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Impacts of Parents' Exercise on Inherited Genes

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Abstract: Physical exercise is considered an essential prospect in cognition. Exercise has a lot of benefits. It increases your body HDL (good cholesterol), controls your weight, prevents heart attacks and diabetes, regulates blood pressure, strengthens your muscles, and improves mood. However, we have minimal information regarding the effects of parents' exercise on the genes they pass down. This research paper reviews three different previous studies done on this topic. The first study is about the research done on the mice to analyze the transmission of the exercise effects of the mice fathers to offspring. The second study is the comprehensive analysis of the epigenetic changes at the molecular level in both mammalian and rodent cells. The third study is exclusively about the research on humans. Later, I presented the research design that I set up to find the answers to my questions, the potential outcomes, and further analysis of the results.

Keywords: Exercise, Epigenetic modifications, microRNA

1. Introduction

First, I will review the following three studies done on the impacts of parents' exercise in inherited genes. These studies are crucial to the conclusion of this paper. They provide more scientific information on if we can justify that parents' exercise can impact the genes they pass down to their children. The researchers who analyzed the results from these experiments organized them into the condensed studies shown later in this research paper.

1.1. Study 1

This design involved exercise performance in the mice fathers, with the patterns running for six weeks. Although mice's intelligence deviates considerably from human memory, intriguing patterns indicate that the lifestyle choices undertaken by a father, whether good or bad, are passed down to their child's genes. Comprehending how a parent's exercise level changes the genes passed down to their offspring necessitates a thorough analysis of the depicted study.

Mothers are considered the major gene carriers in the well-being of their newborns. However, we should remember that a father's habits also impact the child's health. This study revealed that male mice that engaged in exercises produced smarter and brighter offspring than those who did not. Scientists indicate these results are significant since they are repeatable: when mice engage in exercises, their gene behavior changes in their brains and bodies. These changes are eventually passed down to their children.

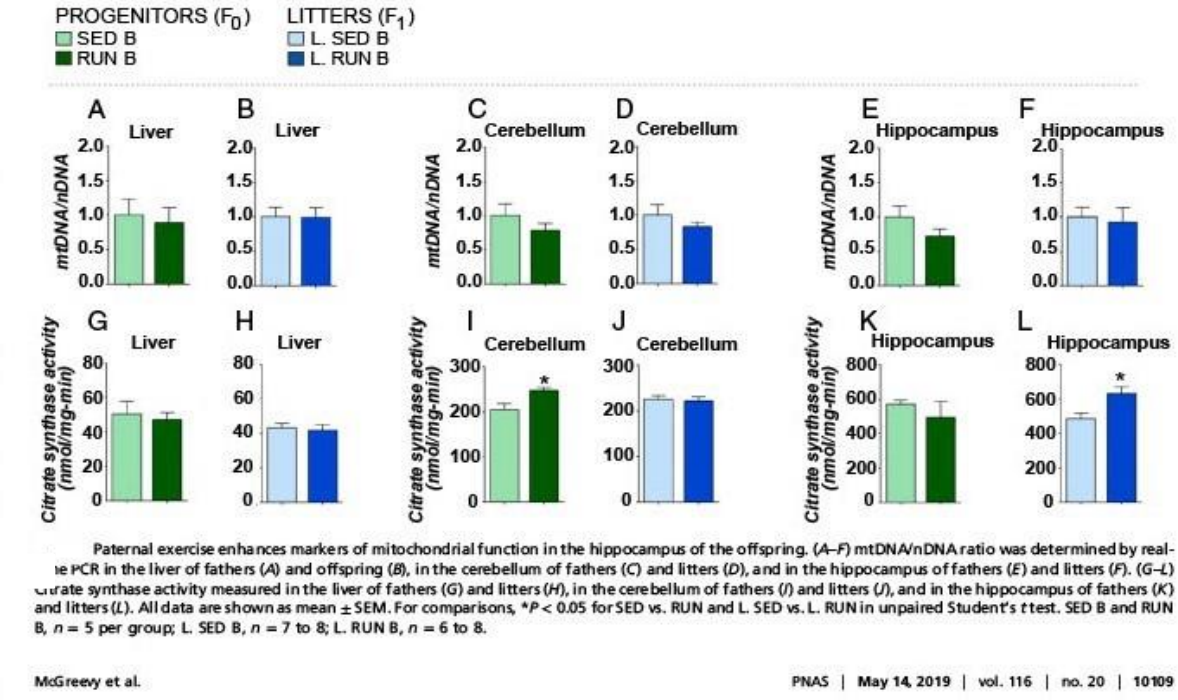
The mice involved in the depicted study underwent long and short-term memory tests (McGreevy et al., 2019). Some of the mice's fathers then engaged in exercises that lasted six weeks. After the exercise

period, the athletic mice seem to have improved memory scores than their counterparts. Exercise is considered an essential part of humans since it increases memory scores. Compared to their compatriots, the athletic mice dads revealed diverse genes in the hippocampus; further, the mitochondria within the brain section depicted more activity levels (Figure 1). These results indicate that the mice produced new brain cells. These brain changes seem to be transmitted from the mice's dads to their children. The mouse litters attributed to the athletic fathers depicted improved memory scores. These scores were compared to their elder siblings, depicting increases in cell population within the brain region.

McGreevy et al. examined exercise-induced effects at the mitochondrial level in the liver, cerebellum, and hippocampus of the fathers and their offspring. First, they figured out that the ratio of mitochondrial DNA (mtDNA) to nuclear DNA (nDNA) stayed the same in the different experimental groups (Fig. 1 A–F), suggesting that there was no increase in the mitochondrial number per cell. Then, they analyzed the activity of citrate synthase, a marker of mitochondrial functionality, and found out that the enzyme activity is very high in the cerebellum of the exercised fathers (Fig 1. I). At the same time, there is no change in the liver and hippocampus (Fig. 1 G and K). They noticed a significantly increased citrate synthase activity level in the offspring's hippocampus (Fig. 1 L). In contrast, not much change was seen in the liver and cerebellum (Fig. 1 H and J). Based on these findings, McGreevy et al. concluded that the increased hippocampal mitochondrial activity, not the differences in the mitochondrial number, leads to cellular and behavioral changes in the offspring.

McGreevy et al. did not find any exercise-induced changes in the DNA methylation in the male sperm and concluded that these changes are majorly passed down from the parent to the offspring through microRNAs. The changes noted within the brain depict microRNAs as coding genetic material within the sperm. They are carried via payloads, thus regulating the gene expression within the child. The sperm microRNAs within the athletic fathers regulate the genes within their child's brain. They confirmed this by performing GSEA (Gene Sets Enrichment Analysis), which showed the overexpression of genes that are targeted by microRNA in the hippocampus of the offspring of the exercised fathers. These prospects are critical since all the litters inherit considerable memory and learning capacity from their parents (McGreevy et al., 2019). Dietary aspects change the microRNA content within the sperm, with obesity also passed down to the progeny. During conception, these changes are notable, with scientists indicating genetic material is passed down to the children through these modes. The effects of lifestyle choices manifest on microRNA, indicating the fathers engaging in exercises pass down improved genes to their children.

Figure1:



Paternal exercise enhances markers of mitochondrial function in the hippocampus of the offspring. (*A–F*) mtDNA/nDNA ratio was determined by real-time PCR in the liver of fathers (*A*) and offspring (*B*), in the cerebellum of fathers (*C*) and litters (*D*), and in the hippocampus of fathers (*E*) and litters (*F*). (*G–L*) Citrate synthase activity measured in the liver of fathers (*G*) and litters (*H*), in the cerebellum of fathers (*I*) and litters (*J*), and in the hippocampus of fathers (*K*) and litters (*L*). All data are shown as mean ± SEM. For comparisons, **P* < 0.05 for SED vs. RUN and L. SED vs. L. RUN in unpaired Student's *t* test. SED B and RUN B, *n* = 5 per group; L. SED B, *n* = 7 to 8; L. RUN B, *n* = 6 to 8.

1.2. Study 2

Xavier et al. explored many research articles in PubMed and other journals and presented a comprehensive analysis. According to Xavier et al., smoking, obesity, and other lifestyle factors can induce oxidative stress in the germline. This oxidative stress can modify histones, telomeres, ncRNAs, DNA, and subcellular structures (mitochondria and centrosome) in the parents. Modifications of cellular structures lead to the altered phenotype of the offspring (Table 1). Xavier et al. found strong evidence that supports the role of DNA methylation patterns, histone modifications, and even non-protein-coding RNA in altering the epigenetic composition of individuals. Furthermore, they stated that these modifications produce long-lasting epigenetic effects that pass down from parents to offspring in humans and rodent species. Xavier et al. further concluded that various mechanisms in the body would erase these epigenetic modifications preventing them from being transmitted to the offspring.

However, few epigenetic changes to the DNA, particularly 8-hydroxy-2-deoxyguanosine (8OHdG) formation, may be transmitted across generations following aberrant or inefficient repair by the oocyte. Spermatozoa are particularly vulnerable to oxidative attack due to their limited capacity for DNA repair ((Smith *et al.*, 2013a, b). Then it is the responsibility of the oocyte to repair this DNA damage after fertilization with the help of 8-oxoguanine DNA glycosylase (OGG-1) (Smith *et al.*, 2013b). This inter-gender co-operation is affected if the oocyte expresses OGG-1 at a relatively low level (Lord and Aitken, 2015). Then the high mutation load is carried by offspring leading to miscarriage, congenital disabilities, and childhood cancers (Ohno *et al.*, 2014).

Table I Common epigenetic modifications and associated effects on the mammalian genome.

Epigenetic modifications	Effect on genome function
DNA methylation	Methylation at promoter sites associated with gene silencing. Methylation in gene region associated with regulation of gene activity.
Histone methylation	Methylation of amino acid residues in histone associated with both transcriptional repression and activation, dependent on residue.
Histone acetylation	Acetylation increases access to DNA for transcription. Allows the genome-wide reprogramming in sperm protamination
Histone phosphorylation	Phosphorylation of histones associated with chromatin compaction. Regulates chromatin structure and chromosome condensation during cell division.
Histone sumoylation	Small ubiquitin-related modifier (SUMO) proteins bind to histones. Associated with transcription activation and gene silencing.
Histone variants	Histone variants, e.g. H2A.Z, CENP-A, H2AX perform various specialized functions including DNA repair, gene regulation and centromere function.
Small non-coding RNAs	Micro RNAs and PIWI-interacting RNA (piRNAs) affect transcriptional repression and activation, and translational repression.
Long non-coding RNAs	Suggested to have high variety of functions, known to regulate large-scale transcriptional repression in imprinting.

1.3. Study 3

A study conducted on the Holocaust survivors' children indicates that most of them inherited stress vulnerability due to the horrendous experiences faced by their parents (Rachel Yehuda et al., 2016). The biological attempt to raise children in a threatening environment results in the children inheriting the stressful conditions faced by their parents.

Between 1993 and 1995, scientists took samples from a subset of a more extensive selection of Holocaust survivors interned in the Nazi camp during World War II. In addition, another sample of comparable subjects, who lived outside Europe during World War II, was taken. The research took place for ten years. At the same time, they started another separate project that recruited both Holocaust survivors and their offspring to evaluate the intergenerational effects of trauma. This sample represents data from 40 parents and 31 offspring. As part of the project, offspring gave samples of their blood and saliva and answered Childhood Trauma Questionnaire.

The main finding of this study is that both Holocaust survivors and their offspring have methylation changes on the same site in a functional intronic region of the FKBP5 gene (Rachel Yehuda et al., 2016). In addition, they found out that children of Holocaust survivors exhibited PTSD, mood, and other anxiety disorders with altered *FKBP5* gene (Table 2).

Table 2: Demographic and Clinical Characteristics for Holocaust Survivors and F0 Comparison Subjects

Parents (F0)	Holocaust Survivors (n = 32) Mean ± SD or n (%)	Jewish Comparison (n = 8) Mean ± SD or n (%)	Group Comparisons F (df) p or χ^2 (df) p
Age	77.9 ± 5.2	73.1 ± 8.5	$F_{1,38}$ = 3.98, p = .053
Gender			χ^2_1 = .46, ns
Male	12 (37.5%)	2 (25.0%)	
Female	20 (62.5%)	6 (75.0%)	
Years of Education	9.2 ± 4.1	12.3 ± 3.0	$F_{1,35}$ = 3.91, p = .056
Current PTSD[a]	16 (51.6%)	0 (0%)	χ^2_1 = 9.86, p = .012
Current Anxiety Disorder Except PTSD[b]	4 (13.8%)	0 (0%)	χ^2_1 = 2.08, ns
Current Mood Disorder[b]	9 (31.0%)	0 (0%)	χ^2_1 = 5.13, ns
Biological Information			
FKBP5 risk allele	18 (58.1%)	3 (37.5%)	χ^2_1 = 1.08, ns

ns, not significant; PTSD, posttraumatic stress disorder.
[a]Clinician-Administered PTSD Scale (42).
[b]Structured Clinical Interview for DSM-IV (41).

2. Analysis

Based on these three studies it is apparent that epigenetic factors can modify and mutate the germline. Over the next few generations, these mutations possibly get stabilized and pass to the offspring. While further studies are needed, these early data suggest exercise can impact intergenerational health through epigenetic modifications. I am proposing a research project to further prove this theory.

3. Research Method and Design

I will visit the nearby gated community to enroll 20 fathers willing to volunteer for my project. To begin with, I will explain to them about my research and let them sign the consent papers. Then, I will ask half of those people to exercise regularly while the other half follow a sedentary lifestyle. Next, I will enroll the fathers from the exercise group in the community gym. I will ask the gym instructor to implement a proper exercise routine and monitor them regularly. I suggest that they exercise for thirty minutes a day, three days a week. They should start this routine at least three years before conception. I will have to select twenty fathers with the same athleticism to make this experiment reliable. After 13-15 years, when the children of these fathers are mature, I will test the children's athleticism through the tests specified below. Same-gender, for example, boys are compared with the boys of the other fathers.

- 40 Yard Dash

The 40 Yard Dash is more accurate than many other running tests because it assesses the timing of the person's muscle reaction. Often the difference between people's 40-yard times is a tenth of a second. That may not seem like a lot, but those tenths of a second are many, especially in 40-yard dashes. In a typical one-mile run, people can build up this endurance throughout their life. In 40-yard dashes, it is difficult to cut the time even by a tenth of a second simply because much of this is genetically inherited. The average time for a 14-year-old boy is 4.8 to 5.5 seconds. All in all, this perfectly suits the designed experiment.

- Standing Vertical Jump

The standing vertical jump measures how high a person can launch into the air without taking extra steps. It tests the body's full explosive power when we jump off the ground. The average standing

vertical jump is 17 inches. However, many elite athletes have a vertical jump of over 30 inches. Of these athletes, only a small number will ever have a vertical jump of over 40 inches, depending on their genes. The vertical jump is primarily determined by the type of muscle fibers we inherit from our ancestors, thus, making this an effective measurement of athleticism for this designed experiment.

- Bench Press

The bench press measures how much a person can lift in one attempt. It measures how well-built a person's muscles are. Like the previous tools to measure a person's athleticism, genetics play a role in performance. Despite the work ethic, many of the best powerlifters have genetics favoring them in terms of muscle fiber types they inherit. The average bench strength of a 14-year-old boy is 1.0 times the body weight, whereas it is 0.7 times the body weight for the same-age girls. Indeed, therefore a bench press test is an excellent measurement for this experiment.

4. Possible Outcomes

4.1 If we receive desired result of study

Suppose the exercised parents' children performed better on these athleticism tests than those who followed a sedentary lifestyle, we can conclude that parents' exercise can modify the genes they pass down to their children. However, we need to confirm this with further DNA and gene analysis.

4.2 If we do not receive desired outcome of study

If there was no significant difference in the performances of the children of the exercised parents and the children of the sedentary parents, then **no, it** can't be concluded that parents' exercise can modify the genes they pass down to their children. Further research must take place. Then, future researchers can review this experiment and create their design with modifications until they can conclude whether or not parents' exercise impacts the genes they pass down to their children.

5. Conclusion

In conclusion, the positive and negative life choices undertaken by parents are passed down to their children. Positive perception is indicated in the analysis of this paper where regular exercise is seen to have lasting effects on children. As noted, athletic mice had improved memory and learning performance than their counterparts. The exercise-induced changes are passed down through microRNAs. MicroRNAs are encompassed within the sperm's payload. Although mice's intelligence differs from humans, the outstanding results depicted intriguing patterns. Most of the studies were conducted in mice and rats. There is only one study so far on human race involving Holocaust survivors. Based on a single study we can't conclude that all the study results of the animals are applicable to humans as well. We need more studies and more data in future to support the hypothesis that the epigenetic modifications could alter the genes' behavior in parents and therefore in their children. However, we can suggest that parents maintain healthy habits, do regular exercise before conception that could have a positive effect on them and their children.

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