The Relationship between the Nervous System and DNA Expression (A Review)

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العلاقة بين الجهاز العصبي والتعبير الجيني (مقالة مرجعية)

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Abstract

Neurotransmitters travel through synapses released by neurons. The DNA inside the neurons does not replicate since it arrests in G1 phase of the cell cycle which explains the absence of replication since DNA replication occurs during S phase which is preceded by G1 phase.

Experiments show that environmental factors can influence the DNA code were tried in both plants and animals kingdoms in last two centuries with great success leading to the belief that environmental factors can force the brain to send signals (neurotransmitters) to somatic cells.

The next question will be "**Is the power of thinking and reasoning are found in the code of DNA or are they are byproducts produced by the functions of the neurons**?

Biotechnology and nano-biotechnology techniques show that (the experiences of life) can switch on/off the DNA expression in neurons which lead to change the way that brain operates.

One hypothesis was assumed that all (changes of DNA expression) occur via a synaptic junction that means that the degree of on (excitatory) versus off (inhibitory) signals determines whether the neuron will be excited to release its neurotransmitter or be inhibited and inactive.

An (electromagnetic field) hypothesis follow (The inverse square law) indicate that the electromagnetic field is exponential, and this was followed by other hypotheses that try to explain the adaptation of genes of *Homo sapiens* comparing with adaptation of genes from other mammals during evolution. This hypothesis claimed that the regulation of genes (gene expression) play a key role that separate (*Homo sapiens*) from other mammals which means the presence of "gene activators and gene dimmers", and not (their gene sequence).

One of the main obstacles is that (Gene regulatory elements) are often a few nucleotides long, which prevent them for calculating and estimating (the acceleration rate) from a statistical point of view.

Researchers suggest that during life-threating accidents, the brain, in order to remember previous experiences, will double-strand break (DSB) the DNA inside neurons to induce rapid gene expression. Those genes produced new connections with cells through synapses, a phenomenon known as (Synaptic plasticity) which plays an important role in learning and saving long and short memories, but more researches are needed to explore the different aspects of synaptic plasticity.

Keywords: Electric current, Neurons, Gene expression, Synapsis, Thoughts.

المستخلص

تنتقل الناقلات العصبية عبر المشابك التي تطلقها الخلايا العصبية، ولا يتكاثر الحمض النووي داخل الخلايا العصبية لتوقف المرحلة G1 من دورة الخلية وهو ما يفسر عدم وجود انقسام لعدم وجود المرحلة S التي تسبقها المرحلة G1، وأظهرت تجارب على كائنات حية (نباتية او حيوانية) خلال القرنين الماضيين امكانية تأثير العوامل البيئية على الشفرة الوراثية للحمض النووي، مما أدى إلى الاعتقاد بأمكانية سيطرة العوامل البيئية (بصورة او باخرى) على الجهاز العصبي واجباره على إرسال إشارات إلى الخلايا الجسدية.

السؤال التالي سيكون "هل قوة التفكير والتفكير موجودة في الشفرة الوراثية للحمض النووي أم أنها منتجات ثانوية تنتجها وظائف الخلايا العصبية؟

تُظهر تقنيات التكنولوجيا الحيوية والتكنولوجيا الحيوية النانوية أن (تجارب الحياة) يمكنها تشغيل/إيقاف تعبير الحمض النووي في الخلايا العصبية مما يؤدي إلى تغيير الطريقة التي يعمل بها الدماغ.

تحدث جميع (التغييرات في تعبير الحمض النووي) عبر مفترق متشابك (في إحدى الفرضيات) مما يعني تحفيز او تثبيط الناقل العصبي اعتماداً على درجة الإشارات المحفزة

مقابل الأشارات المثبطة، بينما تشير فرضية المجال الكهرومغناطيسي (قانون التربيع العكسي) إلى أن المجال الكهرومغناطيسي أسي (exponential)، بينما تحاول فرضيات أخرى تفسير تكيف جينات الإنسان العاقل مقارنة بتكيف الجينات من الثدييات الأخرى أثناء عملية التطور، حيث ذكرت هذه الفرضية أن تنظيم الجينات (التعبير الجيني) وليس التسلسل الجيني يلعب دورًا رئيسيًا يفصل (الإنسان العاقل) عن الثدييات الأخرى، مما يعني اهمية وجود "منشطات ومثبطات الجينات".

إحدى العقبات الرئيسية هي أن (العناصر التنظيمية للجينات) غالبًا ما تكون طويلة من النيوكليوتيدات، مما يمنعها من حساب وتقدير (معدل التسارع) من وجهة نظر إحصائية.

اشارت بعض الأبحاث الى أنه أثناء الحوادث التي تهدد الحياة، فإن الدماغ، من أجل تذكر التجارب السابقة، سوف يكسر (DSB) الحمض النووي داخل الخلايا العصبية للحث على التعبير الجيني السريع. أنتجت هذه الجينات روابط جديدة مع الخلايا من خلال المشابك، وهي ظاهرة تُعرف باسم (Synaptic plasticity) والتي تلعب دورًا مهمًا في التعلم وحفظ الذكريات الطويلة والقصيرة، ولكن هناك حاجة إلى مزيد من الأبحاث لاستكشاف الجوانب المختلفة بذلك.

الكلمات المفتاحية: Electric current, Neurons, Gene expression, Synapsis, Thoughts

Introduction

The nervous system consists of approximately 86 billion nerve cells (or neurons). The neurons are not limited to the brain, but distribute throughout the body forming the central nervous system (CNS) as well as the peripheral nervous system (PNS).

A neuron can be defined as electrically excitable cell. It consists of a soma (the body of the cell containing nucleus and organelles), a single axon (which is long and slender covered by fatty substances (myelin) to insulate it) and very short dendrites (Day *et al*, 2005; Petralia *et al*, 2015).

The function of a neuron is to produce Neurotransmitters (containing information) that travel from axon into dendrites through synapses (an intracellular space between the two neurons in order to communicate). Neurotransmitters are electric, chemicals or electric-chemicals that are released by neurons through its axon in a synapse (Debanne, 2004; Day *et al*, 2005).

Axons differ from dendrites by several features, such as shape and length (dendrites are short with many ramifications while axons are long, tail-like with less ramifications), location (dendrites are found in neurons and all cells of the body while axons are found in neurons only) and function (dendrites receive neurotransmitters whereas axons transmit them) (Petralia *et al*, 2015)

Examples of a neurotransmitter: Dopamine, acetylcholineamine

Each neuron has a DNA molecule (inside the nucleus) that does not replicate since it arrests in G1 phase of the cell cycle which explains the absence of replication since DNA replication occurs during S phase which is preceded by G1 phase, so the DNA cannot replicate in neurons.

A variety of mechanisms controls G1/S regulation and influenced by environmental factors and the neuronal phenotype itself which can leads to

apoptotic of neurons in cases of several diseases such as long-term smoking and Alzheimer (Anazawa *et al* 2004; Frade and Ovejero-Benito, 2015).

Actually, this is the reason, also, why neurons are no affected by x-ray or radioactivity since their DNA cannot be mutated (except in case of heavy doses of radiation).

Environmental factors and DNA

A question is asked always (Are the genes control the brain? or is the brain controls the genes?)

The brain has no effect on the genetic structure of any DNA inside a cell, but this matter is more complicated than one can think about it.

In the past, many scientists believed that all human behaviors were genetically determined. People were wondering if they can have “football genes”, “art genes” or even "leadership genes".

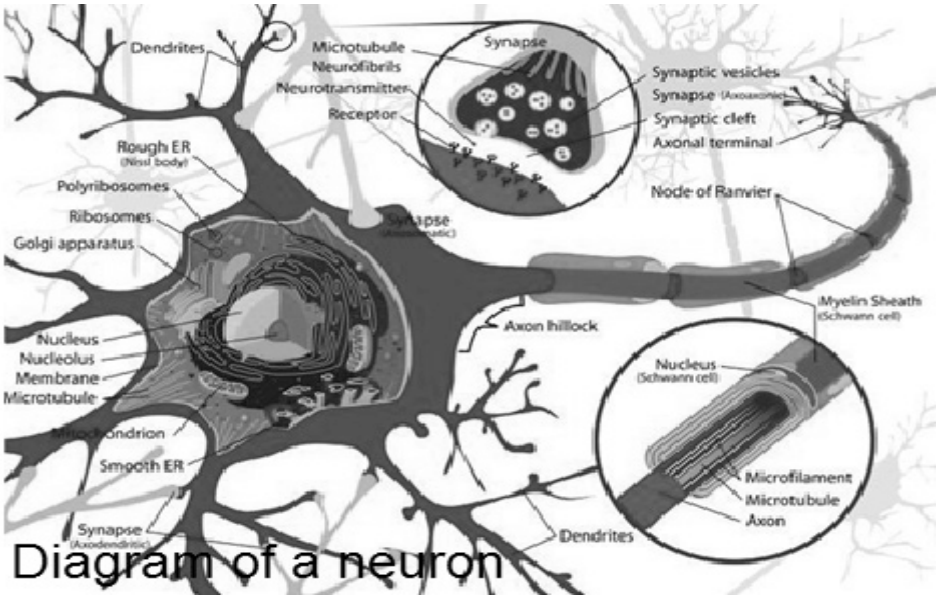

Fig.1. A neuron

This led to many high-level debates about “nature vs. nurture”.

Today, many scientists believe that the only natural instinct remain in human is the sucking of milk by the baby from his mother’ breasts. All other behaviors in humans are taught through traditions, culture, and customs of the society (Zaky, 2015).

Experiments to show that influence of environmental factors can influence the DNA code were tried in both plants and animals kingdoms in last two centuries, for example; The seeds of a single wild mustard plant (*Brassica juncea*) were divided into groups and planted in a certain mountain slope but at different altitudes, with different conditions such as (different soil pH, different amount of rainfall/water, a different number of hours of sunlight, different average temperature, and different concentrations of minerals in the soil).

The seeds, though they all came from the exact same parent plants, they grow into very different types of plants with different appearances that they may not even seem to be the same species. Yet, they came from the very same seed. However, if they had been planted at the same altitude, in the same soil, with the same pH, exposed to the same number of hours of sunlight, and the same amount of rainfall, they would look nearly identical.

From the seeds of a wild single mustard plant, at least 5 different types of plants: Broccoli, Brussel sprouts, kale, cabbage and Kohlrabi are obtained (Nawaz *et al,* 2018; Raekim *et al*, 2010; Sunil and Swaroop, 2020).

Identical twin monozygotic dogs raised in different parts of the world, given different diets, different exercise/play routines, and different types of training will have different behaviors and become two completely different dogs (Aldosari *et al*, 2020).

In humans, the smoking habit will influence at least 30,000 somatic mutations in order to keep the body alive. For example, smoking increases the number of erythrocytes in blood stream by third in order for oxidative phosphorylation will be steady (Bibi *et al*, 2016; Mairi, 2013).

In general, many researchers believe that environmental factors will force the the central nervous system to send signals (neurotransmitters) from its neurons to somatic cells so they may lead change the expression of some DNA inside them (rarely that affect the genetic cells) in order to protect the body of the individual.

The neurotransmitters may lead cells to release hormones that can affect DNA expression in cells throughout the body. Actually, gene expression changes all the time; it's just part of normal cellular function (Singh *et al*, 2018; Hollander *et al*, 2020).

So, the above experiments can indicate that the nervous system can influence the code of DNA in all (or most of) the cells of the body.

Thinking and reasoning

The most important cells in the brain are found in the (region of long memory) and in the (region of short memory). A human being is capable of thinking and reasoning due the experience gained through these two regions in particular.

So, thinking and reasoning may be byproducts produced by the cells of the central nervous system (or brain in particular) since the function of these cells originates and controlled by the DNA found in the nucleus of each neuron cell (Bassett *et al*, 2006; Achard *et al*, 2008).

The problem is that (Thinking and reasoning) may not be byproducts since all the above experiments do not answer the following question:

"**Is the power of thinking and reasoning and the powers of sight, hearing and so on are found in the code of DNA or are they byproducts produced by the functions of the neurons of the brain**?

Since DNA in neurons cannot replicate, so process such as (replication, transcription and translation) seems to play any role on the function of the neurons. Actually replication inside mature neurons can lead to tumors and the apoptosis of the neurons (Yang *et al*, 2001; Yang and Herrup, 2007; Frade and Ovejero-Benito, 2015).

The control of the brain over DNA is more complicated since (the electric-chemical activities of neurons) in the body represent only a minuscule fraction of the electric activity inside the brain itself.

The emergence of biotechnology and nano-biotechnology contribute advanced studies to the physiology and behavior of mammals (and other vertebrates) which have been studied for many decades, but the progress and development of technological-advanced genetic and molecular devices and the presence of advanced programming such as Gene expression programming (GEP) and Multi expression programming (MEP), for example, both are evolutionary algorithms that creates computer models to study genes help so much (Ferreira, 2001).

'**Epigenetics**' is a new area of research studies the effect of (the experiences of life) on DNA such as stress, using of drugs and so on. Therefore, many genes responsible for various behaviors were identified, isolated, and studied inside the brain. Among them:

Cryptochromes (Crygenesfamily)arefoundin plants and animals which are involved in the circadian rhythms (Öztürk, 2008).

NOTCH2NL gene which is coded for a family of three proteins (NOTCH2NLA, NOTCH2NLB, and NOTCH2NLC) in humans which seems to play some kind of role in the growth of brain-cortex (*Fiddes et al, 2018; Suzuki et al*, 2018)

Researches in the past decades prove that nothing can change the sequence of the DNA, but (the experiences of life) can cause the occurrence of methylation (Methyl groups' attachment) to some nucleotide bases which can switch on/off the DNA expression in neurons.

That means, epigenetic changes the DNA expression of neurons which will change the way that brain operates, so, the question isn't exactly 'How does the brain affect the person's DNA?', but '**How do experiences of life affect the DNA in person's brain, and how does this affect the psychology of that person and behavior**?

Even if someone accept that neurons are responsible for changes in DNA expression, no one at present has any evidence (or even a clue) how changes in DNA expression could be achieved.

One can assume (correctly or not) that changes could be (frequency coded), (pattern coded) or just specially (coded by interconnections). None of these make sense in a noisy environment that the cells are and not really answer the question either.

One hypothesis was assumed that all (changes of DNA expression) occur via a synaptic junction. One nerve cell through axon releases a neurotransmitter into the intercellular space of the synapse. The other cell has a dendrite that is positioned exceedingly close to the other neuron's

axon and has a receptor that recognizes the signal from the other neuron. When the neurotransmitter is recognized it, that leads to the propagation of the signal to further neurons. (Giachello *et al*, 2016; Hosseini, 2021)

While it might be easier to think about this like a switch (all-or-nothing), most of the time it is like a dimmer switch. This means that the degree of on (excitatory) versus off (inhibitory) signals determines whether the neuron will be excited to release its neurotransmitter or be inhibited and inactive.

Thoughts and electricity

The phrase "Thoughts should be more than electric currents" is correct somehow since no one is sure what (the biological electric currents) are, or how they operate at the molecular level. Even, no one is sure why they exist or evolve in that way.

In the past, the nervous system (as a whole) was envisioned more as a plumbing system, a system containing pumps and valves with pressure to control the flow of electricity, but in the computer age, the nervous system is seen more like electrical circuitry. (Bullmore, 2004; Sidiropoulou *et al*, 2006)

Many researchers hypothesized that the neurons of most of mammals (including humans) creates an electromagnetic field extended and enclosed the brain that will transfer information to another brain (belonging to another person) and inducing consciousness, knowledge and feelings. The magnetic particles (magnetites) may play significant role in silent communication between individuals (Bullmore *et al*, 2004).

The electromagnetism theory considers the memory a kind of like a USB flash drive. Under this scenario, the electric currents play an important role (Jirsa and Haken, 1996; Tetsuo *et al*, 2016).

To go further with the question, a wide electromagnetic field will follow (The inverse square law) stated that (any specified physical quantity is inversely proportional to the square of the distance from the source of that physical quantity), and that means the electromagnetic field is exponential (Voudoukis, 2017).

This lead to evolve of a new therapy that practiced at present in US and many European countries known as (Transcranial magnetic stimulation (TMS)) that will relieve depression by applying magnetic pulses to the brain and seems to work for some people since their thoughts become clearer. There is a lot of debate on how this treatment works. (Groppa, 2012; Rossi, 2021), so the question remains without answers, if electromagnetic field produces electric current, so who produce the electromagnetic field. Who knows?

Evolution and brain

The brain in *Homo sapiens* differs by only 1 percent from the brain of chimpanzee in protein-coding genomes. A new hypothesis tries to explain how genes of *Homo sapiens* adapted, regulated and went through specific changes during evolution. This hypothesis claimed that the regulation of genes (gene expression) play a key role that separate (*Homo sapiens*) from other mammals which means the presence of "gene activators and gene dimmers", and not their gene sequence (Schibler, 2007).

The researchers create advanced techniques that will able them to recognize and identify vast number sets of gene regulatory regions in the brain. They use both computer models and experimental data in order to pinpoint proteins (involved in gene regulation).

Evolutionary comparisons were performed between human, chimpanzee and gorilla. One of the main obstacle that face researchers is that (Gene regulatory elements) are often a few nucleotides long, which prevent them for calculating and estimating (the acceleration rate) from a statistical point of view (Liu and Robinson-Rechavi, 2020).

DNA and memory

Every common person knows that genes instructed cells to build proteins and those proteins will regulate all functions (directly or indirectly) of the body.

A small number of genes (about 0.1% of the total) are different between people which make persons do not resemble each other. Individually, each person differ in his/her capacity of learning, memorizing or thinking, known as (cognitive function).

Cognitive function cannot be inherited (such as the color of the eye or other physical characteristics which are passed down from parents to their offspring.

That means genes cannot affect cognitive function; or can they?

The size of the brain in a human being makes it impossible for any person to keep all his/her memories from childhood to old age.

Environmental factors (such as the experiences of life, ways of education, health, emotions and others) contribute of 75% of loss of memory, while 25% of loss is contributed to genes.

Groups of researchers all over the globe are trying to identify genes which are responsible for thinking and learning, but so far only a small number have been identified. APOE, PSEN1, PSEN2 and TERM 2 are four non-inherited genes were found.

Some researchers suggest that during life-threating accidents, the brain, in order to remember previous experiences, will double-strand break (DSB) the DNA inside neurons in order to induce rapid gene expression (Bellesi *et al*, 2006).

In order to investigate the full DSB activity, researchers gave mice little electrical zaps to the feet when they entered a box to condition their (fear memory). Several methods were tried after that to assess DSBs and gene expression in the brains of the mice in the next 30 minutes in areas of the brain responsible mainly for producing, sorting and storing conditioned fear memories. All results were compared with (the control group) consists of mice did not experience the foot shock (Suberbielle *et al*, 2013; Madabhushi *et al*, 2015).

The numbers of DSBs were doubled in neurons with the formation of a (fear memory) which affect about 200-300 genes in (fear memory)'s areas (Stott *et al*, 2021).

It seems that those genes produced new connections with cells through synapses, this phenomenon is known as (Synaptic plasticity) which can be defined as (the ability of synapses to increase or decrease their activities leading to strengthen or weakness of their connections)(Abbott and Nelson, 2000; Gerrow and Triller, 2010).

Synaptic plasticity plays an important role in neurochemical foundation of learning and saving long and short memories. More research is needed to solve different aspects of synaptic plasticity and the requirement of DSBs (Abbott and Nelson, 2000; Desai *et al*, 2002; Stott *et al*, 2021).

Some researchers believe that some mother's memories (if used so often) can transfer to the mitochondrial DNA (in mother's neurons) through

a mysterious process (not discovered yet), so memories (usually a way of doing things, not a memory of what happened) can possibly be passed to the next generation. This could explain why children of people in a certain profession are will follow their parents in that profession (Navarro *et al*, 2004, Messing, 2020).

The funny thing is that even when a person has no idea how his/her brain is working? That person accepts and operates according to them regardless and the original question is still asked: What is thought? How do we know we have thoughts? How thoughts and emotions related? And which came first?

Many researches have to be done and will done to answer that question.

Conclusion

DNA inside neuron was arrested in G1 phase of the cell cycle which explains the absence of replication since DNA replication occurs during S phase which is preceded by G1 phase.

Environmental factors can influence the DNA code were tried in both plants and animals kingdoms in last two centuries with great success leading to the belief that environmental factors can force the brain to send signals (neurotransmitters) to somatic cells.

There are many hypotheses are trying to explain the relationship between the function of the brain and the function of DNA.

One hypothesis was assumed that all (changes of DNA expression) occur via a synaptic junction that means that the degree of on (excitatory) versus off (inhibitory) signals determines whether the neuron will be excited to release its neurotransmitter or be inhibited and inactive.

Another hypothesis (electromagnetic field) indicates that the electromagnetic field is exponential, and this was followed by other hypotheses that try to explain the adaptation of genes of *Homo sapiens* comparing with adaptation of genes from other mammals during evolution.

One of the main obstacles is that (Gene regulatory elements) are often a few nucleotides long, which prevent them for calculating and estimating (the acceleration rate) from a statistical point of view.

Researchers suggest that during life-threating accidents, the brain, in order to remember previous experiences, will double-strand break (DSB) the DNA inside neurons to induce rapid gene expression. Those genes produced new connections with cells through synapses, a phenomenon known as (Synaptic plasticity) which plays an important role in learning and saving long and short memories, but more researches are needed to explore the different aspects of synaptic plasticity.

Acknowledgement

The authors are specially grateful and indebted to assistant professor Dr. Rehab S. Ramadhan for all her assistance during the development of this work. They are also like to express their appreciation to the various remarks and suggestions of Mrs. Amal M. Shkara which moved this review into a new horizon.

References

- Abbott, L.F. and Nelson, S.B. (2000). Synaptic Plasticity: Taming the Beast. Nature Neuroscience. 3 Suppl, 1178–83.
- Achard, S., Bassett, D. S., Meyer-Lindenberg, A. and Bullmore, E. (2008). Fractal Connectivity of Long-memory Networks. Phys. Rev. E. Stat. nline. Soft Matter Phys. 77, 036104.
- Aldosari, K.H., Ahmad, G., Al-Ghamdi, S., Alsharif, M.H.K., Elamin, A.Y., Musthafa, M., Abbas, M.Y., Alqarni, A. A., Alqudeebi, S. K., Binsaqer, A. A. and Al-Ghamdi, H. (2020). The Influence and Impact of Smoking on Red Blood Cell Morphology and Buccal Microflora: A case-control study. J. Clinc. Lab. Anal. 34(6), e23212.
- Anazawa, T., Dimayuga, P. C., Li, H., Tani, S., Bradfield, J., Chyu, K-Y., Kaul, S., Shah, P. K. and Cercek, B. (2004). Effect of Exposure to Cigarette Smoke on Carotid Artery Intimal Thickening. Home Arteriosclerosis, Thrombosis, and Vascular Biology. 24 (9),1652–1658.
- Bassett, D. S., Meyer-Lindenberg, A., Achard, S., Duke, T. and Bullmore, E. (2006). Adaptive Reconfiguration of Fractal Small-world Human Brain Functional Networks. Proc. Natl. Acad. Sci. U.S.A. 103, 19518–19523.
- Bellesi, M., Bushey, D., Chini, M., Tononi, G. and Cirelli, C. (2016). Contribution of Sleep to the Repair of Neuronal DNA Double-strand Breaks: Evidence from Flies and Mice. Sci. Rep. 6, 1–13.
- Bibi, T., Rauf, S., Mustafa, H. S. B., Mahmood, T. and Ud-Din, S. (2016). Selection of Stable Mustard (*Brassica juncea L.*) Genotypes Through Genotype Environment Interaction and Stability Analysis Suitable for Punjab, Pakistan. J. Agric. Basic Sci., 01 (01), 15-19.
- Bullmore, E., Fadili, J., Maxim, V., Sendur, L., Whitcher, B. and Suckling, J. (2004). Wavelets and Functional Magnetic Resonance Imaging of the Human Srain. Neuroimage 23 (suppl. 1). S234-249.
- Day, M., Carr, D. B., Ulrich, S., Ilijic, E., Tkatch, T. and Surmeier, D. J. (2005). Dendritic Excitability of Mouse Frontal Cortex Pyramidal Neurons is Shaped by the Interaction among HCN, Kir2, and Kleak Channels. J. Neurosci. 25, 8776–8787
- Debanne, D. (2004). Information Processing in the Axon. Nat. Rev. Neurosci. 5, 304–316.
- Desai. N. S., Cudmore, R. H., Nelson, S.B., Turrigiano, G.G. (2002). Critical Periods for Experience-dependent Synaptic Scaling in Visual Cortex. Nature Neuroscience. 5 (8), 783–9.

- Ferreira, C. (2001). Gene Expression Programming (GEP): a New Adaptive Algorithm for Solving Problems, Complex Systems. 13(2),87-129.
- Fiddes, I. T., Lodewijk, G. A., Mooring, M., Bosworth, C. M., Ewing, A. D., Mantalas, G. L., Novak, A. M., Bout, A. V. D., Bishara, A., Rosenkrantz, J. L. , Lorig-Roach, R., Field, A.R. , Haeussler, M. , Russo, L. , Bhaduri, A., Nowakowski, T. J. , Pollen, A. A. , Dougherty, M. L. , Nuttle, X. , Addor, M-C. , Zwolinski, S. , Katzman, S. , Kriegstein, A. , Evan, E., Eichler, E. E. , Salama, S. R., Jacobs, F. M. J. and Haussler, D. (2018). Human-Specific NOTCH2NL Genes Affect Notch Signaling and Cortical Neurogenesis. Cell. 173 (6), 1356–1369.e22.
- Frade, J. M. and Ovejero-Benito, M. C. (2015). Neuronal Cell Cycle: the Neuron Itself and Its Circumstances. Cell cycle. 14 (5): 712-720.
- Gerrow, K. and Triller, A. (2010). Synaptic Stability and Plasticity in a Floating World. Current Opinion in Neurobiology. 2010. 20 (5), 631–9.
- Giachello, C. N., Scrutton, N. S., Jones A. R. and Baines, R. A. (2016). Magnetic Fields Bodulate Blue-light-dependent Regulation of Neuronal Firing by Cryptochrome. J. Neurosci. 36 (42),10742-10749.
- *Groppa, S., Oliviero, A., Eisen, A., Quartarone, A., Cohen, L. G. and Mall, V.* A. (2012). Practical Guide to Diagnostic Transcranial Magnetic Stimulation: Report of an IFCN Committee*. Clinc. Neurophysiol. 123 (5), 858–82.*
- Hosseini, E. (2021). Brain-to-brain Communication: the Possible Role of Brain Electromagnetic Fields (As a Potential Hypothesis). Heliyon. 7,e06363.
- Hollander, J.A., Cory-Slechta, D.A., Jacka, F.N., Szabo, S.T., Guilarte, T.R., Bilbo, S.D., Mattingly, C.J. , Moy, S.S., Haroon, E., Hornig, M., Levin, E.D., Pletnikov, M.V., Zehr, J.L., McAllister, K.A. , Dzierlenga, A. L., Garton, A. E., Lawler, C. P. and Ladd-Acosta, C. (2020). Beyond the Looking Glass: Recent Advances in Understanding the Impact of Environmental Exposures on Neuropsychiatric Disease. Neuropsychopharmacology. Springer Nature. 1–11.
- Jirsa, V.K. and Haken, H. (1996). Field Theory of Electromagnetic Brain Activity. Phys. Rev. Lett. 77, 960 – 969.
- Kida T, Tanaka, E and Kakigi, R. (2016). Multi-Dimensional Dynamics of Human Electromagnetic Brain Activity. Front. Hum. Neurosci., 19:1-20.
- Liu, J. and Robinson-Rechavi, M. (2020). Robust Inference of Positive Selection on Regulatory Sequences in the Human Brain. *Sci. Adv.* 6 (48), eabc9863.

- Madabhushi, R., Gao, F., Pfenning, A.R., Pan, L., Yamakawa, S., Seo, J., Rueda, R., Phan, PX., Yamakawa, H., Pao, P-C., Stott, R.T., Gjoneska, E., Cho, A.N.S., Kellis, M. and Tsai, L-H. (2015). Activity-Induced DNA Breaks Govern the Expression of Neuronal Early-Response Genes. Cell. 161, 1592–1605.
- Mairi, L. M. (2013). Perceptions of Nature, Nurture and Behavior. Life Sciences Society and Policy. 9(1), 13-21.
- Messing, F., Cecconi, F. and Rodolfo, C. (2020). Do You Remember Mitochondria? Front. Physiol. 11,271-279.
- Nawaz, F., Khan, H., Turi, N.A., Inamullah, Pervez, S., Qayum, S., Andaleeb, F., Gul, S., Maqbool, F. and Bibi, A. (2018). Biochemical and Stability Analysis of Variations of Indigenous *Brassica juncea* Genotypes in Different Egro-climatic Environmental Conditions of Pakistan. I.J.B. 12(6),139-151.
- Navarro, A., Gomez, C., Lopez-Cepero, J.M. and Boveris, A. (2004). Beneficial Effects of Moderate Exercise on Mice Aging: Survival, Behavior, Oxidative Stress, and Mitochondrial Electron Transfer. Am. J. Physiol. Reg. Integ. Comp. Physiol. 286, R505-511.
- Öztürk, N., Song, S.H., Selby, C.P. and Sancar, A. (2008). Animal Type 1 Cryptochromes. Analysis of the Redox State of the Flavin Cofactor by Site-directed Mutagenesis. J.B.C. 283 (6), 3256–3263.
- Petralia, R.S., Wang, Y-X., Mattson, M.P. and Yao, P.J. (2015). Structure, Distribution, and Function of Neuronal/Synaptic Spinules and Related Invaginating Projections. Neuromolecular Med. 17(3), 211–240.
- Raekim, K., Owens, G. and Ikkwon, S. (2010). Influence of Indian Mustard (*Brassica juncea*) on Rhizosphere Soil solution. J. Environ. Sci. 22(1), 98-105.
- Rossi, S., Antal, A., Bestmann, S., Bikson, M., Brewer, C., Brockmöller, J., Carpenter, L.L., Cincotta, M., Chen, R., Daskalakis, J.D., Lazzaro, V.D., Fox, M.D. , George, M.S., Gilbert, D., Kimiskidis, V.K., Koch, G, Ilmoniemi, RJ, Lefaucheur, J.P., Leocani, L, Lisanby, S.H., Miniussi, C., Padberg, F., Pascual-Leone, A., Paulus, W., Peterchev, A.V., Quartarone, A., Rotenberg, A., Rothwell, J, Rossini, P.M., Santarnecchi, E., Shafi, M.M., Siebner, H.R., Ugawa, Y., Wassermann, E.M., Zangen, A, Ziemann, U. and Hallett, M. (2021). Safety and Recommendations for TMS Use in Healthy Subjects and Patient Populations, with Updates on Training, Ethical and Regulatory Issues: Expert Guidelines. Clinc. Neurophysiol. 132 (1), 269–306.
- Schibler, U. (2007). The Daily Timing of Gene Expression and Physiology in Mammals. Dialogues Clinc Neurosci. 9 (3): 257–272.

- Sidiropoulou, K., Pissadaki, E.K. and Poiraz, P. (2006). Inside the Brain of a Neuron. EMBO Reports. 7(9):886-92.
- Singh, K.P., Miaskowski, C., Dhruva, A.A., Flowers, E. and Kober, K..M. (2018). Mechanisms and Measurement of Changes in Gene Expression. Bio. Res. Nurs. 20(4): 369–382.
- Stott, R.T., Kritsky, O. and Tsai, L-H. (2021). Profiling DNA Break Sites and Transcriptional Changes in Response to Contextual Fear Learning. *PLOS ONE*. 16 (7), e0249691.
- Suberbielle, E., Sanchez, P.E., Kravitz, A. V., Wang, X., Ho, K. and Eilertson, K. (2013). Physiologic Brain activity Causes DNA Double-strand Breaks in Neurons, with Exacerbation by Amyloid-β. Nat. Neurosci. 16, 613–21.
- Sunil, K. and Swaroop, M.R. (2020). Impact of Various Sowing Environment and Nutrient Sources on Growth Performance of Indian Mustard (*Brassica juncea*). Indian J. Agron. 65 (4), 465-470.
- Suzuki, I.K., Gacquer, D., Van Heurck, R., Kumar, D., Wojno, M., Bilheu, A., Herpoel, A., Lambert, N., Cheron, J., Polleux, F., Detours, V. and Vanderhaeghen, P. (2018). Human-Specific NOTCH2NL Genes Expand Cortical Neurogenesis through Delta/ Notch Regulation. Cell. 173 (6), 1370–1384.e16.
- Voudoukis, N.F. (2017). Inverse Square Law for Light and Radiation: A Unifying Educational Approach. Eur. J. Eng. Res. Sci. 3(11), 22-29.
- Yang, Y. and Herrup, K. (2007). Cell Division in the CNS: Protective Response or Lethal Event in Post-mitotic Neurons? Biochim. Biophys. Acta. 1772(4), 457–466.
- Yang, Y., Geldmacher, D.S. and Herrup, K. (2001). DNA. Replication Precedes Neuronal Cell Death in Alzheimer's Disease. J. Neurosci. 21 (8) 2661-2668.
- Zaky, E.A. (2015). Nature, Nurture, and Human Behavior; an Endless Debate Editorial. J. Child and Adoles. Behav. 3(6),e107