

HYPOTHESIS 2

Exosomes and free will: Is there any rapport?

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Scientific search for various lines of communication between cells of a living organism gains the important accent today. As Sangani *et al.* (2021) pointed out: the extracellular vesicles are nowadays established as important lines of communication between cells. They are able to efficiently drive changes upon their arrival to recipient cells. The name extracellular vesicle is a general term used to describe three subtypes of vesicles – microvesicles, exosomes and apoptotic bodies. Exosomes are nano-sized biovesicles secreted from cells and released into surrounding body fluids. They were shown to carry cell-specific cargos of proteins, lipids, and genetic information and can be selectively taken up by neighboring or distant cells far from their release and reprogram them (Yuan Zhang *et al.* 2019). They may carry genetic information as fragments of DNA, miRNAs (microRNA) and mRNAs (messengerRNA). Based on such contemporary accepted findings and considering the potential functions of extracellular vesicles, we proposed recently the hypothesis of possible transfer of memory information through exosomes (Lakota *et al.* 2021) between the heart of a donor and brain of a recipient following the heart transplantation. Heart reacts to our feelings and emotions and influences the rational and emotional state of our mental activity. When our hypothesis can be verified as plausible then, maybe, we will add in the future one more parameter for discussing the most suitable donor e.g. from the point of view of possible influence upon a recipient’s mental settings. On the other hand, our hypothesis opens several consequential questions as well.

Already in the 60-ties of the last century Engel (1962) formulated the bio-psycho-social model that is that health and illness is, in essence, highly dependent upon the interplay of biological, psychological, and social factors from the environment we are living in. In spite of this, the contemporary medical curative as well as the current medical research concentrates mostly upon the biological basis of the illness/health. As for the above mentioned hypothesis it also opens the question of the biological basis of our memory mechanisms. Here we point to the difference between biological fundamentals of what one could call “inner” and “outer” memory. These include in the first case, when we have in mind memories stemming from our organism, may be from our organs, even from cells only. That is the memories evoked from physiological mechanisms acting inside of our body. Such memories are stored without the intentional effort. The question is whether they could be subject to exosomes influence also. In the second case, we take into account the memories evoked by the visual, acoustical, haptic, olfactory experiences etc. That is the memories based on the information obtained from the external environment and thus by means of focussing our consciousness as also reflective, but not by intentionally evoked attention at the given moment. The most important question is whether the “memories” as such in the first case stemming from the physiological mechanisms inside our body, even inside the cells are according to our hypothesis encoded and transferred by exosomes. Moreover, whether the exosomes are engaged in their revival also? If we accept for the moment that it could

be possible then the answer must be sought how? Such questions are justified because many of the internal/external signals are carriers of important psycho-social information also and, consequently, they must have biological relevance.

Another discussion may appear in connection to the act of free will. The idea of free will has traditionally been conceived of as a kind of power to control one's choices and actions. Of course, here we will avoid a traditional fellow traveller of free will discussion, namely moral responsibility. Instead, we will try to give a touch to the possible bio-roots of it. The discussion on its biological roots was re-opened also in the eighties last century following the series of publications by Libet and his coworkers (see e.g. Libet *et al.* 1983). They took a look at the results showing that the onset of the recorded cerebral activity (EEG) proceeds by several hundred milliseconds the reported time of conscious intention to act. The subjects executed self-initiated movements in series which were conducted "spontaneously" and capriciously. Having in mind the fact the so-called motor programs of our movements are built, reactivated and fixed repeatedly during our life and thus be permanently at disposal for the initiation of a motor act one can agree with their conclusion that the cerebral initiation of spontaneous freely voluntary motor act can begin "unconsciously", that is, before there is any (at least recallable) subjective awareness. It means that a "decision" to act has already been initiated cerebrally. In this case, the appellation of the recorded readiness-potential is essentially in agreement with the fact that the particular motor program is in a state of availability to initiate the motor act. The subjects in Libet's experiments were aware he/she would launch the motor act. It seems that such awareness may awaken a specific mental set

of a given subject and we may better say that the motor act was not launched "unconsciously" but skilfully initiated by means of the readiness of "inner" memory to act in the train of subject's decision. A skilfully initiated readiness of our brain/mind machine to start an action may at first glance act as manifestation of free will despite our unconsciousness of their neuronal conditionality. The main question is still incommensurate: is there any free will at some time or another? Our brain/mind machine is a parallel and distributed system, with control areas throughout (Gazzaniga 2011). And here we are again in touch with the question of the possible role of communication between cells in a given situation. Exosomes or anything else?

REFERENCES

- 1 Engel, GL.: Psychological Development in Health and Disease. Philadelphia/London, WB Saunders Comp. ISBN-13: 978-0721633909, 1962, 435 pp.
- 2 Gazzaniga M. in: Interview with Michael Gazzaniga (2021). *Ann. New York Acad. Sci.* **1224**(1): 1–8. <https://doi.org/10.1111/j.1749-6632.05998.x>
- 3 Lakota J., Jagla F, Pecháňová O (2021) Heart memory or can transplanted heart manipulate recipient's brain control over mind body interactions? *Act Nerv Super Rediviva.* **63**(1): 49–51
- 4 Libet B, Gleason CA, Wright EW, Pearl DK (1983) Time of conscious intention to act in relation to onset of cerebral activity (Readiness-Potential): The unconscious initiation of a freely voluntary act. *Brain.* **106**(3): 623–642.
- 5 Sangania NB, Gomes AR, Curfs LMG and Reutelingsperger CP (2021) The role of extracellular vesicles during CNS development, *Progress in Neurobiology.* <https://doi.org/10.1016/j.pneurobio.2021.102124>
- 6 Zhang, Y, Liu, Y, Liu, H, Tang WH (2019) Exosomes: biogenesis, biologic function and clinical potential. *Cell Biosci.* **9**: 19. <https://doi.org/10.1186/s13578-019-0282-2>