated interactions.

Mitochondria are positioned to connect this cellular physiology with network dynamics. They produce ATP, regulate calcium, maintain the membrane potential required for oxidative phosphorylation, generate redox signals, support synaptic function, and distribute metabolic capacity within polarized neurons. These functions are coupled: neuronal activity changes mitochondrial demand, while mitochondrial responses modify the conditions under which subsequent activity occurs. The resulting reciprocal relationship provides a plausible interface between intracellular metabolism and large-scale neural organization.

This manuscript develops the hypothesis of neurometabolic criticality: conscious states depend on neural networks maintaining a critical-like dynamical regime, while entry into and persistence within that regime are constrained by mitochondrial regulation of energy, calcium, redox state, membrane potential, synaptic efficacy, and spatial metabolic allocation. Mitochondria are not proposed to generate consciousness independently, encode subjective experience, or provide a sufficient explanation of phenomenology. They are proposed as mechanistic, multiscale regulators of the physiological capacity for integration, differentiation, recurrence, metastability, and perturbational responsiveness.

The decisive empirical distinction is between a permissive and a specific regulatory role. A permissive account holds that mitochondria support neuronal viability and signaling generally, with effects on consciousness appearing only during widespread energetic failure. A regulatory account predicts that selective changes in mitochondrial calcium handling, local ATP supply, membrane potential, respiratory

reserve, redox state, or positioning alter critical-like network properties before generalized neuronal failure. The latter is the falsifiable claim: mitochondrial variables may shift the operating range of neural networks while network architecture, excitation-inhibition balance, neuromodulation, and synaptic organization continue to determine the dynamics themselves.

2. Contemporary theories of consciousness and the missing cellular level

Contemporary theories differ in the variable they place at the center of explanation, but they address complementary aspects of a common problem: how a biological system can preserve differentiated information while coordinating activity across time and anatomical distance. The global neuronal workspace hypothesis emphasizes access and broadcasting. Information becomes conscious when recurrent amplification makes it available to multiple specialized systems, allowing it to guide report, memory, evaluation, and action (Baars, 2005; Mashour et al., 2020). This framework explains large-scale availability and state-dependent access, but it leaves open the cellular conditions that allow some cortical and thalamocortical populations to sustain broadcasting while others fail.

Recurrent processing theory emphasizes feedback within and between neuronal populations rather than a purely feedforward sweep (Lamme, 2006). Recurrence can stabilize ambiguous representations, integrate successive signals, and allow present activity to be shaped by prior processing. Its unresolved cellular question is how feedback loops remain physiologically available. Reliable recurrence requires synaptic release, membrane recovery, calcium control, and sufficient metabolic capacity for repeated interactions. Anatomical feedback therefore does not guarantee preserved effective recurrence.

Integrated Information Theory focuses on intrinsic causal organization, especially the joint presence of integration and differentiation (Oizumi et al., 2014). It explains why consciousness cannot be identified with either global synchrony or independent local events. Its implementation question is how causal distinctions are realized by excitable membranes, synapses, and recurrent pathways. Metabolic regulation may constrain whether these components can express a rich causal repertoire without being identical to the informational structure itself.

Predictive-processing and active-inference accounts describe the brain as a multilevel system that maintains generative models, compares predictions with incoming signals, and updates its organization in response to prediction errors (Friston, 2010). They clarify the roles of hierarchical communication, precision weighting, and neuronal gain, but do not specify how continuous reciprocal signaling meets its energetic and ionic requirements. Mitochondrial state could alter gain, recovery, and synaptic reliability, thereby changing the precision with

which prediction errors are transmitted. It would not itself be a prediction, an error, or a generative model.

Dynamical and criticality-based approaches characterize the temporal regime in which broadcasting, recurrence, causal differentiation, and predictive updating remain flexible. Complexity, metastability, long-range coordination, response diversity, and sensitivity to perturbation connect local events with large-scale organization. Their central unresolved question is how a living network maintains this regime despite changing demand, oxygenation, neuromodulation, and synaptic activity. The neurometabolic proposal addresses this question as a constraint hypothesis: mitochondrial regulation helps determine whether neuronal populations preserve the cellular responsiveness required by these higher-level operations.

The proposed relationship is hierarchical rather than competitive. Workspace mechanisms describe global availability; recurrent processing describes feedback stabilization; integrated-information approaches describe intrinsic causal organization; predictive-processing accounts describe inferential coordination; and dynamical theories describe the regime in which these operations remain flexible. Mitochondrial regulation is positioned beneath and within these levels. It can change the probability that activity propagates, recurs, terminates, or becomes excessively synchronized without determining conscious content or replacing network architecture.

This distinction prevents a category error. ATP, calcium, redox state, and membrane potential are biological mediators and constraints, not phenomenological or computational substitutes. The missing cellular level matters because theoretical descriptions often treat neural elements as functionally available units, whereas their availability is continuously rebuilt by metabolism. Every action potential changes ionic gradients, every synaptic event consumes molecular resources, and every recurrent interaction adds demand. Mitochondria provide one interface through which these local costs can influence large-scale organization. The hypothesis therefore predicts graded and state-dependent changes in network operating range before all-or-none energetic collapse.

3. Neural criticality as a dynamical substrate

Criticality provides a framework for explaining how a neural system can combine broad coordination with preservation of distinct activity patterns. Near a transition between dynamically different regimes, local events may influence distant populations without ensuring that every event spreads globally. The system can retain long-range correlations, a broad repertoire of configurations, and sensitivity to perturbation simultaneously. This differs from excessive order, in which global synchrony suppresses distinctions, and excessive disorder, in which activity terminates locally and fails to coordinate across the network (Chialvo, 2010; Cocchi et al., 2017).

Neuronal avalanches motivate this framework empirically. An avalanche is a cascade of population activity with variable size, duration, and spatial extent. Under some recording conditions, the distributions of these properties approximate scale-free or critical-branching-like statistics (Beggs and Plenz, 2003). Scale-free organization does not prove that the brain occupies an exact mathematical critical point, nor does it imply that every event reaches every region. It indicates that activity is organized across multiple scales without a single characteristic event size dominating the system. Its functional significance may lie in a balance between transmission and containment: activity recruits additional populations but remains capable of terminating.

This balance defines dynamical range. In a subcritical regime, weak inputs may disappear before engaging distributed networks. In a supercritical regime, small inputs may trigger excessive propagation, saturation, or hypersynchrony. A critical-like regime can preserve sensitivity to weak perturbations while avoiding continual runaway activity. Conscious processing requires both responsiveness and selectivity: a system that responds to nothing cannot integrate new information, whereas one that responds identically to everything cannot maintain differentiation.

Integration and differentiation are therefore coupled requirements. Integration concerns the participation of distant or specialized populations in a common process. Differentiation concerns the number and stability of distinguishable patterns the system can express. Metastability adds a temporal condition: a state must persist long enough for coherent processing while remaining labile enough to transition when sensory evidence, internal goals, or perturbations change. Critical-like dynamics may support this compromise by allowing temporary coordination without locking the network into a single attractor.

Perturbational complexity provides a complementary test. The perturbational complexity index combines the spread and richness of evoked responses (Casali et al., 2013). A reduction in PCI may reflect loss of response diversity, loss of integration, or both, and should not automatically be interpreted as reduced firing. Avalanche statistics, PCI, metastability, effective connectivity, and complexity assess overlapping but nonidentical properties; their joint interpretation is more informative than any single metric.

Excitation-inhibition balance helps determine the operating range. Excess excitation can increase propagation while reducing selectivity, producing runaway cascades and global synchronization. Excess inhibition can prevent recruitment of distant populations and reduce dynamic range. Both forms of transmission are metabolically costly because they require vesicle cycling, ion transport, receptor activation, and restoration of gradients. The position of a network relative to a critical-like regime therefore depends on cellular recovery as well as

synaptic architecture.

The brain should not be expected to remain at an exact critical point. Temperature, oxygenation, neuromodulatory tone, sensory input, and metabolic demand change continuously, making a fixed point implausibly fragile. A more realistic concept is a variable critical-like regime: a family of operating states sharing scale-spanning coordination, response diversity, and flexible transitions. Regions may occupy different portions of this regime, while the whole brain moves through it as arousal changes. Mitochondrial physiology may shift the boundaries of the accessible region by changing excitability, synaptic efficacy, recovery time, calcium buffering, and propagation probability.

Loss of consciousness consequently need not involve uniform neural silence. An anesthetized or otherwise unconscious brain may retain substantial activity while losing differentiated, integrated, and perturbation-responsive organization. Critical-like dynamics are a candidate substrate for conscious processing, not a complete theory of phenomenology. Neurometabolic criticality adds that the cellular conditions supporting this organization may be selectively narrowed or displaced before neurons cease firing, producing a testable link between mitochondrial state and network-level dynamics. Keppler's formulation of critical brain dynamics likewise motivates treating criticality as a candidate organizational condition rather than as a complete explanation of experience (Keppler, 2024).

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4. Neurometabolic criticality hypothesis and causal architecture

The central hypothesis is that conscious states depend on neural networks maintaining a critical-like dynamical regime, while entry into and persistence within that regime are constrained by mitochondrial regulation of energy, calcium, redox state, membrane potential, synaptic efficacy, and spatial metabolic allocation. The causal architecture is reciprocal rather than metabolism-first: neuronal activity → metabolic demand → mitochondrial response → ATP/Ca²⁺/redox/membrane-potential regulation → cellular excitability and synaptic efficacy → network dynamics → renewed metabolic demand.

The first stage includes action potentials, synaptic release, postsynaptic currents, calcium entry, and recurrent excitation or inhibition. These events increase ion fluxes and molecular work. Metabolic demand therefore includes ATP required to restore Na⁺ and K⁺ gradients, remove Ca²⁺, recycle synaptic vesicles, and maintain intracellular homeostasis. Demand is spatially heterogeneous and depends on firing rate, synchrony, synaptic location, and recent activity history.

The mitochondrial response couples workload to cellular regulation. Calcium entry and local activity can increase oxidative metabolism, alter membrane potential, and change the distribution of reducing equivalents. ATP production, calcium buffering, redox signaling, and

membrane potential then influence pumps, channels, presynaptic release, receptor function, and recovery. The immediate cellular outputs are changes in membrane thresholds, action-potential reliability, release probability, postsynaptic integration, and recovery kinetics, potentially without any alteration in anatomical wiring.

Network outcomes include propagation probability, recurrent amplification, effective connectivity, synchronization, avalanche structure, metastability, complexity, and perturbational responsiveness. These outcomes feed back into demand by determining which populations are recruited, how long activity persists, and where repeated signaling occurs. A small local mitochondrial change may therefore be amplified or dampened by network organization. A pathway with slightly lower release reliability may become functionally disconnected during a demanding state, while a compensatory pathway carries more traffic and incurs greater metabolic load.

The loop operates on at least three temporal scales. Fast processes include membrane charging, synaptic release, calcium entry, mitochondrial calcium uptake, and ATP-consumption changes during individual events or short bursts. Intermediate processes include respiratory adjustment, ATP replenishment, redox signaling, vesicle-pool recovery, ionic restoration, and changes in synaptic gain over seconds to minutes. Slow processes include mitochondrial transport, anchoring, remodeling, biogenesis, turnover, and longer-term metabolic allocation. Similar network phenotypes may therefore arise from rapid buffering failure, intermediate respiratory limitation, or slow redistribution of mitochondria, although their temporal signatures should differ.

The variables have distinct causal roles. Mitochondrial calcium handling, membrane potential, local ATP availability, and redox state are candidate cellular mediators. Oxygenation, vascular supply, neuromodulation, temperature, synaptic architecture, and excitation-inhibition balance are modulators. Complexity, PCI, avalanche statistics, effective connectivity, integration, differentiation, and metastability are network outcomes. Neuronal viability, membrane integrity, firing capacity, and global ATP depletion are controls that distinguish specific regulation from generalized failure.

The key consequence is a change in accessible dynamical phase space rather than independent determination of network dynamics. Anatomical connectivity may remain constant while effective connectivity changes because transmission reliability, latency, and recovery have changed. Selective mitochondrial perturbation should be able to move a network toward fragmentation, excessive synchrony, or reduced metastability while leaving basic firing and cell survival relatively intact. If the relationship is causal, rescue of the targeted mitochondrial function should restore the prior dynamical range.

Severe mitochondrial failure supports only a permissive role because it produces nonspecific energetic collapse. Specific regulation requires selectivity, dose dependence, temporal precedence, preserved viability, and preferably reversibility or rescue. The model is therefore ontologically modest: mitochondrial variables constrain the conditions under which global availability, recurrence, causal differentiation, predictive dynamics, and critical-like complexity can emerge and persist, but they do not replace those higher-level organizations or independently determine consciousness.

5. Mitochondrial mechanisms linking cellular physiology to network dynamics

5.1 Local ATP production

After depolarization, the Na^+/K^+ -ATPase restores transmembrane gradients, calcium pumps remove cytosolic Ca^{2+} , and synaptic terminals power vesicle docking, fusion, endocytosis, and recycling. Activity-driven local ATP synthesis is especially important because demand is concentrated at axons, dendrites, and synapses and rises rapidly during sustained transmission (Rangaraju et al., 2014). Local insufficiency can increase synaptic failure or prolong recovery before global neuronal dysfunction appears. The network consequence is a change in timing and reliability: anatomical connections remain present, but effective connectivity weakens, propagating cascades may terminate prematurely, and recurrent amplification may fail.

5.2 Mitochondrial calcium handling

Calcium is both a signal of activity and a potential source of stress. Mitochondrial uptake can stimulate oxidative metabolism so that energy production tracks workload while also shaping cytosolic calcium transients (Rizzuto et al., 2012; Llorente-Folch et al., 2015). Altered uptake or buffering changes calcium-dependent channels, neurotransmitter release, postsynaptic integration, and recovery. Too little local buffering may prolong calcium elevations and distort release during repeated activity; excessive buffering may weaken action-potential-to-fusion coupling. In a near-critical network, these changes can shift propagation probability, recurrence, oscillatory coordination, and the balance between integration and differentiation without immediate structural injury.

5.3 Membrane potential and respiratory reserve

The mitochondrial membrane potential supports oxidative phosphorylation and calcium uptake, while respiratory reserve determines how far oxidative phosphorylation can increase when demand rises. Partial depolarization or reduced reserve may leave baseline firing apparently intact while narrowing the range of sustained or perturbed activity a neuron can support. The network may consequently lose long-range coordination, response diversity, or recovery after repeated perturbations before total ATP levels collapse. This dissociation would indicate regulatory impairment rather than

simple energetic failure.

5.4 Physiological redox signaling

Mitochondrial respiration produces reactive oxygen species. Excessive accumulation damages proteins, membranes, and nucleic acids, but physiological redox signals can regulate enzymes, channels, and synaptic proteins (Murphy, 2009). A moderate redox shift could change neuronal gain, release probability, and recovery kinetics without representing oxidative injury. Increased excitability might favor excessive synchronization, whereas impaired transmission and recovery might favor weak propagation and fragmentation. Redox signaling is therefore treated as a modulator of response properties, not as the cause or content of consciousness.

5.5 Presynaptic mitochondrial function

Presynaptic terminals have high and fluctuating energy demands. Mitochondria in these terminals support vesicle cycling, calcium buffering, and the maintenance of release probability during sustained activity. Their positioning and function are critical for reliable synaptic transmission. When presynaptic mitochondrial function is compromised, short-term plasticity and recovery from synaptic depression are impaired, which can lead to use-dependent synaptic failure. This selectively weakens active pathways and alters the effective connectivity of networks, particularly during high-frequency activity, without necessarily affecting basal transmission at low rates.

5.6 Anchoring and microtubule-dependent transport

Energy sensing can retain mitochondria near active presynaptic sites, where local ATP production supports sustained transmission (Li et al., 2020). Transport along microtubules distributes mitochondria through axons and dendrites and positions them according to local energetic and calcium requirements (Sheng and Cai, 2012). Disrupted transport may impair a distant terminal or dendritic branch even when somatic respiration appears preserved. The resulting change in effective connectivity is spatially selective: a projection remains anatomically intact, but its functional influence declines because repeated transmission cannot be sustained. The relevant variable is therefore the distribution of metabolic capacity across computationally important sites, not average mitochondrial content.

These mechanisms form a coupled regulatory system rather than a single quantity called energy. ATP availability affects recovery; calcium affects both metabolism and excitability; membrane potential and respiratory reserve limit sustained demand; redox state modifies cellular gain; presynaptic mitochondria shape transmission; and anchoring and transport determine where support is available. Together they can influence propagation, recurrence, integration, differentiation, perturbation sensitivity, and metastability. Connectivity, neuromodulation, vascular supply, excitation-inhibition balance, and synaptic organization still determine network dynamics

within the physiological range that mitochondria help maintain.

6. Astrocytes and cytoskeletal infrastructure as complementary components

Neural criticality is sustained within a multicellular metabolic environment rather than by isolated neurons. Astrocytes take up neurotransmitters, regulate extracellular potassium, provide metabolic substrates, and participate in neurovascular coupling. Glutamate uptake can stimulate astrocytic glycolysis and couple neuronal activity to local energy supply (Pellerin and Magistretti, 1994). By terminating excitatory signaling and limiting spillover, astrocytes help regulate excitation-inhibition balance. Potassium buffering constrains extracellular K^+ changes that would otherwise shift membrane potentials and firing thresholds. These processes affect propagation, synchrony, recurrence, and the dynamic range in which critical-like activity is possible.

Astrocytic processes also organize the relationship between local demand and vascular supply. Neurovascular coupling helps deliver oxygen and substrates when demand rises, while limitations in substrate delivery can reduce respiratory reserve even when synaptic architecture is unchanged. Adequate support may allow mitochondria to meet transient increases in demand and preserve distributed integration. These are enabling conditions for neural dynamics, not an independent theory of conscious experience.

The neuronal cytoskeleton supplies complementary spatial infrastructure. Microtubule-dependent transport moves mitochondria through axons and dendrites and retains them near sites where ATP demand and calcium buffering are high. Impaired transport can produce local synaptic unreliability while leaving somatic mitochondrial measurements relatively normal. The resulting effective-connectivity change may be selective, altering which pathways support integration, recurrence, or metastability without directly changing anatomical wiring. Astrocytes and microtubules are therefore incorporated as components of the neurometabolic context while mitochondria remain central. Neither astrocytes nor microtubules is proposed as an independent substrate of consciousness.

7. Testable predictions, experimental strategy, and limitations

The hypothesis is most strongly supported if selective mitochondrial perturbations change network dynamics before generalized neuronal failure. Experiments should therefore combine graded manipulation, temporal precedence, simultaneous cellular and network measurement, and rescue. A first test would alter mitochondrial calcium uptake or buffering while measuring mitochondrial and cytosolic calcium, synaptic transmission, cell viability, membrane integrity, and network activity. Modest perturbations should be

applied before severe calcium loading, which serves as a positive control for nonspecific injury. A regulatory effect would involve dose-dependent changes in complexity, avalanche distributions, integration, differentiation, recurrence, effective connectivity, metastability, or PCI while basic signaling and viability remain substantially preserved.

Second, mitochondrial membrane potential and respiratory reserve should be manipulated while measuring oxygen consumption, ATP, membrane integrity, and neuronal viability. Partial depolarization or reduced reserve should be calibrated so that the intervention does not simply reproduce hypoxia or global metabolic poisoning. If these variables help define the operating range, the predicted effects include reduced recovery after perturbation, narrower dynamic range, earlier loss of long-range coordination, or a shift toward excessive synchrony or fragmentation. Oxygen delivery should be maintained, and an oxygen-limitation control should be included because hypoxia may produce a different cellular signature.

Third, local ATP supply should be tested at synapses rather than inferred from whole-cell ATP. Measurements should include presynaptic release probability, vesicle-pool recovery, postsynaptic gradient restoration, local ATP signals, and effective connectivity. Selective impairment at active terminals should reduce transmission reliability and recurrence before widespread dysfunction. Conversely, preserving local ATP during increased demand should help maintain response complexity and metastability if local energy availability is limiting. Uniform ATP depletion would provide a comparison and should produce less spatially specific effects.

Fourth, physiological redox signaling should be manipulated without inducing oxidative injury. Changes in neuronal gain, propagation, integration, differentiation, or metastability should track the redox manipulation and be reversible or preventable by pathway-specific intervention. Measurements of oxidative damage, membrane integrity, and respiratory failure are essential controls; otherwise, an apparent redox effect could simply reflect toxicity.

Fifth, mitochondrial positioning should be examined by disrupting transport or anchoring while measuring local ATP, calcium buffering, synaptic release, and network dynamics. A spatially restricted deficit should alter selected pathways without changing anatomical projections, and rescue of positioning should restore local physiology.

The measurement platform should combine high-density electrophysiology, perturbational stimulation, and mitochondrial imaging. Electrophysiology can quantify oscillations, avalanches, propagation, synchrony, and state transitions. Perturbation can estimate PCI, integration, differentiation, response diversity, and recovery. Imaging or validated reporters can measure mitochondrial and cytosolic calcium, ATP-related signals, membrane potential, redox

state, and positioning. Effective connectivity should be estimated with methods sensitive to direction and time, while anatomical connectivity is measured independently. This distinction is essential: a change in effective connectivity without rewiring would support the proposed cellular mechanism.

Controls must distinguish mitochondrial regulation from general neuronal failure. Studies should monitor cell viability, membrane integrity, firing capacity, synaptic release, oxygenation, glucose or substrate availability, temperature, and extracellular potassium. Sham and vehicle controls, non-mitochondrial calcium controls, oxygen-limitation controls, matched firing-rate changes, and toxicity assays are required. A manipulation that changes complexity only when neurons stop firing, membranes fail, or ATP is globally depleted supports a permissive account. A selective change in PCI, avalanche structure, or effective connectivity during preserved firing and viability supports regulation.

General anesthesia is the primary test case because it provides controlled transitions in responsiveness and an opportunity to test temporal precedence. Critical dynamics in spontaneous EEG have been associated with anesthetic-induced loss of consciousness and perturbational complexity (Maschke et al., 2024). Simultaneous electrophysiology, PCI, mitochondrial calcium, membrane potential, ATP-related signals, oxygenation, and redox measurements could determine whether mitochondrial changes precede, covary with, or follow loss of critical-like organization. Pharmacological, genetic, or optical interventions could then test whether changing a candidate mediator shifts the threshold, timing, or reversibility of the transition.

Sleep provides a complementary physiological context. The model predicts reduced integration, altered metastability, and mitochondrial changes that precede or accompany transitions into deeper sleep, while recognizing that sleep includes cycling neuromodulation, vascular adaptation, and homeostatic regulation rather than a direct anesthetic action. Sedation may provide an intermediate, graded test, with possible dissociations between spontaneous activity and evoked responses. Disorders of consciousness are clinically important but heterogeneous; mitochondrial capacity may relate to residual PCI or integration, although injury, inflammation, vascular disruption, and regional disconnection can produce effects not present in anesthesia or sleep.

Across contexts, the strongest evidence would combine time-resolved measures with targeted intervention and show that criticality-related changes precede generalized failure, are quantitatively linked to mitochondrial state, and can be prevented or reversed by restoring the targeted function. Temporal precedence alone is insufficient because mitochondrial and neural variables may both respond to a third factor. Stronger causal evidence requires dose-response relationships, mechanistic specificity, anatomical localization, state dependence,

reversibility, and rescue.

Several limitations constrain interpretation. Direct evidence linking mitochondrial regulation to conscious-state transitions remains indirect. Mitochondrial dysfunction clearly affects neuronal and cognitive function, but this does not establish a specific role in consciousness. Criticality measures are methodologically sensitive: avalanche statistics, scaling relations, complexity, PCI, and metastability depend on recording modality, preprocessing, spatial scale, sampling rate, and model assumptions. Apparent changes may reflect signal-to-noise ratio or firing rate rather than altered organization.

Mitochondrial variables are difficult to measure noninvasively in humans, and available proxies may average across heterogeneous cell types and regions. Neurons differ in morphology, firing pattern, synaptic workload, mitochondrial density, and reliance on oxidative metabolism. Mitochondria may have partial and context-dependent effects because neuromodulation, thalamocortical organization, excitation-inhibition balance, vascularization, astrocytic support, and synaptic architecture also shape network dynamics. The theory would be weakened if selective manipulations changed criticality-related measures only after ATP depletion, hypoxia, widespread synaptic failure, or cellular injury, or if mitochondrial changes consistently followed transitions and could not alter them when manipulated independently.

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8. Conclusions

Neurometabolic criticality proposes that conscious states depend on distributed, integrated, differentiated, recurrent, metastable, complex, and critical-like neural dynamics whose biological realization is constrained by mitochondrial regulation. Established physiology shows that neuronal signaling requires continuous energy expenditure, ionic-gradient restoration, calcium control, synaptic recycling, and coordination with astrocytic and vascular support. Mitochondria regulate more than ATP production: they participate in calcium handling, membrane-potential maintenance, redox signaling, presynaptic function, respiratory reserve, and spatial metabolic allocation.

The proposed mechanism is specific but limited. Mitochondrial state may alter the accessible dynamical phase space by changing transmission reliability, recovery, excitability, calcium buffering, and responsiveness to perturbation. The same anatomical network could therefore occupy different effective configurations under different mitochondrial conditions. Mitochondria are not proposed to be consciousness, to encode subjective content, or to replace network architecture, neuromodulation, thalamocortical organization, or excitation-inhibition balance.

The decisive distinction is between permissive support and specific

regulation. Support would be indicated by effects restricted to global energetic failure. Regulation would be indicated by selective, dose-dependent, temporally preceding, reversible, and rescuable changes in complexity, integration, differentiation, avalanche structure, effective connectivity, metastability, or PCI while neurons remain broadly viable. Multimodal experiments in anesthesia, supplemented by sleep and disorders-of-consciousness studies, can test this distinction. As perspectives for future research, this framework calls for coordinated multimodal studies linking cellular bioenergetics with network-level measures across anesthesia, sleep, and disorders of consciousness, and for the development of noninvasive proxies of mitochondrial state suitable for human research. The evidential status remains provisional, but the framework is sufficiently mechanistic and falsifiable to guide experiments without reducing consciousness to a molecular variable.

Author Biography

Roberto Garcia Sanchez was born in Santa Cruz de Tenerife, Canary Islands, Spain. He holds a degree in Psychology (Universidad de La Laguna, La Laguna, Canary Islands, Spain, 2014), a Master's degree in General Health Psychology (Universidad de La Laguna, La Laguna, Canary Islands, Spain, 2017), and a PhD in Logic and Philosophy of Science (Universidad de La Laguna, La Laguna, Canary Islands, Spain, 2021). He previously served as Director of the Doctoral Studies Department and Vice-Rector for Research at TECH Universidad Tecnológica.

He is currently a Professor at the Universidad Europea de Canarias, La Orotava, Tenerife, Spain, and an external professor at the Universidad de La Laguna. He is Principal Investigator of the Applied Humanities Research Group at the Universidad Europea de Canarias, President of the NUMES Research Institute (Nutrition, Metabolism and Health), Coordinator of the NUMES Working Group (Nutrition, Metabolism, Mental Health and Lifestyle) of the Spanish Association of Neuropsychiatry, and Secretary General of the Spanish Institute of Lifestyle Medicine.

His research interests include the study of personality, consciousness, psychopathology, nutrition and metabolism in mental health, as well as the medical humanities. He serves on the scientific committees of the journals *Egle* and *Médica Review*, and on the editorial boards of *Abaco* and *Análisis y Modificación de Conducta*. He also serves as a reviewer for several high-impact journals indexed in the Journal Citation Reports (JCR) and Scopus. He is the recipient of the Best Review Award from the journal *Canarias Pediátrica*.

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