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Epigenetic and neuroplasticity in neurodevelopmental disorders: possibilities of physical exercise

Abstract

This article deals with the relationship between the mechanisms of neuroplasticity and epigenetics provided through the regular practice of physical exercise for the treatment of neurodevelopmental disorders. The aim of the study was to focus on the benefits of early interventions, especially physical exercise, in cases of neurodevelopmental disorders through epigenetic and neuroplasticity mechanisms. For this, a critical review of a narrative nature was carried out in the Scielo, PubMed and PsycInfo databases, as well as consultation in books on the subject. The results show us that exercise seems to promote epigenetic improvements, which can prevent the onset of neurodevelopmental disorders and also promote changes through neuroplasticity, which can mitigate the deficits caused by pathologies, especially if it occurs during early childhood. We can then understand that exercise tends to improve neurodevelopment, but a more robust base of empirical studies on this subject is needed.

Keywords: neurodevelopmental disorders, exercise, epigenetic, neuroplasticity

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Introduction

Neurodevelopmental disorders have increased considerably, as in the United States alone it is estimated that approximately 15% of children have some neurodevelopmental disorders (National Center for Health Statistics, 2015). Among the disorders with the highest incidence in the population, we can highlight the attention deficit hyperactivity disorder (ADHD) with an estimated 2.27% of the American population and the autism spectrum disorder (ASD), with 0.64% of occurrence in the United States.[1] This is even more worrying if we take into account that most cases are underdiagnosed in developing countries, that is, the percentages are probably even higher than those presented in the literature.[2] Despite these high rates that seem to be on the rise in recent years (GBD, 2019), there are some alternatives to treat or even prevent the development of these disorders in early childhood, when most of them manifest. Early intervention is essential to mitigate the progression of these pathologies, as it affects neural mechanisms of neuroplasticity and epigenetics.[3,4] Through neuroplasticity (the brain's ability to adapt to changes) (how to treat or even cure) the literature tells us that experiences as a medium can provide changes to the typical and atypical neural development process,[5] so that promoting neuroplasticity in the brain can reduce the deleterious impacts of several neurodevelopmental disorders such as autism spectrum disorder and attention deficit hyperactivity disorder.[6,7]

While from the perspective of epigenetics this relationship of early interventions seems to occur through avoiding the involvement of pathologies,[8] that is, through the activation or non-activation of pathological genes that trigger these disorders.[9,10] These neuroplasticity and epigenetic mechanisms are then activated in early interventions in the gene-environment relationship, in which, through experiences with the environment, the child may or may not develop a certain disease to which their genetics is predisposed. One of these early treatment environmental alternatives is physical exercise, which seems to be directly related to these avoidance and treatment mechanisms by stimulating the secretion of substances such as irisin and brain-derived neurotrophic factor (BDNF).[3,11,12] Therefore, the objective of this critical review of the literature is to focus on the benefits of early interventions, especially physical exercise, in cases of neurodevelopmental disorders through mechanisms of epigenetics and neuroplasticity.

Epigenetics and neuroplasticity: gene-environment interaction in neurodevelopmental disorders

Even with genetic predispositions with various aspects of the formation and development of an organism, genetics alone is not a final determinant for the onset and worsening of a neurodevelopmental disorder. That is, phenotypes depend on genetic transcription and this will occur especially in the individual's relationship with the environment.[13]

Studies that evaluated the etiology of disorders with ADHD showed that the triggering of the disorder occurs from interactions of multiple environmental factors before and after birth, that is, events in the environment for the mother, in particular, affect the fetus and after birth, experiences, especially in early childhood, have enormous potential for epigenetic changes. These environmental changes add to the inherited genetic predisposition.[14,15] This reinforces the role of epigenetics as chemical molecules (or markers) linked to a gene that change the way the cell reads its DNA (Papalia & Martorell, 2022). This cell activation occurs from the various environmental factors that trigger the referred gene. As, for example, prenatal stress is associated with prematurity, as well as low birth weight.[16] Several studies have sought to identify the effects of environmental interactions on organisms. Studies with monkeys show that maternal deprivation of social contact disturbs the mother-infant relationship, leading to important emotional and social disturbances and behavioral abnormalities in the infant,[17] as well as early mother deprivation of life causes epigenetic alterations that make the animal more vulnerable and with less cognitive capacity.[18] Given these factors, it is evident the need to invest in factors that provide positive reinforcing environments where mechanisms to enrich development and learning are created. Identifying those genetically predisposed is important, however the essential and most relevant factor is to provide healthy environments that protect dignity and essential aspects.

Physical exercise, environmental enrichment and neurodevelopmental disorders

Early intensive behavioral intervention studies demonstrate that an intervention initiated at preschool age and maintained for 2 to 3 years results in substantial improvements for a large subset of children with neurodevelopmental disorders, especially with ASD.[19,20,4] In

addition, the epigenetic alterations caused by experiences with the environment seem to be transmitted between generations, as is the case with physical exercise. Studies show that a mother who practices regular physical exercise can pass her deactivated genes to the fetus, that is, it is estimated that the non-activation of pathologies due to epigenetic mechanisms activated by the mother may even not transmit the pathological genetic load or attenuate its development in the fetus. The literature also tells us that physical exercise during pregnancy can produce a healthy intrauterine environment so that the fetus develops cognitively better.[21,22]

In this way, exercise acts in 2 ways in the reduction of neurodevelopment disorders, through epigenetics, in which through successful experiences the individual may not activate certain pathological genes (suppress their activation), preventing the children from developing the disorder or even by mechanisms of neuroplasticity, where the disorder only triggered, but can still be treated early and attenuated or even retrogressed depending on the stage of the disorder.[9,11] Thus, environmental enrichment, especially physical exercise, seems to promote large neural gains in individuals with neurodevelopmental disorders, as demonstrated in the enriched environment model shown in Figure 1.[3] Therefore, we can see that physical exercise has great neurobiological potential to prevent the emergence of neurodevelopmental disorders, but further empirical studies are still needed to demonstrate and better understand the real impacts on these pathologies.

Effects of environmental enrichment in animal models of neurodevelopmental disabilities

Disorder	Behavioural effects	Cellular effects	Molecular effects
Down Syndrome[18]	Improved cognitive (spatial learning and memory) and visual function recovery	Restored long-term synaptic plasticity in a neural circuit	Reduced inhibitory transmission, bringing GABA release in the synaptosomes
Fragile X Syndrome[19]	Rescued behavioral abnormalities displayed by adult Fmr1-KO mice: hyperactivity, social and cognitive deficits	Increased dendritic spine plasticity (especially in the hippocampal and amygdala)	Not determined
Rett Syndrome[20]	Ameliorated motor coordination and motor learning	Enhanced synaptic plasticity and regulation of synapse formation and stability in the cerebral and cerebellar cortex	Increased BDNF expression
Epilepsy[21-23]	Increased resistance to seizures; attenuated deficit in exploratory activity; improved learning and spatial memory	Decreased apoptosis; increased neurogenesis	Increased GDNF, BDNF, pCREB, ARC, HOMER1A and ERG1

Figure 1 Environmental enrichment model.

Fonte: Cioni et al.[3]

Conclusion

We can see those changes through environmental enrichment, in particular physical exercise, seem to promote neuroplasticity, which will safeguard the usual synapses and neurons, as well as better develop the brain, mitigating or preventing various neuropsychological disorders. Therefore, it is necessary to continue investigating how physical exercise variables can intervene in neuroplasticity and epigenetics mechanisms, promoting the refinement of successful interventions in several clinical cases, thus improving brain functionality and the development process of a general way.

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Conflicts of interest

The author declares there is no conflict of interest.

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