Energy transduction and the mind–mitochondria connection

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The body and mind are fuelled by energy. But where does the energy come from? The sun beams energy through space as photons that are captured by plants, which store that energy in the improbable separation of carbon and oxygen. By reuniting carbon and oxygen in their mitochondria, breathing animals power their warm bodies, thoughts, feelings, minds and consciousness. Thus, the life-giving flow of energy proceeds from light, through chemistry, into life. Mapping the mechanisms of energy transformation among mind-imbued organisms is the challenge for the field of mitochondrial psychobiology. Emerging evidence positions energy as the substrate of the mind–body connection, linking the molecular processes in the organism and the subjective experiences in our mind. Building a bioenergetic psychobiology framework can stimulate the health sciences in three main ways: it provides an empirical foundation to examine the *interconnectedness* of people and their environment, highlights health as a *dynamic process,* and may eventually illuminate *new approaches and strategies to optimize* the energetic mind–body crosstalk that is the basis of human health.

The body–mind unit

Human beings are both body and mind. We know our existence through our conscious, subjective experience of the world around us, i.e., what we experience in our mind. And, as far as we know, the essential condition for having a mind in the first place is having a living brain and body. Thus, the mind and body are two expressions of the same creature.

For further evidence that mind and body are interlinked, let us consider a few examples. The fear of speaking in public, within seconds, makes your heart race and your blood pressure rise; it activates the sweat glands in your clammy hands. For the athlete, the anticipation of the race alone is enough to flood the blood with powerful hormones (adrenaline, cortisol) that liberate and mobilize metabolites to fuel the energy needs of the upcoming challenge. The immune cells in your blood also are under emotional regulation of stress hormones released by the brain and endocrine glands, which trigger changes in the (epi)genome and dictate when and how genes are expressed. The mind, subjective as it is, regulates bodily biology and physiology.

On the other hand, processes within the body elicit subjective experiences. Our athlete again, now running and experiencing the burning of acidity in their contracting muscle, begins to experience the discomfort and anxiety of losing the race. Other interoceptive processes – afferent input signals informing the brain of peripheral processes – shape our feelings, moods and emotions. Air hunger – a blocked trachea making us run out of oxygen – triggers panic within seconds. Pain likewise modulates how energetic and optimistic we feel about the future. The body, as objectively biological as it is, shapes the mind. Mind and body are linked by a two-way stream.

But a stream of what? The mind–body unit is a two-way stream of energy, transformed from one form to another. It carries information, from one place to another, connecting cells and organs to one another into a coherent whole. Without energy animating the body, living beings are merely an agglutination of a few trillion inanimate cells – with their genomes, proteins and metabolites frozen in time. But animated by energy, the body is enlivened and gives rise to the mind: feelings and emotions, thoughts, ideas, hopes and love. The mind–body connection is an energetic one, and examining how this connection arises at the subcellular level can bring new insights into the forces and mechanisms that sustain human health.

Energy-based information transfer between mind and body

Transmitting mind states into bodily states, and vice versa, is essential to life. But it requires energy. In fact, keeping the brain and body alive consumes the biggest share of our daily energy budget (called basal metabolic rate). Although a relatively small organ, the brain is energivorous. It consumes large quantities of energy to process, anticipate (and occasionally ruminate), plan and regulate physiological functions. Carrying information to and from the brain via nerves and hormones involves the transmission of action potentials, the synthesis, release, reuptake and degradation of neurotransmitters, the sprouting and pruning of synapses, the regulation of genes, etc. At every step in our biology, molecular operations underlying brain–body communication consume precious energy.

But energy flow doesn't just keep us alive; it makes us who we are. Energy powers ion pumps, enzymes, ribosomes and molecular motors in our neurons, glands and muscles. In turn, these activities underlie our behaviours. Studies in animals show that altering energy transformation alone changes how animals behave and respond to stress. Imagine for an instant interacting with the same person when their energy level are *low* (in a food-deprived state, late at night, after having ran a marathon) or *high* (well rested, at a mid-morning brunch, after a cup of coffee). The interaction is not the same experience. Our decisions are also shaped by our physiological, energetic state. Energy flow shapes social behaviours – in humans and in animals.

From sun to cells

In addition to influencing our behaviours, energy flow generates body heat and keeps us warm. Where does the warmth and energy come from? Ultimately, of course, it comes from the sun (Figure 1). Energy from the nuclear fusion of hydrogen in our closest star, the sun, is projected and beamed down to Earth as photons – a form of electromagnetic radiation. The photons' energy is then absorbed by pigmented chloroplasts in leafy plants and trees and used to do the thermodynamically improbable. Chloroplasts condense atmospheric carbon dioxide into starch, fruits and vegetables, expelling molecular oxygen in the process and releasing it into the air. The photons' energy thus becomes trapped in new carbon–carbon bonds of food and also 'stored' in the chemical possibility that oxygen and carbon atoms may reunite again (the technical term is *electronegativity*, which refers to the tendency of oxygen to attract shared electrons when forming a chemical bond). The sun's energy is thus stored in the separation of oxygen from

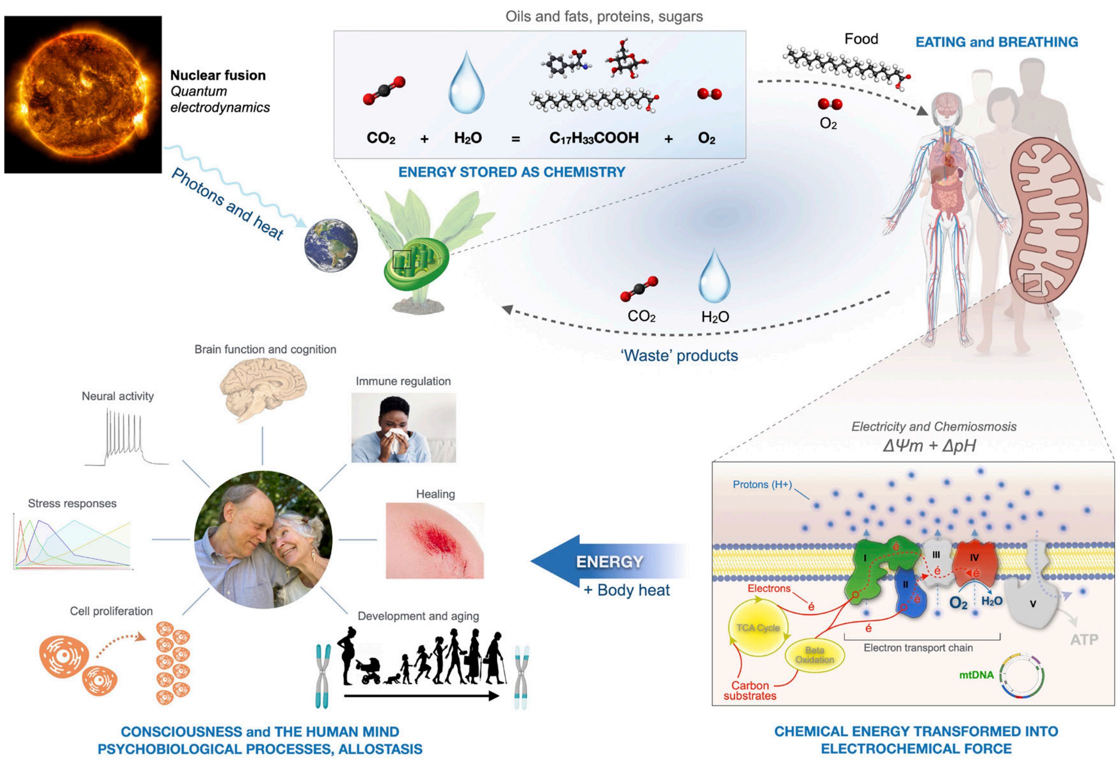

Figure 1. Energy flow from sun to cells to minds. Energy released from nuclear fusion in our closest star is beamed down to Earth as photons. Plants capture and use the photons' energy to separate carbon and oxygen, producing food substrates and molecular oxygen (O_2) in the process. Animals eat sun- and plant-derived food substrates and breathe plant-derived O_2 to feed their mitochondria. In mitochondria, the reunification of carbon-derived electrons with oxygen provides the driving force to generate the electrochemical charge ($\Delta\Psi m + \Delta pH$) across the inner mitochondrial membrane. This powerful charge provides the driving force for all life-related processes in the human mind and body and keeps the body warm. Energy flow is the basis for the mind–body connection that shapes human health.

the food's carbon. Should we wish to unleash the sun's energy and heat, all we need is something to set off the exergonic reaction reuniting carbon and oxygen.

How so? Just heat up a piece of wood sufficiently and voilà! Oxygen jumps onto the trapped carbon–carbon bonds of the wood with sufficient vigour that it steals an electron, releases heat and a flame arises. Rapidly, the released energy ignites neighbouring molecules into a chain reaction. We call this chain reaction *fire*. In the process, both the carbon bonds of the wood and the oxygen from the air are 'consumed' – finally rejoined and returned into carbon dioxide (CO_2). The other main product of this reaction is heat – large amounts of heat, released at times destructively, and always together with light. Thus, the heat and light of the sun radiate from the flame, liberated from organic matter by the action of oxygen.

But there is another way to unleash the sun's energy without burning yourself – an ingenious way evolved by aerobic cells on Earth. This way is as follows: first, break down carbon-based food substrates to small manageable sizes (usually 2-3 carbons in length). Then pull out, one by one, the electrons that make up the carbon–carbon bonds, and load these electrons onto special carriers (called reducing equivalents). Then have a series of metal ions strategically arranged into a kind of electric cable (called the electron transport chain) to carry these electrons from the carriers to their most desired destination – the one they have been longing for ever since captured by a green leaf: oxygen. The electronegativity of molecular oxygen, coupled with free electrons, creates this almost unimaginable drive – a thermodynamic gradient, giving rise to an electric (i.e., electron flowing) current. The trick here is to capture the energy from the flow of electrons down the electron transport chain and turn it into something that can power life.

Turning raw energy into complexity in mitochondria

Life is complex and requires many different kinds of molecular operations. If energy was transformed into only one kind of operation, then life would be limited by this simplicity, even if large amounts of carbon-electron-oxygen energy were available. The key then is to transform the electron flow into a kind of malleable or highly versatile energy form, one that can be used to power dozens, hundreds or thousands of different molecular operations. This is accomplished by energizing the proteins that hold the electron transport chain's 'metal wire' into doing something masterful. To achieve this, the closely interacting proteins are embedded into a special fluid membrane called the inner mitochondrial membrane. The electron flow is then coupled to the pumping across the membrane of the smallest and simplest imaginable element in the universe – the proton (H^+).

The proton is a hydrogen (number one in the periodic table of the elements, used in the stars for nuclear fusion) without an electron. Coupling the quantum flow of electrons to the translocation of protons across the 5-nm membrane gap generates a powerful force – an electrochemical gradient called the mitochondrial membrane potential ($\Delta\Psi m + \Delta pH$). This force stands at ~16,000,000 volts/m, an order of magnitude larger than that of a lightning bolt. It is like having a formidable battery in your pocket (in fact in each of your cells) to power your phone, flashlight, laptop, car and anything that works with electricity. By pulling electrons from carbon substrates, creating a path for their reunification with oxygen and extracting energy from chemistry, food is turned into a versatile, flexible form of energy that can power complex, multicellular life. In this process, heat is naturally generated, and perhaps also small amounts of sunlight as biophotons.

In your body, this magnificent sequence of events turning condensed sun energy into membrane potential and electricity takes place in a special organelle – a 'cellular organ' called the *mitochondrion*. Each cell in our body contains hundreds to thousands of mitochondria, depending on how much energy they consume. Mitochondria are dynamic organelles that move around, fuse and interact with each other, occasionally moving from one part of the cell to another and even between cells, sensing and signalling information about the metabolic state of the organism. They have two membranes: one outer membrane that encapsulates their >1,300 different proteins and compartmentalizes their operations from the rest of the cell; and the special inner membrane where the electron transport chain sits, and where oxygen pulls on electrons to charge the mitochondrion.

With their *membrane potential* (referring to the energy potential to perform work), mitochondria indeed perform dozens of molecular functions. The precious transmembrane charge is used to import hundreds of proteins from the cytoplasm, to uptake signalling ions such as calcium and sodium, to import metabolic substrates to feed the electron carriers, and to metabolize neurotransmitters and hormones. This includes all of the sex and stress hormones that make new life possible (e.g., estradiol, progesterone) and that the mind can request to fueld the stress response (e.g., cortisol). Energized mitochondria also synthesize the building blocks needed to make DNA and replicate the nuclear genome, produce signalling molecules including reactive oxygen species that modulate the expression of genes in the nucleus, and synthesize iron–sulphur clusters and haeme molecules without which our cells cannot survive. Importantly, an impressive turbine and rotor-like component (the F_0F_1 ATP synthase) embedded in the inner membrane can harness, on demand, the membrane potential to synthesize adenosine triphosphate (ATP). ATP is one of the chemical intermediates or cellular energy 'currency' that carries energy throughout the cell. ATP is also relatively versatile and used widely to power the pumps, enzymes, ribosomes and motors within our axons, glands and other organs that connect mind and body processes.

The mind–mitochondria connection and mitochondrial psychobiology

The cross-talk of mind and body as a coherent unit shapes and colours our daily experiences and our health. As we have seen, this cross-talk requires energy – transformed from chemistry to psychobiology within our mitochondria. The energy flow described earlier is universally shared across breathing creatures. Conscious minds of variable levels of sophistication, therefore, depend on the energetic *interface* between molecular operations of cells and organelles and the subjective aspects of our human experiences.

Most researchers in the life and biomedical sciences share the common goal to understand the functioning of living organisms and to use that knowledge to improve human and planetary health. How can the above integrative understanding of energy flow on Earth and in the human mind–body unit be harnessed in research?

This integrative energy-centric understanding creates a framework to think about health. This framework is the foundation for an emerging discipline based on bioenergetic principles and focused on elucidating mind–body processes: *mitochondrial psychobiology*. This discipline is concerned with how bioenergetic processes within mitochondria relate to specific aspects of the human experience, including moods and emotions, psychosocial factors including social connections, stress and trauma, psychopathology and positive psychological states, among others. Understanding the energetic basis of mind–body processes can have at least three positive effects on the health sciences.

First, the energetic connection of all living things and of the body–mind unit provides an empirical foundation to appreciate the *interconnectedness* of things in the world. It reminds us how fundamentally interdependent we exist with plants and other living organisms, including other humans who breathe and eat the same sun-derived air and food. Second, because energy flow must be constantly sustained, it helps us appreciate health as a *dynamic process*. This in turn provides the theoretical foundation to build increasingly accurate causal frameworks discerning what is upstream and primary (energy and communication processes) from what is downstream and secondary (molecular pathology, accumulation of damage) in the chain of events linking energy, cells, minds and health. Third, an energetic framework may eventually illuminate approaches and strategies to nourish the energetic mind–body connection, and thus optimize health across the lifespan. Applied broadly, an energetic framework of mitochondrial psychobiology has the potential to guide research and uncover new ways to ensure that every person can reach their full health potential.

Mapping the instructive role of energy flow in human health is the task, challenge and opportunity ahead for the evolving field of mitochondrial psychobiology. ■

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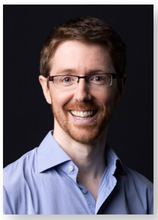

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