Human evolution and mutation in FOXP genes: a hypothesis on Atavism and neurological disorders

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Abstract. Atavism is a concept that encompasses the idea of the reappearance of traits considered "ancestral" or "archaic" in evolved organisms, possibly resulting from genetic mutations or variations. Accordingly, this article explores such a principle through the lens of FOXP genes, which are key in the development of neural networks associated with speech and language. The goal is to understand the rise in cases related to speech disorders and delays in human communication. This approach is based on the premise that behavioral changes driven by environmental evolution may have the potential to induce mutations, particularly in the form of motor and cognitive neurological conditions, especially among children and adolescents.

Keywords. Atavism; Communication; evolution; FOXP; Autism

1. Introduction

The FOXP genes influence cognitive neuromotor functions and regulate the expression of other genes associated with the development of neural circuits for speech, playing a fundamental role in the construction and formation of human language. As such, this gene represents a significant evolutionary distinction between humans, primates, and other species. Mutations in FOXP genes can lead to disorders such as Speech Apraxia and KE syndrome, and have also been linked to attention-deficit/hyperactivity disorder (ADHD) and Autism Spectrum Disorder (ASD) (Clifton et al., 2018).

2. Methodology

This study is based on hypothesis formulation through a systematic review of the scientific literature on Atavism and neurological disorders associated with gene mutations in the FOXP family. The article selection was conducted using scientific relevance criteria, including in vivo experimental studies, such as those developed by the Autism Science Foundation, and epidemiological data provided by the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC). The convergence of the data obtained enabled the construction of the central hypothesis of this article, establishing a theoretical foundation for future discussions.

3. Discussion

Linguistic atavism and the current communication problems

Research indicates that approximately 5% of school aged children currently exhibit speech disorders, with a particular emphasis on apraxia. Furthermore, it is estimated that there are 70 million individuals on the autism spectrum (WHO). Additionally, the U.S. Centers for Disease Control and Prevention (CDC) compiled a database with information from 2009 to 2017, revealing that at least 17% of children aged 3 to 17 are on the autism spectrum associated with hyperactivity and attention deficit disorder (ADHD).

These data evidence the advancements in medicine, enabling quick and easy diagnoses; however, the reasons behind the increase in cases – compared to previous decades – remain unclear. In light of this, this study will explore “linguistic atavism”, following the premise that humans do not evolve uniformly with the environment in which they are situated, resulting in the degradation of communication and the recurrence of behavioral traits – even if subtly – that had been lost through evolution.

Behavioral changes as triggers of new hereditary patterns

For this discussion, globalization and the establishment of the food industry will be used as a parameter. This niche reached its peak starting in the 1940s, grounded in the idea of food associated with convenience and a sense of fulfillment. Consequently, in addition to drastically changing their lifestyles due to automation in general, individuals began to excessively consume processed products high in sodium, sugars, and fats, leading to acute cases of diabetes and hypertension—conditions that were previously acquired and have now also become hereditary. Currently, these diseases affect more than half of the global population (IDF et al., 2023), including children and adolescents. Therefore, it is possible to assert that the rapid evolution of the environment induces behavioral changes, which in turn lead to new genetic patterns in subsequent generations.

Using this analogy as a basis, it is possible to correlate the increasing speech and cognitive disorders in new generations with the environments in which they are immersed: hyper-stimulated and chronically addicted to technology.

With the popularization of computers (also in the 1940s) and their continuous improvement, coupled with the emergence of social networks (beginning in the 1960s), new communication patterns have been adopted, particularly among younger groups. Vocabulary has become filled with abbreviations and slang, while non-verbal modes (emojis, GIFs, memes) have gained significant prominence. Furthermore, by the 1990s, a 556% increase in the prevalence of autism cases was recorded between 1991 and 1997 by the US Department of Developmental Services. Subsequently, with the ideals of convenience and necessity, it became common for every individual to own at least one smartphone, which is now considered an essential resource. Access to the internet is regarded as a facilitator for all social niches, including parents who turn to technology to balance their personal tasks with the growth of their babies. Thus, the use of screens by young children has become routine, and alongside chronic addiction, the "internet language," once characteristic of a single "social bubble," has become customary and normalized for all users of social networks.

These factors are strong contributors to the incidence of issues such as social isolation, anxiety, and ADHD itself (GOMES, Corrêa Julia, et al. 2018), symptoms currently observed in younger age groups. From this perspective, it is possible to infer that the prevalence of cognitive and socialization syndromes in these new generations is a hereditary reflection of the human inability to keep pace (from a genetic standpoint) with the abrupt evolution of the environment and its own habits.

The FOXP genes and the manifestations of mutations

There is a variety of studies correlating FOXP genes with neurodevelopmental conditions such as Autism, ADHD, and speech apraxia. The FOXP family (Forkhead P) comprises transcription factors that regulate other genes responsible for the formation of various organs in the human body, particularly the brain, cerebellum, and spinal cord, which are fundamental for neural migration, differentiation, and motor connectivity (Dasen, De Camilli, 2008). The variations within this family include FOXP1, FOXP2, FOXP3, and FOXP4, whose expressions are directly linked to the formation of the cortex, thalamus, hippocampus, and cerebellum.

FOXP1 and FOXP2 are key points in the study of neurological disorders, as they are the most abundant in humans, expressed in the cortex and deep cerebellar nuclei, structures associated with the modulation of motor activities. Their variations can be characterized by deletions or duplications, as well as by linear "disorder" in the variability of amino acids (Viscardi, Lucas Henrique; 2024), compromising the production of proteins such as FOXP2.

These genes trigger different neurological disorders also due to their structural components. Notably, the polyglutamine tract (Co, Marissa et al., 2019) is a protein portion that, during gene expression, translates to contraction or expansion of the sequence, potentially affecting neurons. Thus, disorders are provoked by either excessive or limited expression of this protein. Furthermore, all of them possess the capability for hetero- and homodimerization to bind to DNA molecules, thanks to the leucine zipper domain. In vivo experiments revealed the co-immunoprecipitation of these proteins associated with gene dysregulation—FOXP1/2—in the brains of mice (Mendoza & Scharff; Araujo et al., 2015).

It is essential to study the FOXP2 gene and its target group, CNTNAP2, which encodes the CASPR2 protein linked to neuronal growth and connectivity. This is because FOXP2 binds to protein sites and inhibits its expression (Vernes et al., 2008). Studies have shown

that this mechanism resulted in poor communicative behavior in children, associated with intellectual disability disorders (Whitehouse et al., 2011), such as Childhood Apraxia of Speech (CAS) and Autism Spectrum Disorder (ASD).

CAS is one of the most common conditions among children and is characterized by motor difficulty in speaking, meaning that the necessary movements and articulations are challenging, resulting in nearly incomprehensible speech. In this case, mutations can be observed in both the FOXP1 and FOXP2 genes, also occurring alongside the dysfunction of the DYX1C1 and KIAA0319 genes, which are responsible for the motor development of speech and are associated with dyslexia (T. A. Currier, M. A. Etchegaray, J. L. Haight, A. M. Galaburda, G. D. Rosen). Such variations are also studied through the lens of epigenetics, where alterations in genes arise from external factors—whether congenital inheritance or influences during the gestational period.

Autism and ADHD are increasingly prominent conditions in new generations. Scientific studies address the relationship between these conditions and mutations in the FOXP1 and FOXP2 genes, as they are associated, respectively, with the development of cognition and language, as well as with the neural circuits linked to communication and social interaction. The FOXP3 gene, although primarily associated with the immune system, has correlations with brain plasticity, suggesting its association with manifestations of Autism, particularly in relation to learning difficulties and adaptation to new situations.

Within the FOXP subfamily, the PAX6 group stands out, possessing highly conserved binding sites with FOXP2 (Coutinho et al., 2024). Although its expression is primarily linked to the formation of the ocular field, it also acts as a transcription factor for the differentiation of neural cells and the formation of cortical layers. Thus, alterations related to the expression of FOXP genes may be associated with Autism.

These genes, in turn, are regulated by the transcription factor Tbr1 (T-box brain protein 1), responsible for the development of the Central Nervous System (Hoed, Joery den et al., 2021), starting from the development of layer VI neurons in the cortex, establishing communication with the thalamus and essential intercortical connections for processing sensory expressions, as well as regulating glutamatergic neurons (neuronal migration). This factor has been studied in the context of autism spectrum disorders, as alterations lead to behavioral deficits that impact socialization and communication, characteristics present in individuals with this condition. In addition to interacting with FOXP1/2, it also regulates genes such as AUTS2 and RELN, which are associated with Autism due to their links to neural development.

4. Results and Conclusion

The analysis carried out revealed a significant (and apparently exponential) increase in cases of neurological disorders compared to previous decades. From that, it was possible to understand the critical role of FOXP genes in cognitive and motor functions, which are essential for the development of human language. The literature review clarified the connection between mutations in these genes and neurological disorders (such as Autism and Speech Apraxia) that compromise human communication. Thus, the study was relevant for elucidating the concept of linguistic atavism, positing that the recurrence of precarious communication traits, as well as the prevalence of cognitive disorders in current generations, has roots in environmental evolution.

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