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The Human Microbiota and the Immune System; Reflections on Immortality

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Article Info

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Abstract

In this Editorial I discuss implications arising from the novel interpretation of the human microbiota as integral part of the immune system with the ability to learn, memorize and have consciousness. The ship of Theseus as example of continuity as it relates to immortality is discussed. Finally, analogies between the human microbiota and the rhizome as proposed by Deleuze and Guattari are explored.

Your third brain will live forever

This rather strong statement might sound quite odd or even inappropriate to some, since the themes of life and death, or life after death, are usually reserved to books of religion or philosophy. However, a deeper insight into the ramifications and the consequences of having discovered that we are only minimally "human", inevitably leads to such speculations. Before entering into this area of thought, let's summarize the terms of the question:

1. The third brain. With this term I indicate the human microbiota as it relates to the first brain and to the immune system with its capacity of learning and retaining memories [1].
2. What we call "human" is not a homogeneous living being, but rather a complex ecosystem made by cells that interact with each other: only few - about 10% - of these cells are human and have their genetic information encoded in human DNA. The remaining 90% is constituted by microbial cells, thousands of different strains, and their information is encoded in microbial DNA [2].
3. Human and microbial cells continuously exchange information and are reciprocally influenced by each other. The microbiota is shaped by these interactions and rapidly becomes as unique as the sequence of human DNA [3].
4. Therefore, identity does not reside solely in the sequence of human DNA but in the combination of human and non-human DNAs. This is so true that non-human DNA is used for forensic analyses exactly as human DNA [4]. The information in the non-human DNA is 100 folds that of human DNA, if not more; from the genetic point of view we barely are 1% human [2] [3].
5. Although the topic of death is a complex one, it is assumed that what actually dies is the individual identity; the molecules and the atoms of the body remain, but they are no longer assembled as in a living body. Human cells die, their DNA is

fragmented, the information contained in the sequence of DNA is lost, and we assume that the person holding that DNA is dead. This could not be the case.

6. If identity does not reside only and uniquely in human cells and in their DNA, then what actually dies is only 1% of the genetic information that makes the ecosystem we call "human". For example, when we assume antibiotics, a great number of bacterial cells in our microbiota dies. The number of dead microbial cells may even be higher than the total number of human cells we have in our bodies. We lose a great deal of information and we may suffer some side effects because of microbiota alterations; nevertheless, even if a great number of our microbial cells are dead, we do not feel dead at all.

To make it simple: microbial cells survive the human cells and, since the information in these microbial cells has been shaped by the reciprocal interaction with the human cells, this information is not lost after the death of the human body. Essentially, it lives forever.

This concept may be hard to digest; however, it is consistent with a philosophical argument of antiquity as well as with more modern concepts.

The ship of Theseus

It was around the year 1,260 B.C. when the ship of Theseus sailed from Crete to Athens to announce the victory over the Minotaur. According to Plutarch's "Life of Theseus", the ship was kept in the Athenian harbor as a memorial for several centuries.

"The ship wherein Theseus and the youth of Athens returned had thirty oars, and was preserved by the Athenians down even to the time of Demetrius Phalereus, for they took away the old planks as they decayed, putting in new and stronger timber in their place"[5].

According to the tradition, the ship had to be maintained in a seaworthy state, because, in sign of gratitude for Theseus's successful mission, the people of Athens had pledged to honor the god with the ship of Theseus sailing from the harbor to the temple of Apollo every year. The need to maintain the ship in a seaworthy state for centuries, however, poses a substantial problem that, ever since, is known to students of philosophy as the Theseus paradox.

"Is a thought experiment that raises the question of whether an object which has had all of its components replaced remains fundamentally the same object? The paradox is most notably recorded by Plutarch in Life of Theses from the late first century. Plutarch asked whether a ship which was restored by replacing each and every one of its wooden parts remained the same ship. The paradox had been discussed by more ancient philosophers such as Heraclitus, Socrates, and Plato prior to Plutarch's writings; and more recently by Thomas Hobbes and John Locke. This thought experiment is 'a model for the philosophers'; some say, 'it remained the same', some saying, 'it did not remain the same' ".

More recently, the paradox has been used in cognitive psychology by a researcher from the Department of Psychology of the University of British Columbia, Canada, who performed three experiments on 480 participants [6]. Dr. Hall concluded that "knowledge about specific kinds of objects and their canonical transformations exerts an increasingly powerful effect, over the course of development, upon people's tendency to rely on continuity as a criterion for attributing persistence to objects that undergo change". Such a conclusion implies that today, as in the past, we have the tendency to think that the identity of the ship does not reside in the individual parts that were changed during the years because of their decay, but in its design that is the way the individual planks had been originally assembled by the shipmaster of Theseus. Roland Barthes, a French philosopher writing on this subject in the seventies of the last century, saw in the persistence of the form of the ship a key structural list principle that defined identity [7].

If we apply the Theseus paradox and its solution to the human-microbiota ecosystem, we see that all the components of this system change, just like the planks of Theseus's ship were changed as they decayed. It is calculated that all our human cells are renewed every 7 years and the microbial cells much faster. However, the identity remains according to the structurallist principle. Both for human cells and microbes, the identity that remains lays in the information contained in the sequence of DNA, and this information is inextricably interconnected.

It is well known that the microbes of the microbiota survive our human cells and, from the standpoint of sheer numbers, we may say that 1% or less of our information dies with our human cells. It is as if the ship of Theseus had lost 1% of its timber; it can be presumed that the Athenians would not have noticed the loss and they would have sailed and venerated the ship for centuries just the same.

The question then is: does the microbiota retain the information it has acquired during its time in symbiosis with the human cells, that is during the timeframe we define "our lifetime"? From the standpoint of genetic information in DNA the answer is unambiguously affirmative. Microbial genes are continuously modified by what we eat, drink or breathe, by our mental states or lifestyles [8]. Likewise, the microbes deeply influence our lifestyle to increase their fitness up to the point that researchers write of microbes manipulating humans [9]. In other words, human genes are continuously modified by the interaction with information contained in microbial genes. This does not mean that our commensal microbes cause mutations in our DNA, but that they modify the expression, i.e. how the information contained in the human genes is read and interpreted. In other words, the microbial genes modify the human epigenome, the superstructure that directs the working of the genome [10].

There is no doubt that our lifestyle leads to information that shapes the microbial information and viceversa. Such a reciprocal exchange of information was well described by

Blythe and Pacini in a very recent report [11]. In this study, the Authors "describe the changes associated with three months of intermittent fasting and probiotic yogurt consumption in a 72-year-old marathon runner with chronic lymphocytic leukemia for a number of years". They observed that probiotic yogurt consumption was associated with significant elimination of toxicants that the subject had accumulated during his many years of urban running, notably, Monoethyl phthalate (MEP) and 2-Hydroxyisobutyric acid (2HIB). According to the Authors, "the toxicants, whose excretion was increased concomitantly with implementation of intermittent fasting and probiotic yogurt consumption, are among the most common environmental pollutants. It may be argued that elevated initial levels of phthalates were associated with Dr. JB's consistent running and consumption of water from years of soft, plastic water bottles possibly containing phthalates. 2HIB is also a metabolite of gasoline additives that indicates exposure to environmental pollution that could be associated with activities such as running in urban environments" [11] [12]. From this study, it can be deducted that changes of the microbiota due to consumption of a specific probiotic yogurt led to elimination of toxicants known to affect the information in human DNA, thus reinforcing the concept that there is a constant exchange of information between our cells and the cells of the microbiota.

Such an exchange of information shows all features of recursion as the case reported above exemplifies; a certain lifestyle (running in urban environment) changes the information exposing human and microbial cells to toxicants that modify DNA [13]; another lifestyle (consumption of a probiotic yogurt) changes that microbiota that, in turn, leads to elimination of those toxicants that affects DNA information and so on, in an almost endless recursion [14]. This example supports the concept that the microbiota retains the information it has acquired during its interaction with the human body and, therefore, this information persists after the death of the human cells of the body.

However, even accepting that the microbiota retains the information it acquires during its stay with the human part of ourselves, and also assuming that the microbiota outlives the human part of our body, we still have to confront the challenge of whether the microbiota is endowed with self-consciousness, i.e. whether the microbiota realizes it exists as an individual entity shaped by interactions with the human cells.

The issue of self-consciousness is amply debated in these days when we wonder whether computers with artificial intelligence will be aware of their own existence [15] and goes beyond the scopes of this article. However, if we consider the commonly accepted notion of human consciousness, there are no theoretical obstacles in accepting the existence of a collective consciousness residing in the microbiota, in particular when we consider the interactions with its human counterpart. The commonly accepted concept postulates that consciousness resides in neuronal interconnections shaped by experience, i.e. by interaction with the environment [16]. It follows that the electrochemical information responsible for this neuronal network-based human consciousness is superimposable to the genetic information contained in the DNA inside the nucleus of neurons following the principle of isomorphism as Wittgenstein had once demonstrated [17].

According to this principle, human consciousness is superimposable to the information contained in human DNA as it relates to interactions with the environment. Since the DNA of the microbiota has the same nature of the human DNA, there are no theoretical obstacles in hypothesizing that the microbiota has consciousness of itself, a consciousness that is shaped by its interaction with the human part of our bodies as well as with the more general concept of "environment". If green plants are endowed with intelligence, cognition and language without the need of having a brain made by neurons [19]. the microbiota could fall in the same category of unconventional (for human eyes) consciousness.

This hypothesis is further corroborated by the observation that the microbiota exchange signals within itself, as neurons in our brains do. Arguably even in a much more efficient way, since bacteria, unlike human cells, are able to exchange genetic information with direct transfer of genes, without intermediaries as our human cells are obliged to do. In addition, the microbes of the microbiota produce the same neurotransmitters that are at work inside our heads, thus further resembling a fully organized network of information that is difficult to imagine devoid of consciousness.

The idea that the microbes of the microbiota are endowed with self-consciousness may appear odd at first, but it is consistent with the most modern philosophic theories of consciousness based on quantum physics. For example, the philosopher David Chalmers postulates

"That consciousness might be universal and that every system down to the elementary particles has degrees of consciousness. This view is also called panpsychism in philosophy or nonduality in the mystical traditions. Chalmers believes that the universality of consciousness is what can help us bridge the gap between consciousness and the physical world in science, leaving the equations in physics as they are while using them to describe the flux of consciousness. From this perspective the answer to the famous question of Stephen Hawking "What puts fire into the equations?" is that consciousness is not outside of the physical world but it's the fire at its heart. Chalmers further proposes that this "new" view can transfigure our relationship to nature leading to profound social and ethical consequences" [19].

The microbiota, our third brain, will then survive the death of the human body and retains 99% of its consciousness. If this is a concept difficult to digest, the following hypotheses that derive from our knowledge of the microbiota may be even more intriguing.

The rhizome

Before entering into these concepts, we have to familiarize with an obscure object of modern French philosophy that is the rhizome. This is a philosophical concept developed by Gilles Deleuze and Félix Guattari in their project entitled "Capitalism and Schizophrenia" (1972–1980). It is what Deleuze calls an "image of thought," based on the botanical rhizome, that apprehends multiplicities [20]. The concept is so obscure that Wikipedia warns: "This article may be too technical for most readers to understand. Please help improve this article to make it understandable to non-experts, without removing the technical details. (December 2014)". As of today, apparently no one has been able to interested, in making it more understandable [21].

Deleuze and Guattari postulate that human culture and knowledge and, hence, human consciousness, behave like a botanical rhizome that dynamically permeates the entire biosphere with no boundaries in terms of space or time, with all consciousness forever interconnected.

According to Deleuze and Guattari:

"In this model, culture spreads like the surface of a body of water, spreading towards available spaces or trickling downwards towards new spaces through fissures and gaps, eroding what is in its way. The surface can be interrupted and moved, but these disturbances leave no trace, as the water is charged with pressure and potential to always seek its equilibrium, and thereby establish smooth space"[21].

The two philosophers enunciate 5 principles governing the behavior of the rhizome, principles that can be applied, with no exception, almost literally, to the microbiota:

1&2. Principles of connection and heterogeneity: "any point of a rhizome can be connected to any other, and must be".

3. Principle of multiplicity: only when the multiple is effectively treated as a substantive, "multiplicity" that it ceases to have any relation to the One.

4. Principle of asignifying rupture: a rhizome may be broken, but it will start up again on one of its old lines, or on new lines.

5&6. Principle of cartography and decalcomania: a rhizome is not amenable to any structural or generative model; it is a "map and not a tracing".

Although Deleuze and Guattari were discussing human culture and consciousness as it was interpreted in the seventies, now that we know that human culture and consciousness comprise the third brain, i.e. the microbiota, it is easy to understand that, without knowing, they were describing the features of the microbiota. It is ironic to notice that Deleuze and Guattari defined the rhizome "an answer to a question that has not been asked". Or: "we have more answers than questions". We now know, some forty years later, that the question is: "how do you define the characteristics of the microbiota as it relates to human consciousness?" And the answer is: "The eternal and boundless rhizome".

This means that our microbiota-based consciousness not only survives the human side of our bodies, but it continually expands all over the world. Every breath we exhale, every surface we touch, every time we go to the bathroom, we disseminate our microbiota-based consciousness in the live environment where it permeates, shapes, and is shaped by, the other microbiota-based consciousness that are there, in the soil, in the water, associated with plants, humans or animals, in a sort of inextricable network of consciousness that evolves without interruption for 3.5 billions of years, the estimated time of appearance of the first (microbial) cell on this earth.

In the information contained in the nucleic acid of that primordial cell there was, in embryo, the project of the entire biosphere and we, as well as all the living beings before and after us, are developing that project that has never had any interruption, despite mass extinctions or the death of any single individual, in perfect accordance with the 4th principle of the rhizome: "Principle of asignifying rupture: a rhizome may be broken, but it will start up again on one of its old lines, or on new lines". From dinosaurs to mammals, individual life on earth may be broken, but it will start up again and the consciousness will not be broken.

Conclusion

Assuming that the microbiota-based consciousness of ours outlives the human part of our bodies, what will be of it once the sun will have consumed its fuel and the earth will precipitate into the dying sun? Will it be the end of it? I do not think so: microbes survive quite well in the outer space, thrive in the tails of comets and outside human space stations [22]. The concept of panspermia [23]. i.e. the hypothesis that life exists throughout the Universe, distributed by meteoroids, asteroids, comets, planetoids, self-replicating spacecraft and, man-made spacecraft in the form of unintended contamination, is very well contemplated by biologists up to the point that astrobiology is taught in schools [24].

Therefore, we may reasonably assume that our third brain will live forever, at least in this universe. Whether will it live, and how, in other parts of the multiverse [25] will be the topic of another article.

Disclosures

Marco Ruggiero is the founder and CEO of Silver Spring Sagl, the Swiss company producing the Bravo yogurt that was used in the study quoted as reference n. 11. He had no prior knowledge of the nutritional plan followed by subject described in the study nor of the results of the analyses. Marco Ruggiero is member of the Editorial Board of Madridge Journal of Immunology and is waived from the Article Processing fee for this contribution; he receives no remuneration for his editorial work.

Ethics

This article is original and contains material that has not been submitted or published in any other scientific journal.

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