(REVIEW ARTICLE)

Autism spectrum disorder and molecular imaging following environmental stress: Functional aspects of the risk using multi-omics

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Abstract

Autism Spectrum Disorder (ASD) is characterized by complicated phenotypic symptoms, including intervention with social activity, communication, and unusually behavioral abnormality. ASD is a lifelong developmental condition affecting one in 88 children and is considered one of today's most urgent public health challenges. Individuals with ASD tend to respond inappropriately in conversation and may struggle to build relationships. Currently, the prime cause of ASD remains unclear, even though emerging findings emphasize the role of genetic and environmental factors in the development of autistic behavior could be examined. At present, risks such as exposure to unknown chemicals as an environmental factor in ASD are less appreciated. This review will discuss potential risks include air pollution and particle matters in alignment with detection strategies, like multidimensional Omics and the transcriptomic approach, which may empower the capability of predicting potential risk from gene expression to phenotype level as a hallmark of transformation outcome. In addition, this genomic-driven validation process saves time and quality of accuracy in the process of finding molecular determinants in the early stage of disease onset. Currently, the genomics era brings prediction models with various algorithms, and its intervention alternatives speed up to analyze the environmental risk of chemical stressors, such as hazardous chemicals, air pollutants, and/or nanoparticles, in compliance with regulatory measures of exploring molecular determinants associated with chronic disease and metabolic disorders. The value chain of disease prevention along with surveillance platform closely interacts with the prediction of risk assessment using a molecular-based platform. Efficacy of a sequential workout, including exploring, monitoring, and the translational application process in cellular or in vitro systems, could crosstalk with a transgenic animal model. Targeting molecule implication, such as gain- or loss-of-functional reverse genetic technology to verify its functional analysis, multi-dimensional omics could be beneficial in the field of environmental risk assessment, including safety evaluation: food and drug screening in ASD combined with imaging technology.

Keywords: Autism Spectrum Disorder; Biomarkers; Interactome; Metabolomics; Diagnostic marker; Toponomics

1. Introduction

To date, increasing environmental stress attributes to health complications in children: maternal health. Prenatal health was associated with urbanization and industrialization, leading to an increase of air pollution with industrial productivity and development of new environmental chemicals to facilitate energy consumption on-demand in developmental countries. In the environment, heavy metals are a permanent and existing threat; they contaminate the food chains and cause numerous health issues because of their toxicity. A real danger to living species is prolonged exposure to heavy metals in the atmosphere [1].

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Air pollution is emerging as a global issue. In western countries, pregnancy exposure to air pollution has harmful effects on the offspring. Air pollution remains a significant threat to public health globally, with nearly 9 million deaths each year. In early human development, air pollution can have multiple malignant health impacts, such as gastrointestinal, cardiovascular, behavioral, and perinatal diseases, and lead to infant mortality or chronic adult illness. Ambient exposure to particulate matter (PM) in industrialized countries, especially in urban areas, induces massive numbers of excess adverse health events [7].

Due to the sensitivity of the brain to environmental changes during the early development stages, exposure of mothers to air pollution during pregnancy is extremely dangerous and may result in severe damage to synaptic plasticity, which reflects cognitive functions (learning and memory), motor activity, and mood-related symptoms (depression and anxiety). This is in addition to the findings of research conducted on the dangers resulting from exposure to polluted air, including brain disease, attention deficit, hyperactivity, and autism spectrum disorder (ASD), Alzheimer's, and impaired cognitive development in children exposed to air pollution [2-9]. Autism spectrum disorder (ASD) refers to a range of conditions characterized by some degree of impaired social behavior, communication, and language, sometimes accompanied by a narrow range of interests and activities unique to the individual and carried out repetitively. ASD begins in childhood and tends to persist into adolescence and adulthood. In most cases, the conditions are apparent during the first five years of life [10]. Prevalent studies of ASD conducted in recent years have been the source of an important debate because of a steady and highly significant increase in estimates of the total prevalence of pervasive developmental disorders. Increasing evidence supports that the interaction of genetic and environmental factors could trigger the onset of pathogenesis in the development of ASD behavior, and related symptomatic phenotypes could be cross-linked. Recently, it was reported up to 40–50% of the variance in ASD liability might be determined by environmental risk. Environmental exposure to lead (Pb), mercury (Hg), arsenic (As), cadmium (Cd), manganese (Mn), and aluminum (Al) have been associated with neurodevelopmental disorders, including ASD [2]. One study found significantly higher levels of lead in the hair of patients with ASD than those of controls. In addition to this gene-environment correlation, environmental factors could interact with genetic components on various levels. It has been suggested that some environmental factors, certain toxins, and vitamin D deficiency increase the risk of the gene mutation that in turn can lead to an increased risk of ASD [5]. Other evidence shows that a specific polychlorinated biphenyl congener, PCB-95, might modify the number of copy number variations that lead to deletion or duplications of 15q11-q13, which is a genetic cause of ASD [8].

Interestingly, other reports indicate the production of numerous autoantibodies that react with specific brain proteins and brain tissues in children with ASD. These autoantibodies can also act to alter the function of the respective brain tissue. Studies show that anti-brain antibodies are associated with more severe cognitive and behavioral profiles in children with ASD. In line with this premise, one study led by Kern et al. found that certain brain auto-antibodies correlate with mercury levels in children with ASD. These findings suggest that children with ASD have limited thiol availability and decreased glutathione (GSH) reserve capacity, resulting in a compromised detoxification capacity and increased oxidative stress [4].

Over the last decade, altered risks from lifestyle, medical, chemical, and other factors have emerged through various study designs: whole population cohorts linked to diagnostic and/or exposure-related databases, extensive case-control studies, and smaller cohorts of children at elevated risk for ASD. Due to the genomic era (i.e., next-generation sequencing, human genome sequence, and exon sequence) and the advent of genomic editing, a molecular diagnostic can detect interaction, molecular alteration and phenotypic change as part of real-time healthcare services using genomics-based family care. Omics technologies can be utilized to define the risk of ASD pathogenesis, identify novel biomarkers that refer to ASD, its drug safety, examine family genetic stability and the risk of exposure within the family niches, evaluate the health impact of mental health and modulating factors, identify genetic predispositions relevant to behavioral patterns, and diagnostics via imaging.

2. Air pollution, mental health in a prenatal and maternal relationship, and ASD

There is a suspected relationship between long-term exposure, ambient air pollution, and mental health in the period of prenatal phase, including subjective stress, depressive disorders, health-related quality of life (QoL) due to socioeconomic factors, drug misuse, and suicide. The risk of mental disorders using multiple logistic regression analysis depends on the quartiles of air pollutants such as particular matter 10 μm (PM10) or fine particle matter. A high concentration of PM10 causes the prevalence of high stress, poor QoL, depressiveness, and suicide ideation. In a previous report, men were more susceptible to the increased risk of stress, poor QoL, and depressiveness from air pollution exposure than were women. Long-term exposure to ambient air pollution may be an independent risk factor for mental health disorders ranging from subjective stress to suicide ideation [10]. Mental health status was also associated with various sociodemographic features, health-related behaviors, and medical factors. The risk of subjective

stress (e.g., emotional and environmental) decreased their quality of cognitive health with older age, education less than 12 years, and unemployed participants. Subjects who were current smokers and drank alcohol more than one time per week represented a low risk of depressiveness and depression diagnosis by a doctor [10]. Genetic abnormality and vulnerability of mutation (i.e., deletion and duplication in several chromosomal regions) like copy number variation (CNV) and single nucleotide polymorphism (SNP) was reported in the case of ASD patients whose phenotypic features may alter dysfunction of chromosomal aberration along with synaptic malfunction due to functional gene modification, for examples neuroligins, SHANK and neurexins [12, 13]. Recently gene-phenotypic interaction was supported by epigenetic modification following exposure of various environmental risks including air pollution and chemical intoxication in the prenatal or pregnancy period. Future studies are required to explore the connectivity between disease complexity and molecular networks utilizing multi-dimensional molecular driven risk validation equipped with imaging skill to visualize molecular behavioral change resulting in phenotypic complications.

3. Conclusion

Autism spectrum disorder (ASD) is a complicated genetic disorder that features associated with cognitive failure to adapt at social, educational, and psychological levels. Future work needs an integrative approach to understand the genetics and development of ASD and explain connectivity between exposure of environmental risk among affected individuals and its family lifestyle, including food style. To explore the network of molecular connectivity between environmental risk and genetic abnormality, further research will be beneficial to structure interactome paired with risk and functional map use molecular-driven risk detection tools, like multidimensional Omics platform, for example metabolomics, genomics, proteomics, epigenomics, nutrigenomics, toponomics, and fluxomic. Those skill sets will improve risk assessment focusing on individualized and family care treatments and its follow-up monitoring and surveillance purposes which could mitigate medical costs early in the life of a child that was diagnosed with a malfunction of behavior and brain development.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflict of interest.

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