Editorial

A Genomic and Epigenomic Approach for Studying Neuropsychiatric Disorders Associated to Early-life Stress: Part I

Early Life Stress (ELS) profoundly impairs child's brain development and behaviour giving rise to either temporary or permanent effects on cognitive, behavioural and psychological functions. Furthermore, possible long-term cumulative effects of various types of early adversity may show up in adulthood [1]. ELS-related pathological consequences greatly vary among individuals and depend on genetic and environmental factors. With regard to the onset of neurodevelopmental and psychiatric disorders associated to ELS exposure, great emphasis must be laid on the influence of various pre-, peri- and post-traumatic components in the environmental social context in which childhood abuse occurs. Namely, other influence factors related to the nature of the early trauma, such as its duration, chronicity, and severity, strongly predispose towards either pathological outcomes or resilient reactions. Together, genetic and environmental factors influence the individual stress responses although the most remarkable effects of such an interplay are those concerning a critical period of vulnerability spanning from fetal to post-natal development and adolescence. During this developmental window, the genome within neurons appears to be more plastic and sensitive to both positive and negative environmental stimuli. These gene-environment interactions contribute to optimal brain development, establishing a proper neural and behavioural developmental trajectory [2]. As previously anticipated, it is now clear that there is a causal link between ELS and the onset of neuropsychiatric and behavioural consequences, both with short- and long-term effects [3].

With the advent of Omic technologies, we are getting a considerable amount of information on the gene-environment interplay mechanisms, and learning biological underpinnings of those long-lasting changes that influence the pathological effects of ELS during the development of brain and behavioural traits [4]. In recent years, we have witnessed the rapid evolution of knowledge about several potential mediators responsible for the high phenotypic heterogeneity observed among individuals exposed to ELS. Ultimately, epigenetic changes in response to stress signalling are also known to influence the development and susceptibility to early trauma-related pathologies. Epigenetic variations depict potentially reversible and transitory biochemical changes that cause altered gene expression without modifying the DNA sequence and dynamically switch transcription rates in response to a multitude of environmental stimuli and developmental states. These epigenetic changes mirror the great flexibility of diverse biological processes of the organism including the modulation of proper and adaptive neurobiological responses to various stressor agents throughout the life. However, experiencing prematurely a stress challenge causes widespread alterations in brain plasticity and neuroendocrine system that correlate with marked and persistent changes in functional activity of a large number of stress responsive genes [5]. It follows that the epigenetic deregulation may be implicated in many long-term pathological consequences of physical and mental health.

The above key concepts are well represented by the seven reviews selected for the present Special Issue, which aims to provide an extensive overview of the interplay between ELS and the genome. This Special Issue is divided into two parts: the first comprises two papers and features a very constructive analysis of ELS-driven processes that program the cerebral decline to neurodevelopment and neuropsychiatric disorders. To this end, Drake *et al.* examine the intriguing and relatively little-known mechanisms linking preterm birth with neurodevelopmental effects. From the viewpoint of clinical neuroscience, there is substantial interest in studying the delayed effects of ELS in neurodegeneration. Therefore, the scope of the paper by Lemche is to provide a highly informative overview of genomic association studies supporting the relevance of ELS as a powerful mediator of Late-Onset Alzheimer's Disease (LOAD).

Taken as a whole, the pioneering works of this first part of the Issue invite the readers to discover some interesting genomics and epigenomics insights into the programming of the neuronal cell fate during the developmental age. These new findings build the foundation for precision medicine to improve the treatment of neuropathological sequelae induced by ELS injury, develop preclinical screening and, possibly, offer more reliable and integrative therapeutic models.

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