

Five reasons why Brain Research merits a change of Focus

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Abstract

In spite of remarkable achievements in the field of molecular biology, neuron-glia partnership, regenerative medicine and systems neuroscience the primordial faculty of a unicellular organism for handling sensation, information and phenomenon in local and nonlocal way are still relevant in directing the research on the brain.

Key Words:

Cognition, Mind, Phenomenon, Self, Brain-research

The journey of a unicellular organism over millions of years through struggle for survival, natural selection and reproductive success of its genetic and epigenetic machinery to evolve into a multicellular organ like brain, the organ of cognition, attitude and psychomotor skill of the organism, has perplexed everyone. The unique feature of this process is that the organ brain has not merely preserved the primitive cognitive faculty of a unicellular organism but fine-tuned this property to a remarkable degree concomitant with its evolutionary status as a system of sophistication and complexity. The brain is supposed to be the most complex organ of this universe. While constituting 2% of body mass in human being with 100 billions of neurons and 1000 billions of glial cells, the brain is nourished by 10% of cardiac output, consumes 20% of total body energy and expresses more than one third of 23,000 genes encoded in the human genome. The scientists declared the last decade of twentieth century as the decade of the brain. The outcome of last twenty years' research is a definitive *systems neuroscience*¹, studying the circuits in the highly cellular brain and relating them with its functions, activities, cognition and behavior with advanced techniques in electrophysiology, PET (Positron Emission Tomography) and fMRI (functional Magnetic Resonance Imaging). The regional area of the brain has thus been mapped in conditions like anesthesia to synaesthesia, mania to schizophrenia, sexual ecstasy to spiritual ecstasy, state of joy to state of dementia. Another exemplary achievement in last two decades is advancement in molecular biology in understanding many of neuron's and glia's extraordinary functions in terms of signal transduction, intracellular and intercellular transport of informational molecules and pathogenesis of several important diseases in terms of genetic linkage, polymorphism, gene-gene interaction and epistasis^{2,3}. The third remarkable advancement is in the field of regenerative medicine with stem cell therapy in neurodegenerative disease like Huntington's and Parkinson's disease⁴. The fourth outstanding achievement is the recognition of neuron-glia partnership^{5,6,7,8} in the process of generation and migration of neurons, in development and evolution of the brain⁹, in pathogenesis of several neuronal diseases^{10,11} in metabolic-neural coupling¹² and information-channeling within the brain^{13,14} which have brought a renaissance in the science of the brain. However, in spite of these advancements it is felt that research in science of the brain requires changing its focus. What follow are the reasons why?

1. Informatics:

The brain is the organ with the highest information density per unit volume and mass. In the brain, information is channeled through four cellular networks; neuron-neuron, neuron-astrocyte, astrocyte-neuron and astrocyte-astrocyte network. The networks in the brain differ from material hardware by the fact that both neuron and glia are alive. Brain's hardware is a living hardware. Astrocytic intervention in flow of information through neuronal channels is primarily meant to prevent informational chaos which the extremely non-linear neuro-neuronal, glia-neuronal and neuron-glia channeling is prone to. Neural network and its applications like AI, Expert systems are yet to consider and apply the functionality of this neuron-glia partnership. Further to note, information channeling and information processing are different. Information is processed by what is called mind which is programmed by 'self'. 'Self' is categorically identical with consciousness, customized and informationally conditioned as operational unit of consciousness within the system. Besides, there are differences between 'inactive' and active information. What makes inactive information active in the brain is new frontier of research. What a sense organ can perceive are 'form' and movement. How information, seemingly nonsensical, contributes in creation of new ensemble of space and time ('form') in the event-horizon as manifested by the brain's behavior is another interesting field to ponder on. Mind is the logical choice for what brings out 'form' within *information* as new space and time and there is possible release of a new kind of information-based energy during this information-split¹⁵. But the question remains, how?

Further, if information is omnipresent, if it can act in both local and nonlocal way then the cerebral cortex in its present human form cannot be the last footprint of evolution, and the brain cannot be considered an informationally 'closed' system. However, how information outside the system brain is exchanged with information inside or, how extraneous information communicates with inside infrastructures without any compromise of the integrity of the system, whether all of it happens in the information channel or in the processing system, are not known and are required to be worked out. For all practical purpose any material hardware is informationally closed. However this cannot be true for a living hardware constituted by cellular network. The issue of openness to information is particularly relevant to its software equivalent, the mind. Extrasensory and nonsensory perceptions, information purging during deep sleep¹⁶, communication with extracerebral natural world during dream, and cross-modality sensory perception could be better explained if there exists a transcortical route of information exchange between inside and outside the brain. Should such route exist, then does the dendritic mat in the uppermost layers of cerebral cortex and non-synaptic spines in the apical dendrites of cortical pyramidal neurons play any role in such communication? What are the 'catchment areas' in the cerebral cortex for such activities? These are all new areas which make frontier neuroscience.

2. Local and Nonlocal science:

Like information, the mind and often the 'self' behave in both local and nonlocal ways. The brain is the play-ground of such both local and nonlocal players. By local players it is meant energy and matter confined within defined space and time. Nonlocal players are those which are not consistently confined to a specific space and/or adhered to a definitive time. Therefore, with knowledge pertaining to only local players, explaining brain function with the help of local theories of science and adhering to use of local investigative tool, we are far from understanding the brain as a whole. There are preliminary data¹⁷ available in science on nonlocal behavior in the brain activities and we are to find out how we can outreach this domain. Two titans, local science and nonlocal science meet within the science of the brain. This issue has not been adequately addressed so far. Like any cell, an organ which works locally and has the ability to communicate nonlocally reserves the chances for evolution. Unlike kidneys and liver or lungs or spleen, the brain with its constituents, neuron and glia belong to such group.

3. Sensation, Information and Phenomenon:

The rooting of brain's excellent output could be found out in its integrating capacity (Sherrington). Starting from local spinal reflex to somatic, autonomic and somato-autonomic function, integration is brain's characteristics. The brain has handled the sensory world. The brain has also been handling the world of information. The latest imperative in evolution of the brain is to gain ability to handle the phenomenal world. Sensori-motor integration centre in the upper brain stem has been well-defined. Autonomic integration occurs through hypothalamic centers. Mind integrates information-rooted brain functions. The capacity of the brain to handle information-world has co-evolved with mind. What does the brain need during this transition from handling of sensation to information to phenomenon? As the sensory apparatus is sensitive to physical world and the mind is sensitive to information, so the 'self' is sensitive to phenomenon. A phenomenological integration center in the brain, therefore, requires a robust operating 'self' rooted in the brain. This is also required for balancing and integrating the cognitive (knowledge), psychomotor (skill) and affective (attitude) functions of the brain. This kind of integration is absolutely essential for better survival in a phenomenal world sensed by 'self'. Phenomenal world, in contrast to sensory and information worlds, is more difficult to combat with. This is true for an individual cell, an organ or a system. The direction of brain-research, therefore, should focus on and shift towards this rooting of 'self' within the system brain.

4. Consciousness; identifying the real issue:

Every cell, although, is conscious in its own way, the brain remains the organ for consciousness, which is precious to all of us as being. The infrastructure of the brain supports conscious states and participates in manifestation of consciousness, while 'self' experiences it all and retains that as episodic memory. In contrast mind retains semantic memory of information it processes. The spectrum of this issue of consciousness in the brain extends from one pole of matter-based study of consciousness to another pole of consciousness-based study of matter. The issue extends from consciousness as an epiphenomenon in collective neuronal activity to consciousness as the driver and user of the infrastructure of the system brain. Since each and every individual neuron and glia are alive and conscious, the issue here is not how matter or energy is related to consciousness. As a live cell, both neurons and glia exchange matter and energy with their micro-environment. The issue here is of life, information and consciousness. There may be debate on origin of 'life' from matter. However, that living cell generates matter is a fact. All matters in the brain are products of neuron and/or glial cell. If our neurocentric view of consciousness were true, the cause for property like preferential neuron-philic of consciousness and consciousness-philic of neurons are yet to be found out. How consciousness, mind and self of individual neuron and glia make a unitary experience of consciousness, mind and 'self' as a whole within the brain is the issue. The binding element involved in this process of unification is suggested to be information. The closest approximation of the 'abstract' consciousness at the concrete plane, therefore, in most likelihood is the conformational geometry of information involving various group of neuron-glia at different hierarchical levels operating in different contexts.

5. Cosmology and the Brain:

Finally, the cosmic sense of the organism has co-evolved with the brain as an organ for operation of 'self', mind and consciousness. Beside the fact that there is an astonishing identity between number of stars (10^{11}) in a galaxy or the supposed number galaxy in a universe (10^{11}) and the number of neurons (10^{11}) inside the brain, in human being the brain is the organ that connects finite with the Infinite, mortal with the Immortal, evanescent with the Eternal. It is the organ which is responsible for Love seen as Action, Worship seen as Work, Divinity seen as Material. The purpose of evolution of the brain as an organ is to unify the consciousness within and the

consciousness without. In this grand biological design the dominant neurons and the humble glias are equal partners.

Concluding Comments

The primitive faculty of a cell to handle the physical world with sensory apparatus, information world with mind and phenomenal world with 'self' remains relevant in further evolution of the brain and this property also influences research focus for the science of the brain. In the perspective of brain's evolving cosmic sense the time has come when the brain should not be looked as if it is at the centre of the universe. The brain is required to be placed at the boundary of the universe so that it can look at the operation of multiple universe(s), the multiverse. In 1895, William James first used the term 'multiverse' for multiple universe(s), which is now an astrophysical reality¹⁸. Most of the interesting events happen at the boundary of a system, be it a cell, a universe or the brain! Whatever is transcortical is trans-universal as well! Einstein once was asked what he wanted to do after knowing so much about the universe. Einstein's reply was that he wanted to know what God's will is. It is felt that the time has come to connect the 'free will' generated from the brain with the 'will' behind this generation of multiple universe(s). This would take the science of the brain to the platform it deserves.

References

1. Hemmen, J.L., & Sejnowski, T.J. *23 Problems in Systems Neuroscience*. Oxford University Press, Oxford, New York (2006).
2. Combarros, O., Cortina-Borja, M., Smith, A.D., & Lehmann, D.J. *Neurobiol. Aging* 30, 1333–1349 (2009).
3. Mansoori, N., Tripathi, M., Luthra, K., Alam, R., Lakshmy, R., Sharma, S., Arulselvi, S., Parveen, S., & Mukhopadhyay, A.K. *Neurobiol. Aging* (2011). PMID: 22015309.
4. Lindvall, O., Kokaia, Z., & Martinez-Serrano, A. *Nat. Med. Suppl*: S 42-50 (2004).
5. Fields, R.D., & Stevens-Graham, B. *Science* 298 (5593), 556-562 (2002).
6. Banaclocha, M.A. *Brain Res. Bull.* 73, 21-27 (2007).
7. Allen, N.J., & Barres, B. A. *Nature* 457, 675-677 (2009).
8. Araque, A., & Navarrete, M. *Philos. Trans. R. Soc. Lond. B. Biol. Sci.* 365, 2375-2381 (2010).
9. Oberheim, N.A., Takano, T., Han, X., He, W., Lin, J.H.C., Wang, F., Xu, Q., Wyatt, J.D., Pilcher, W., Ojemann, J.G., Ransom, B.R., Goldman, S.A., & Nedergaard, M. *J. Neurosci.* 29, 3276-3287 (2009).
10. Aamodt, S. *Nat. Neurosci.* 10, 1349 (2007).
11. Lobsiger, C.S., & Cleveland, D.W. *Nat. Neurosci.* 10, 1355-1360 (2007).
12. Magistretti, P.J. *J. of Expt. Biol.* 209, 2304-2311 (2006).
13. Panatier, A., Theodosis, D.T., Mothet, J.P., Touquet, B., Pollegioni, L., Poulain, D.A., & Oliet, S.H.R. *Cell* 125(4), 639-641(2006).
14. Pereira, A., (Jr) & Furlan, F.A. *Prog. Neurobiol.* 92, 405-420 (2010).
15. Mukhopadhyay, A.K. *Frontier Perspectives* 16 (2), 19-29 (2008).
16. Crick, F., & Mitchison, G. *Nature* 304, 111-114 (1983).
17. Grinberg-Zylberbaum, J., Delaflor, M., Attie, L., & Goswami, A. *Physics Essays* 7 (4), 422-428 (1994).
18. Jenkins, A., & Perez, G. *Scientific American*, 302 (1) 42 (2010); DOI: 10.1038/scientificamerican0110-42