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Physical Exercise as an Epigenetic Factor Determining Behavioral Outcomes

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Editorial

The science of behavior has been afforded much fuel for advancement of notions of lifespan development through the emerging observations of (i) *physical exercise* as an intervention for disease states and health assurances [1-8] and (ii) *epigenetics* as the biological avenues determining whether or not individuals well-being or ill-being [9,10].. Any bodily activity that enhances or maintains physical fitness implies the involvement of regular and frequent exercise [11,12] have defined exercise as a planned, structured physical activity with the purpose of improving one or more aspects of physical fitness and functional capacity. Epigenetics may be defined as the study of heritable phenotypic expressions resulting from changes in a chromosome without alterations in the DNA sequence. It has been applied in developmental psychology to examine psychobiological development emerging from an ongoing, bi-directional interchange between heredity and the environment through mechanisms of temporal and spatial control of gene activity during the development of complex organisms thereby shaping the behavior of individuals and organisms; as an experimental aspect of psychology it investigates how the life-span of 'nurture' orchestrates the biological heredity of 'nature'. It refers to heritable changes in gene expression (active versus inactive genes) that does not involve changes to the underlying DNA sequence; a change in phenotype without any alteration of genotype. These changes present regular and natural occurrences and are influenced by several factors such as age, the environment/lifestyle, and disease state. Epigenetic modifications may be manifested in the manner through which cells differentiate terminally to induce skin cells, liver cells, brain cells, and so on or may induce damaging effects that may lead to somatic, e.g. tumours, or behavioral conditions, e.g. clinical depression. At least three systems including DNA methylation, histone modification and non-coding RNA-associated gene silencing contribute to the initiation and sustenance of epigenetic alterations. According to these notions, physical forces may shape human/animal memory, behavioral traits/attributes, e.g. impulsiveness, and abnormal behavior [13,14]. Thus, a framework for the science of clinical and experimental is provided that encompasses how environment and experiences determine the expressions of genes to produce the variations and individual differences in multiple behavioral domains, including cognition, emotion, personality, behavioral disorders and psychological health.

The manifest health-beneficial expressions of physical exercise over individuals' life-cycles, whether normal or in ill-health, may be encapsulated within several domains of welfare: (i) exercise and academic performance, (ii) exercise and the developmental trajectory, (iii) exercise for the alleviation of affective disorders, and (iv) the epigenetic manifestations of physical exercise. Surprisingly, the effects of exercise may be determined relatively quickly: just eight weeks of pre-season training on body composition, physical fitness, anaerobic capacity, and isokinetic strength in collegiate taekwondo athletes in endurance gave improvements on all these parameters, as assessed by relative peak power and anaerobic capacity and angular velocity [15]. Although conclusions concerning exercise effects upon epigenetic modifications are still relatively premature, physical activity-dietary manipulations are being selected may quantify those changes occurring among individuals particularly with immune system inflammaging. Despite issues linked to population selection and quantification of exercise, the overall pattern emerging appears to be a product of the utilization of global methylation as an outcome measure, not depicting changes in DNA methylation at the gene-specific level. Thus, particular genes may be methylated differentially in response to exercise-activity; nevertheless, certain genes may be hypomethylated, and others hypermethylated, thereby causing little to no global alteration [16]. By applying the rat model of acute restraint stress, using Wistar rats, to examine the influence of stress on the global DNA methylation and on the expression of the Dnmt1 and Bdnf genes of hippocampus, cortex, hypothalamus and periaqueductal gray [17], found that the stress treatment induced a decrease in global DNA methylation in hippocampus, cortex and periaqueductal grey matter of sedentary animals and an increased expression of Bdnf, brain-derived neurotrophic factor in the periaqueductal grey matter whereas in the exercised rats no changes in DNA methylation were associated with stress, although it was linked with abnormal expression of Dnmt1 and Bdnf in cortex, hypothalamus and periaqueductal grey matter. These authors concluded that physical exercise demonstreates the potential to modulate changes in DNA methylation and gene expression consequent to stress treatment; a case of a positive epigenetic influencing counteracting negative influences.

Exercise intensity benefits for positive epigenetic changes in terms of mitochondrial biogenesis have been amply demonstrated [18]. Here, healthy male subjects performed interval cycling at 73, 100 or 133% of peak power output (PPO) and post-exercise changes in gene expression of PGC-1α (peroxisome proliferator-activated receptor gamma coactivator 1alpha, a protein encoded by the PPARGC1A gene) and its regulators were estimated in skeletal muscle biopsies. Cycling at 100% of PPO was observed to increase PGC-1α mRNA more than cycling at 73% PPO, although supramaximal exercise seemed to blunt this response, so that a lower increase in levels of PGC- 1α mRNA was seen when compared to both 100% and 73% PPO. Notably, increases in the mRNA levels of the regulators Sirt-1, PDK4 and RIP140 occurred in a manner independent of exercise intensity and muscle activation (ibid) [19] identified imprinted genes in skeletal muscle gene networks and observed exercise-associated DNA methylation alterations. These exercise-associated DNA methylation modifications make possible the propensity to rewind the 'epigenetic clock' over the course of the aging process [20] using an exercise regime consisting of sprint

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interval training, have shown that the cardiorespiratory fitness of individual participants, 12 healthy young men (18 to 24 years) and their maximal running performance, and decreased low-density lipoprotein cholesterol concentration in conjunction with genome-wide DNA methylation changes. Several CpG island and gene promoter regions were de-methylated after exercise, indicating increased genome-wide transcriptional changes, including epidermal growth factor (EGF; involved in cardiovascular disease) which was de-methylated and displayed reduced mRNA expression. They observed also that in microRNAs miR-21 and miR-210 (microRNA encoded by the *MIR21* gene), gene DNA methylation was altered by exercise causing a cascade effect on the expression of the mature microRNA involved in cardiovascular function. The viability of health-promoting epigenetic changes arising from exercise must endower attainable advantages for an aging brain and body [21] studied the contribution of DNA methylation and associated transcriptomic changes emerging from exercise-training regimes. They obtained consistent and associated modifications, DNA methylation in enhancers, gene bodies and intergenic regions and to a lesser extent in CpG islands or promoters, in methylation and expression, concordant with observed health-enhancing phenotypic adaptations. Physical exercise and activity, as epigentic interventions, provide essential contributions to respiratory and cardiovascular health and regeneration [22].

Exercise, as a potent epigenetic regulator, implies the potential to counteract pathophysiological processes and alterations in most cardiovascular/respiratory cells and tissues not withstanding a paucity of understanding the underlying molecular mechanisms and dose-response relationships. A study by [23] exemplifies the unique of role exercise as in the clinical and experimental context: they examined the influence of exercise on global DNA methylation and expression of the *Dnmt1* gene [for the DNA (cytosine-5-)-methyltransferase 1 protein] in the rat brain and verified, additionally, its potential to modulate responses evoked by repeated restraint stress, an animal model of depression. Rats were assigned to four treatment groups and treated, as follows: i) Exercise group: were physically active animals that received swimming exercise during postnatal days 53-78; ii) Stress animals submitted to repeated restraint stress during postnatal days 75-79; iii) Exercise-stress animals submitted to swimming during postnatal days 53-78 and to repeated restraint stress during postnatal days 75-79, and iv) Control group: animals that were not submitted to these interventions. Hippocampal, cortical and hypothalamic tissues were obtained on postnatal day 79. They observed significant increases in methylation from the exercise group (i) compared with the control group (iv). There were also significant increases in global methylation by the exercise-stress group (iii) compared with the stress group (ii) thereby demonstrating physical exercise modulation of repeated restraint stress responses. There was a reduced expression of the *Dnmt* gene in the hippocampus and thalamus of the exercise-stress group (iii). Since repeated restraint stress presents an animal model of depression it is interesting to note that electroconvulsive shock treatment increased *Dnmt3* expression [24] and aberrant *Dnmt* gene regulation is implicated in the pathophysiology of mood disorders [25]. Finally, there is accumulating support for the notion that physical activity plays a major role in promoting mitochondrial biogenesis in skeletal muscle tissues through the increased expression of genes encoded in both the nuclear and the mitochondrial genome [26] with nuclear receptors providing key signalling proteins capable of integrating environmental factors and mitochondrial function, thereby providing a potential link between exercise and mitochondrial biogenesis.

The necessity of physical exercise is linked to the assurance of normal, healthy developmental trajectories for structure and function over the complete lifespan of individuals, as evidenced from global public health physical activity guidelines [27]. It restores the healthy homeostatic regulation of stress, cognitive-emotional affective status and the balance of the hypothalamic-pituitary adrenal axis together the amelioration or reversal of performance deficits observed in neurocognitive tasks under conditions of neurologic or psychiatric disorder.

References

1. Archer T (2011) Physical exercise alleviates debilities of normal aging and Alzheimer's disease. Acta Neurol Scand 123: 221-238.
2. Archer T (2012) Influence of physical exercise on traumatic brain injury deficits: scaffolding effect. Neurotox Res 21: 418-434.
3. Archer T (2013) Physical exercise as intervention in Parkinsonism. In: RM Kostrzewa (ed.), Handbook of Neurotoxicity.
4. Archer T (2014) Health benefits of physical exercise for children and adolescents. J Novel Physiother 4: 2.
5. Archer T (2015) Exercise as therapy: Health and well-being. J Intellect Disabil Res 3: 76-81.
6. Archer T, Garcia D (2014) Physical exercise improves cognition and health in ADHD. J Novel Physiother 4: 208.
7. Archer T, Garcia D (2014) Physical Exercise Influences Academic Performance and Well-being in Children and Adolescents. Int J Sch Cogn Psychol 1: e102.
8. Archer T, Kostrzewa RM (2012) Physical exercise alleviates ADHD symptoms: regional deficits and development trajectory. Neurotox Res 21: 195-209.
9. Archer T, Blum K (2012) Epigenetics in neuropsychiatry. In: (1st Edn). CRC Press.
10. Archer T, Beninger RJ, Palomo T, Kostrzewa RM (2010) Epigenetics and biomarkers in the staging of neuropsychiatric disorders.
11. Blum K, Braverman E, Waite RL, Archer T, Thanos PK et al. (2015) Neuroquantum theories of psychiatric genetics: can physical forces induce epigenetic influence on future genomes? NeuroQuantology 13: 1-6.
12. Morris M, Schoo A (2004) Optimizing Exercise and Physical Activity in Older Adults. Butterworth Heinemann, Edinburgh.
13. Archer T, Oscar-Berman M, Blum K, Gold M (2012) Neurogenetics and Epigenetics in Impulsive Behaviour: Impact on Reward Circuitry. J Genet Syndr Gene Ther 3: 1000115.
14. Blum K, Braverman E, Waite RL, Archer T, Thanos PK, et al. (2015) Neuroquantum theories of psychiatric genetics: can physical forces induce epigenetic influence on future genomes? NeuroQuantology 13: 1-6.
15. Seo MW, Jung HC, Song JK, Kim HB (2015) Effect of 8 weeks of pre-season training on body composition, physical fitness, anaerobic capacity, and isokinetic muscle strength in male and female collegiate taekwondo athletes. J Exerc Rehabil 11: 101-107.
16. Horsburgh S, Robson-Ansley P, Adams R, Smith C (2015) Exercise and inflammation-related epigenetic modifications: focus on DNA methylation. Exerc Immunol Rev 21: 26-41.
17. Rodrigues GM Jr, Toffoli LV, Manfredo MH, Francis-Oliveira J, Silva AS, et al. (2015) Acute stress affects the global DNA methylation profile in rat brain: modulation by physical exercise. Behav Brain Res 279:123-128.
18. Edgett BA, Foster WS, Hankinson PB, Simpson CA, Little JP, et al. (2013) Dissociation of increases in PGC-1Î± and its regulators from exercise intensity and muscle activation following acute exercise.
19. Brown WM (2015) Exercise-associated DNA methylation change in skeletal muscle and the importance of imprinted genes: a bioinformatics meta-analysis. Br J Sports Med.
20. Denham J, Nelson CP, O'Brien BJ, Nankervis SA, Denniff M, et al. (2013) Longer leukocyte telomeres are associated with ultra-endurance exercise independent of cardiovascular risk factors. PLoS One 8: e69377.
21. Lindholm ME, Marabita F, Gomez-Cabrero D, Rundqvist H, Ekström TJ, et al. (2015) An integrative analysis reveals coordinated reprogramming of the

epigenome and the transcriptome in human skeletal muscle after training. Epigenetics 9:1557-1569.

22. Zimmer P, Bloch W (2015) Physical exercise and epigenetic adaptations of the cardiovascular system. Herz 40: 353-360.

23. Kashimoto RK, Toffoli LV, Manfredo M, Volpini VL, Martins-Pinge MC, et al. (2015) Physical Exercise Affects the Epigenetic Programming of Rat Brain and Modulates the Adaptive Response Evoked by Repeated Restraint Stress. Behav Brain Res.

24. Dyrvig M, Gøtzsche CR, Woldbye DP, Lichota J (2015) Epigenetic regulation of Dnmt3a and Arc gene expression after electroconvulsive stimulation in the rat. Mol Cell Neurosci 67: 137-143.

25. Higuchi F, Uchida S, Yamagata H, Otsuki K, Hobara T, et al. (2011) State-dependent changes in the expression of DNA methyltransferases in mood disorder patients. J Psychiatr Res 45: 1295-1300.

26. Perez-Schindler J, Philp A (2015) Regulation of skeletal muscle mitochondrial function by nuclear receptors: implications for health and disease. Clin Sci (Lond) 129: 589-599.

27. Dawson IG, Dohle S (2015) Towards an understanding of adult judgments of synergistic health benefits. Br J Health Psychol.