DOES ENRICHED ENVIRONMENT ALTER GENES?

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Abstract: The objective of the paper is to not only shed light on the scientific studies in neuroscience but also reveal criticality of enriched environment to the teaching community for the cause of optimal learning. It showed the shift off belief that the human growth and behavior are output of genes to the possibility of altering genes through the enriched environment. The paper exhibited the two different functions of genes, one of which facilitate learning of genes from the environment. It further focused on concept of enriched environment along with the aiding research studies from animal models to be extrapolated to human brain with good consistency.

Key Words:Genes, learning cells, enriched environment, research studies with consistency

1. Introduction

According to Jensen (2006),"Mendelian Genetics" swayed both scientific and medical world for the past two centuries leaving all to believe "we are with what our parents gave" and "much cannot be altered at least pertaining to brain" The prevailing paradigm is that brain has a fixed capacity, which can be filled by the experiences in the lifetime. Most of the educational policies were grounded on uniform belief that each child has fixed allotment of brainpower, which was supposedly determined by the unalterable genetic inheritance,in other words, genes that were passed to a child from its parents, stuck the child's brainpower accordingly. It developed a belief "nature-nurture." Eric Kandel exploded the idea of fixed genes. Jensen (2006) quoted his findings

"The subjective experiences of human consciousness, our perception of free will, behavior, and social dynamics can modulate gene expression, and vice versa. The regulation of gene expression by social factors makes bodily functions, including all functions of the brain, susceptible to social influences (p.8)."

According to Kandel(1998), social influences such as living states, environments, relationships biologically incorporated in altered expressions of specific genes in specific nerve cells of the brain. Berezovskii, Zelenskaia, Serebrovskaia, Zverkova, and Il'chevich (1986) studied that even twins who were brought up in different climates had the difference in their physical development and metabolic rate. Therefore, gene expression is powerful to influence what is used to be sacred between identical twins and their metabolism rates. Thus genes expressions can be influenced by the environment, for instance, the alterations in genes activity can bring change in height, weight, response to stressors, immune system etc.,. This complex process is influenced by some environment activators such as stress, trauma, nutrition, and exercise for gene expression. The sensors of the cells pass the incoming data from the environment to genes and genes to proteins in both ways and the interaction between environment and genes determines the life of organism.

2. Helix Structure of DNA

Watson and Crick understood genetic code as elegant double helix structure of DNA molecule that governs it. Many biologists believed that genes held the information needed to guide growth of all cells of the body and they were considered blueprints that make copies called RNA(Ribo Nucleic Acid, a messenger and translator), which activate transcription factors that further activate proteins to influence behavior. A few years ago, scientists thought that there might be two hundred thousand genes, which were believed responsible for human complexity. Groundbreaking research project in 1999 found that there were only twenty to twenty-five thousand genes,moreover human complexity cannot come only from genes. Therefore understanding genetic code is not yet helpful to understand human behavior.

3. Communication among the Cells

According to Giancotti and Ruoslahti (1999), human body has fifty trillion cells and each of them had tulip-shaped structures called receptors to receive information. Those cells have different receptor sites for different molecules. They will be activated by histamines, stress hormones, nutrition, and androgens. The receptor sites not only receive the information but also initiate electrochemical cascade of activity, which finally effect genes. Though there is core of genes to regulate basic functions, thousands of genes are responsive to environment stimuli. Therefore, genes are grouped according to their types. They are:

1. Early activated
2. Intermediate activated
3. Late activated
4. State dependent
5. Activity dependent

According to the complexity of environment signal genes allow an inter play among them. The type of signal is the determining factor of their response. An experience activates the expression of multiple genetic factors to make changes based on the experience called "gene expression." Hagmann stated that old view is one-way street, in which genes influence our lives whereas now science found two-way street view, according to which genes influence our lives and our lives influence genes. It is a revolution in biology and education. Therefore, it is possible to influence gene expression purposefully.

4. Functions of Genes in Every Cell

Genes have two core functions: They serve as highly reliable templates that can replicate perfectly. Every gene in every cell of the body provides high quality copies of its information. Not every day experience changes the information but only rare or random mutations will influence the quality of the copies. The second function is transcriptional, in the sense they can influence the structure, function, and other biological characteristics of the cell in which each is expressed. Though every cell has all the genes of the body, a particular cell activates small portion of its gene. When genes are expressed in a cell, the activation alters the phonotype of the cell and directs to manufacture of specific protein that characterizes the cell. The former function as a "blue print" is unaffected by the outside environment whereas the latter function "transcription" is susceptible to the environment.

5. Environment Changes the Behavior of Cell

Cairns, Overbaugh, and Miller (1988) studied from their seminal experiment with bacteria and observed that not all the mutations were random but they were able to change themselves. Bacteria consumed unaccustomed food by mutating into forms that could use available sources to survive in highly stressful environment. This biological event was replicated in the following experiments. According to Reik, Dean, and Walter (2001), after conception prenatal stress influenced the genetic matters in the newborn baby. Wolffe and Matzke (1999) mentioned another research, which found heritable changes in genes expression can be seen without changing DNA sequence. Therefore the studies show that environment even more to do with the outcome in behavior than we expected.

6. What is Enrichment?

Jensen (2006) defined enriched environment as positive biological response to contrasting environment, in which measurable, synergistic, and global changes take place. Enrichment stimulates proper brain activity at each turn and effect the course of entire life.

According to Jensen (2006), the learning about plasticity of brain and its potentiality to enrichment come from laboratory-based enrichment studies. The factors of enrichment are relevant to educators who look to improve the quality and quantity of not only special learners but also for all learners.Barnea and Nottebohm (1996) stated that enrichment is the response from a measure of difference. The enrichment can be measured only by comparison with something in experimental setting.Therefore, the law of contrast is all the matter in the field of enrichment research. If no measurable difference from the baseline, no enrichment response can be found.Renner and Rosenzweig (1986) explained that enrichment response is

something that affects subjects differently in terms of more encompassing, effective, and longer lasting than usual learning. Brain's structural and safety limitations determine the limit of learning, if the new learning is unlimited, it will cause massive cognitive instability because of overloaded networks, and it results in trauma. According to the rule, the older the brain, it protects more the past knowledge. Therefore, in the course of time the brain can take huge amount of new learning.

7. Brain Research from animal models

Since the study of human brain involved a couple of impediments to establish, and execute, the studies on the brains of rats were available to understand human brain. The studies on rats are desirable for the following reasons:

1. Though the brain of rat is smaller and less folded, there is less variation from human brain
2. Less cost of the study
3. Good understanding in less time
4. Easy to work with them

Limitations:

Though the research from animals may be useful to understand certain things relating to human beings, it has some limitations. Everything of the animal studies never have one-to-one correspondence with human studies but some simple transferable methodology models such as experiments and measuring new learning, spatial memory, and the changes of brain.

Overman and Bachevalier (2001) mentioned a study on dilemma in animals verses human models, which had found that certain safe and appropriate procedures of some selected animal testing could be generalized and applied to the children. The safe and appropriate procedure include simple behavioral tasks, learning, memory or nutrition but not tasks of learning language, complex learning, or specific latency studies.

8. Classical Studies on Enriched Environment

Many believed Donald Hebb, Canadian psychologist is the original trial blazer in the world of changing brain. He is first one who realized that the environment change brain and his book "Organization of Behavior" in 1947 remained classic for today but required better research. The two published studies in 1962 changed the view about learning, environment, and brain: one of them was discovered by Rosenzweig, Krech, Bennett, and Diamond (1962) in which the growth of the cerebral cortices of rats were observed in three different environments such as enriched environment, standard environment, and impoverished environment.A group of rats was set in the environment, which was enriched with full of toys and cage mates of rats and the toys were changed daily with boxes, tubes, and wheels and other objects of curiosity to the rodents. Another group of rats was set in the impoverished environment in which rats were left alone without toys and cage mates. After several weeks of leaving the two groups of rats in the particular environments, the development of their cerebral cortices of brain was measured and found that the cortices of rats in the enriched environment were 100% thicker than the cortices of the rats in the impoverished environment and had complex dendrites. Whereas the cortices of the rats in impoverished environment look like chemically fixed thin slices. Therefore, it is understood that complex outside environment, which makes the brain busy can alter the physical structure inside the brain.

Another is Altman's (1962) discovery of birth of new neurons in adult mammals but it was discounted at the time because it simply destroys a century old doctrine that no neurons will be produced in adult brain. Only after 40 years, the researchers Eriksson, Perfilieva, Bjork-Eriksson, Alborn, Nordborg, Peterson, and Gage (1998) confirmed the discovery of Altman about neurogenesis. Jensen(2006) stated that Bill Greenough at university of Illinois conducted dozens of studies, which were now considered classic on enrichment. Now enrichment of environment is widely accepted concept.

9. Enriched Environment Changes the Structure of Brain

Greenough (1976) stated that the learning changes the structure of brain. According to Eriksson et al (1998) extended by saying that even adult brain generate new neurons every day because of certain variables. Therefore, Jensen (2006) concluded that the brain structures and procedures could be altered by employing the selected behaviors. He believed that the enriched environment spearheads to alter the structures of brain and aid to maximize learning of so-called low-learners just as so-called gifted learners. Kandel (1998) asserted that the effect of enriched environment on impoverished brain lasts long years.

Van Praag, Christie, Sejnowski, and Gage (1999) studied that the voluntary gross motor activity of mice gave them better brains than that of rodent left with sedentary life style. Brown, Cooper-Kuhn, Kempermann, Van Praag, Winkler, Gage, and Kuhn (2003) conducted a study with mice in five different environments. They observed the mice that were set in a cage with a wheel had 50 % growth of new neurons than the mice in any other condition, but the mice in the complex and enhanced environment had 85% survival rate of cells in their brains. Therefore, it is understood that the running seems to generate more brain cells than the sedentary lifestyle but enriched environment helps the neurons to survive. It is assumed that running shall be incorporated in enriched environment as it has the effect of neurogenesis. Van Praag hesitated to extrapolate rodent data to human population but she told that the data of experiment changedher lifestyle by stimulating her to start jogging and she desires a school where plenty of gross motor activities will be maintained for her children.

10. Consistency of Research Studies on Affect of Enriched Environment

According to Jensen (2006), the research studies on the brains of animals found the important changes in the brain such as enhanced functioning, development of areas related to cognitive strength, learning, memory, and resilience. Based on the design of the study, the results witnessed were growth of neurons, longer dendrites, more connections, increase in the weight of brain, growth of the brain mass, more intra and inter connected activity, and enlarged capillaries. The researchers used both old school methods, which include behavioral tasks and smart new methods, which include MRI scans, marker dyes, and autopsies to understand, measure, and validate the changes. According to Jensen(2006), environment stimulation can affect the brain in several ways. He noticed six fundamental effects that are consistent in the research studies:

1. Metabolic Allostasis: Allostasis refers to readjusting the level of baseline properties of brain. Nobrega, Saari, Armstrong, and Reed (1992) studied that environmental stimulation had changedin regional cerebral metabolism in terms of enhanced blood flow in the brain and also enhanced levels of chemicals which are important for learning, mood, and cognition.Westhead, Slidel, Flores, and Thornton (1999) found the enhanced blood flow in specific regions such as thalamic, cortical, and hippocampal plays vital role for learning, consciousness, and memory. Serotonin, dopamine, acetylcholine are the important neurotransmitters for communication within the brain, and the chemicals associated with learning, mood, and memory. Rosenzweig and E. L. Bennett (1969) studied in the brains of rats that acetylcholine which is known for formation of memory was enhanced when environment was enriched. Clarke, Dalley, Crofts, Robbins, and Roberts(2004) found that the efforts of environment enriching enhancedserotonin, which stimulate mood and cognitive flexibility. According to Belz, Kennell, Czambel, Rubin, and Rhodes (2003),this research is highly relevant to stress since the enrichment protocol decrease stress-related hormones and ensure protection from stress disorders. Honess and Marin (2005) stated that the change of specific chemicals because of enrichment effect in the environment reduce non-human primate aggression.

2. Enhanced anatomical structures: enriched environment alters anatomical structure, which may serve as scaffolding necessary for increased cognitive tasks. Black, Isaacs, Anderson, Alcantara, and Greenough (1990) studied that enrichment protocol efforts enhanced vascular system which increased oxygen to neurons in the brain. Sirevaag and Greenough(1991) noticed the growth of glial cells that are closely connected to the neurons. Besides the studies of Diamond, Green, Greenough, and Schlumph (1983) found increment in length of dendrites, more complex branching on dendrites to make more connections in the future. Kolb (1995) observed that the enriched environment enhances 7% to 10% weight of the brain after 60 days.

3. Increased connectivity:

Globus, Rosenzweig, Bennett, and Diamond (1973) noticed the increase in synapses from both connections and dendritic spine counts. Turner and Greenough (1985) understood the correlation between more dendrites and synapses of the neuron with the increased connectivity, which may be considered important for processing and cognition. Another competing model of connectivity was proposed by Greenough and his colleagues at the university of Illinois, which showed that motor learning induces the formation of new synapses in mouse models. Geinisman, Disterhoft, Gundersen, McEchron, Persina, Power,

van der Zee, and West(2000) studied that the associative learning changed the size of synapses which may facilitate neurotransmission, though it did not increase the number of synapses in hippocampus. These contrasting models suggest that there may be developmental phases against the same stimulus.

4. Responsiveness and Learning efficiency:

Green and Greenough (1986) studied that the tissue of learning and memory in hippocampus turn to be better at electrical signal conduction point. According to Sharp, McNaughton and. Barnes (1985), effective enriched environment increased field potentials of synapses in hippocampus. Wang, B. W. Scott, and J. M. Wojtowicz(2000) noticed the ability of cells of rat in enriched environment was increased to the plasticity. According to Engineer, Percaccio, Pandya, Moucha, Rathbun, and Kilgard (2004), these changes will also affect the other senses such as auditory and visual. Wallace, Withers, Weiler, George, Clayton, and Greenough (1995) asserted that enriched environment influences protein synthesis and gene expression. The rats in enriched environment showed RNA messenger, which is crucial for memory at higher level. Lee, Hsu, Ma, Lee, and Chao (2003) observed that the frequent stimulations changed neurons to be very responsive and rats performed mazes, remembered spatial cues better, and learnt faster. Electrophysiological data showed that the brain could easily activate a function associated with new learning and plasticity

5. Increased neurogenesis and growth factors:

Kempermann discovered a brand of new brain cells in ratsin 1998 by using ingenious staining technique that involved using green fluorescent protein, which was extracted from jellyfish. The team was able to identify and photograph the newly dividing neurons. Kempermann, Brandon and Gage (1998) injected the same dye with the permission into brain of patients with inoperable cancer. When the patients died Kempermann and his team were able to autopsy their brain and knew the neurogenesis in the adult human brain. Kempermann, Gast, and Gage (2002) studied that the adult animals and humans within the enriched environment generated new neurons, the quantity of which was 500% more than the generation of new neurons in control group adult animals and humans within the non-enriched environment. The groundbreaking study of Eriksson, Perfilieva, Björk-Eriksson, Alborn, Nordborg, Peterson, and Gage (1998) showed that enrichment efforts not only influence growth of new brain cells but also the rate of growth. According to Gomez-Pinilla, So, and Kesslak (1998), the critical chemicals, which regulate growth and survival of brain cells that are linked to increased rates of cognition, are growth factors. The growth factors are responsible for proliferation, survival, and functionality of new neurons. Praag, Kempermann, and Gage (1999) observed that rats in enriched environment had higher survival rate of new neurons (85%) than that of rats in control and other experimental group whose survival rate range between 46% and 56%.The production of new neurons is genetic and partly modifiable by human experience.

Manipulation of environmental protocols results not only in production of more neurons but also increasing their survival rates to enhance in turn learning and memory.

6. Recovery from trauma and system disorders

Kempermann, Brandon, and Gage (1998) studied that the mice that bred for slower learning do worse on maze tasks and they have lower neuronal production than do their genetically bred typical counterparts, improved dramatically in enriched environment in terms of neuronal production and learning performance. Hellemans,Benge, and Colmstead (2004) conducted a study on animals that reared in isolation, increased anxiety, poor learning, and memory but later the enriched environment reversed all the deficits induced by isolated rearing. Waterland and R. Jirtle (2003) showed that the enriched environment could override mutation in mice that caused obesity. Animal studies have the advantage of inducing mutation and placing the animal in research environment to verify the results. Though human beings suffer many challenging insults, some of them were tried with animal studies and repaired with enriched environment. Dobrossy and S. B. Dunnett (2004) stated that enrichment benefits were found against the exposure to head injuries, alcoholism, and stroke. According to Guilarte, Toscano, McGlothan, and Weaver (2003), the studies with contrasting environment showed that those in enriched environment showed more protective strength and faster recovery. The studies showed that the enriched environment might facilitate under-achieving and special care learners for their progressive learning and memory.

11. Conclusion

The paper attempted to understand how genes were being altered by the enriched environment and provided scientific research studies to appeal the educators to change theirperspective genes domination over human behavior. The paper showed the two-way mechanism of genes that genes determine properties and growth of human body on one hand responding to the signals environment on the other. The paper looked into reasonability of extrapolation of results of studies from animal models to human beings and also fundamental and consistent effects of environment on the behavior of sampling of certain breed whose behavior is identical.

References:

[1] Altman, J. (1962). Are new neurons formed in the brains of adult mammals? *Science,135,* pp.1127–1128.

[2] Barnea, A., & Nottebohm, F. (1996). Recruitment and replacement of hippocampalneurons in young and adult chickadees: An addition to the theory ofhippocampal learning. *Proceedings of the National Academy of Sciences of the UnitedStates of America, 93,* pp.714–718.

[3] Belz, E., Kennell, J., Czambel, R., Rubin, R., & Rhodes, M. (2003). Environmentalenrichment lowers stress-responsive hormones in singly housed male and female rats. *Pharmacology, Biochemistry, and Behavior, 76*(3–4), pp. 481–486.

[4] Berezovskii, V. A., Zelenskaia, T. M., Serebrovskaia, T. V., Zverkova, A. S. &Il'chevich, N. V. (1986). Degree of concordance of the adaptive reactions in twins undermountain climate conditions and their relationship to the reactivity of thephysiological connective tissue system, *Fiziol Cheloveka, 12*(6), pp. 992–998.

[5] Black, J. E., Isaacs, K. R., Anderson, B. J., Alcantara, A. A., & Greenough, W. T. (1990). Learning causes synaptogenesis, whereas motor activity causes angiogenesis,in cerebellar cortex of adult rats. *Proceedings of the National Academy of Sciences ofthe United States of America, 87,* pp.5568–5572.

[6] Brown, J., Cooper-Kuhn, C. M., Kempermann, G., Van Praag, H., Winkler, J., Gage, F. H., & Kuhn, H. G. (May, 2003). Enriched environment and physical activity stimulate hippocampal but not olfactory bulb neurogenesis. *European Journal ofNeuroscience, 17*(10), pp. 2042–2046.

[7] Cairns, J. Overbaugh, J. and Miller, S.(1988). The origin of mutants. *Nature*, pp. 335,pp.142–145.

[8] Clarke, H. F., Dalley, J. W., Crofts, H. S., Robbins, T. W., & Roberts, A. C. (2004). Cognitive inflexibility after prefrontal serotonin depletion. *Science, 304*(5672),pp. 878–880.

[9] Dobrossy M. D., & Dunnett, S. B. (2004). Environmental enrichment affects striatalgraft morphology and functional recovery. *The European Journal of Neuroscience,19*(1), pp. 159–168.

[10] Engineer, N. D, Percaccio, C. R., Pandya, P. K., Moucha, R., Rathbun, D. L., &Kilgard, M. P.(2004). Environmental enrichment improves response strength, threshold,selectivity, and latency of auditory cortex neurons. *Journal of Neurophysiology,92*(1), pp. 73–82.

[11] Eriksson, P. S., Perfilieva, E., Bjork-Eriksson, T., Alborn, A. M., Nordborg, C., Peterson, D. A., & Gage, F. H. (1998). Neurogenesis in the adult human hippocampus.*Nature Medicine, 4*(11),pp. 1313–1317.

[12] Geinisman, Y., Disterhoft, J., Gundersen, H., McEchron, M., Persina, I., Power, J., van der Zee, E., & West, M. (2000). Remodeling of hippocampal synapses afterhippocampus-dependent associative learning. *The Journal* of *ComparativeNeurology, 417,* pp.49–59.

[13] Giancotti, F. G. & Ruoslahti, E. (1999). Integrin signaling, *Science, 285,* pp. 1028–1032.

[14] Globus, A., Rosenzweig, M. R., Bennett, E. L., & Diamond, M. C. (1973). Effects ofdifferential environments on dendritic spine counts. *Journal of ComparativePhysiological Psychology, 84,* pp.598–604.

[15] Gomez-Pinilla, F., So, V., & Kesslak, J. P. (1998). Spatial learning and physical activity contribute to the induction of fibroblast growth factor: neural substrates forincreased cognition associated with exercise. *Neuroscience, 85,* pp.53–61.

[16] Green, E. J., Greenough, W. T., & Schlumph, B. E. (1983). Effects of complex or isolated environments on cortical dendrites of middle-aged rats. *Brain Research, 264,* pp.233–240.

[17] Green, E. J., & Greenough, W. T. (1986). Altered synaptic transmission in dentate gyrus of rats reared in complex environments: evidence from hippocampal slicesmaintained in vitro. *Journal of Neurophysiology, 55,* pp.739–750.

[18] Greenough, W. T. (1976). *Neural mechanisms of learning and memory.* M. R. Rosenzweig and E. L. Bennett (Eds.). Cambridge: MIT Press, pp. 255–278.

[19] Guilarte, T. R., Toscano, C. D., McGlothan, J. L., & Weaver, S. A. (2003). Environmental enrichment reverses cognitive and molecular deficits induced by developmental lead exposure. *Annals of Neurology, 53*(1), pp. 50–60.

[20] Honess, P. E., & Marin, C. M. (2005). Enrichment and aggression in primates. *Neuroscience Biobehavioral Review,30*(3), pp. 413–436.

[21] Jensen, E.P. (2006). Enrich the brain. San Francisco, CA: Jossey-Bass.

[22] Kandel, E. (1998). "A New Intellectual Framework for Psychiatry?" *American Journal of Psychiatry,155,* p.461.

[23] Kempermann, G., Brandon, E. P., & Gage, F. H. (1998). Environmental stimulation of129/svj mice results in increased cell proliferation and neurogenesis in the adultdentate gyrus. *Current Biology, 8,* pp.939–942.

[24] Kempermann, G., Gast, D., & Gage, F.(2002). Neuroplasticity in old age: sustainedfivefold induction of hippocampal neurogenesis by long-term environmentalenrichment. *Annals of Neurology, 52*(2), pp. 135–143.
[25] Kim G., HellemansLuis,C., Benge, C., &Mary,C (June, 2004). Adolescent enrichment partially reverses the social isolation syndrome. *Developmental Brain Research, 150(2), pp.103-115.*
[26] Kolb, B. (1995). *Brain plasticity and behavior.* Mahwah, NJ: Lawrence Earlbaum Associates.
[27] Lee, E. H., Hsu, W. L., Ma, Y. L., Lee, P. J., & Chao, C. C. (2003). Enrichment enhances the expression of sgk, a glucocorticoid-induced gene, and facilitates spatiallearning through glutamate ampa receptor mediation. *The European Journal ofNeuroscience, 18*(10), pp. 2842–2852.
[28] Nobrega, J. N., Saari, M. J., Armstrong, J. N., & Reed, T.(April, 1992). Neonatal 6-OHDA lesions and rearing in complex environments: Regional effects on adult brain14C-2-deoxyglucose uptake revealed by exposure to novel stimulation. *Developmental Psychobiology, 25*(3), pp.183–198.
[29] Overman, W., & Bachevalier, J. (2001). Inferences about the functional development of neural systems in children via the application of animal tests in cognition. InC. Nelson and M. Luciana (eds.). *Handbook of Developmental Cognitive Neuroscience*Cambridge: MIT Press.
[30] Reik, W., Dean, W., & Walter, J. (2001). Epigenetic reprogramming in mammaliandevelopment. *Science, 293,* pp.1089–1093.
[31] Renner, M. J.,& Rosenzweig, M. R. (1987) . *Enriched and impoverished environments: effects on brain and behavior.*New York: Springer.
[32] Rosenzweig, M. R., Krech, D., Bennett, E. L., & Diamond, M. C. (1962). Effects ofenvironmental complexity and training on brain chemistry and anatomy. *TheJournal of Comparative Physiological Psychology, 55,* pp.429–437.
[33] Sharp, P. E., McNaughton B. L., & Barnes, C. A. (1985). Enhancement of hippocampal field potentials in rats exposed to a novel, complex environment. *BrainResearch, 339,* pp.361–365.
[34] Sirevaag, A. M., & Greenough, W. T.(1991). Plasticity of GFAP-Immunoreactiveastrocyte size and number in visual cortex of rats reared in complexenvironments. *Brain Research, 540*(1–2), pp. 273–278.
[35] Turner, A., & Greenough, W. T. (1985). Differential rearing effects on rat visual cortex synapses. i. synaptic and neuronal density and synapses per neuron. *BrainResearch, 329,* pp.195–203.
[36] Van Praag, H., Christie, B. R., Sejnowski, T. J., & Gage, F. H. (1999). Running enhances neurogenesis, learning and long-term potentiation in mice. *Proceedings of theNational Academy of Sciences of the United States of America, 96,* pp.13427–13431.
[37] Van Praag, H., Kempermann, G., & Gage, F. H. (1999). Running Increases CellProliferation and Neurogenesis in the Adult Mouse Dentate Gyrus. *NatureNeuroscience, 2*(3), 266–270.
[38] Wallace, C., Withers, G., Weiler, I., George, J., Clayton, D., & Greenough, W.(1995). Correspondence between sites of ngfi-a induction and sites of morphologicalplasticity following exposure to environmental complexity. *Molecular BrainResearch, 32,* pp.211–220.
[39] Wang, S., Scott, B. W., & Wojtowicz, J. M. (2000). Heterogeneous properties of dentate granule neurons in adult rats. *Journal of Neurobiology, 42,* pp.248–257.
[40] Waterland, R., & Jirtle, R. (2003). Transposable elements: targets for early nutritionaleffects on epigenetic gene regulation. *Molecular and Cellular Biology, 23*(15),pp. 5293–5300.
[41] Westhead, D. R., Slidel, T. W., Flores, T. P., & Thornton, J. M. (April, 1999). Protein structural topology: Automated analysis and diagrammatic representation. *Protein Science,8*(4), pp.897–904.
[42] Wolffe, A. P., & Matzke, M. A. (1999). Epigenetics: regulation through repression.*Science, 286*(5439), pp. 481–486.