A Comprehensive Literature Review on The Interplay Between Genetic and Environmental Factors in Mental Illnes

Yitong Jin *

Jinan Xinhang Experimental Foreign Language School, Jinan, China

* Corresponding Author Email: jinyitong20061013@163.com

Abstract. This essay examines genetic factors and explores environmental factors while considering gene-environment interactions. Using a specific disorder, commonly perceived as influenced by either genetic factors or environmental factors, it illustrates how genetic predispositions and life experiences intertwine. Lastly, it discusses the role of epigenetics, where environmental factors lead to stable changes in gene expression, ultimately affecting mental health. This discussion supports the view that the relative significance of genetic factors versus environmental factors in causing mental illness depends on the type of disorder under consideration. Furthermore, it underscores the pivotal role of gene-environment interactions in the majority of mental disorders.

Keywords: Genetic factors, environmental factors, gene-environment interactions, epigenetics, mental illness.

1. Introduction

The debate of genetic factors versus environmental factors in mental illness is multifaceted and complex. While many researchers have found that genetic factors carry more weight in mental illness, highlighting their significant role in neurodevelopmental and neurodegenerative disorders. A growing body of evidence suggests that environmental factors also play a significant role in the development and progression of these conditions. However, as asserted by Kendler et al. (2005) in their comprehensive study published in 'The American Journal of Psychiatry,' the environment's impact on mental health encompasses aspects such as life experiences, social relationships, and living conditions.

2. Genetic Factors in mental illnesses

2.1. Genetic factors in Neurodevelopmental disorders

In some mental illness, genetic factors are particularly influential.

Neurodevelopmental disorders (NDDs), often stem from genetic mutations (Cardoso et al., 2019). An example is Down syndrome, mostly caused by chromosomal rearrangements, specifically trisomy 21, which has been observed to influence DNA methylation patterns, particularly in the brain. Studies have noted a tendency for increased methylation in the cells of individuals with Down Syndrome compared to those with a typical chromosomal arrangement (Antonarakis et al., 2020). The changes in methylation patterns can influence gene expression and function. This, in turn, impacts brain structure and functionality during early development. Studies have shown that individuals with Down Syndrome often have a reduced volume in the temporal lobe, including the hippocampus, and exhibit cerebellar hypoplasia, slowing the cognitive development of children which declines in their IQ scores (Liogier d'Ardhuy et al., 2015). Gene mutations like copy number variants (CNVs), small indels, and nucleotide substitutions contribute to mental illnesses as well. CNVs, by altering gene copies in brain development and neural pathways, disrupting the normal balance and connectivity of neural networks. It could affect amygdala to damage

memory processing, causing autism spectrum disorders (ASDs) (Sebat J et al. -n.d.). Similarly, small indels and nucleotide substitutions can disrupt critical genes for brain development, influencing disorders like schizophrenia and bipolar disorder (Cardoso et al., 2019).

2.2. Genetic factors in neurodegenerative disorders

In addition to certain neurodegenerative disorders, there is a progressive loss of brain functions and overlapping clinical syndromes caused by genes. (Gan et al., 2018). Having problems in immune function and lipid metabolism cause the accumulation of amyloid-beta (Aβ) and the formation of neurofibrillary tangles (Jones L et al. -nd). And the central role of Aβ overproduction and deposition in Alzheimer's Disease (AD) pathogenesis is emphasized in recent studies. Apolipoprotein E (APOE) is shown to have specific effects on Aβ, aggravating neuropathology and cognitive impairment associated with Aβ (Huang et al., 2014). In addition, Huntington's disease, the gene mutation cause poly-glutamine expansion in the Htt protein, causing resulting in Htt misfolding and cell death (Gomez-Pastor et al. 2017). It is found that an expansion mutation involving CAG trinucleotides in the HTT gene, responsible for producing Huntington protein, leads to a progressive disorder characterized by movement difficulties, dementia, and behavioral issues (Ross et al., 2014). So, it would cause Huntington's disease as its diagnosis is based on the presence of characteristic motor signs.

3. Environmental factors in mental illnesses

3.1. Major life related event cause mental illnesses

In some mental illnesses, environmental factors are significant. Major life related event can reduce well- being and disrupt normal daily activities. PTSD, often triggered by terrifying events like experiencing or witnessing domestic violence, is a case where environmental factors are crucial. Domestic violence, as ongoing,

Repetitive trauma causing physical, emotional, and psychological harm, can lead to stress reactions, increased physiological arousal, and persistent re-experiencing of traumatic events. This results in PTSD symptoms such as recurring traumatic memories, avoidance of related stimuli, emotional numbness, hyperarousal, sleep disturbances, and irritability. In populations of women in shelters, it has been observed that PTSD symptoms are not solely due to domestic violence. Factors like homelessness, lack of social support, lower income, and histories of multiple victimizations, such as childhood abuse, also significantly contribute to the likelihood of developing PTSD (JONES et al., 2001). In addition, some mental illness caused by the change in culture norm such as the eating disorder. In our daily lives, people often follow the trend and aesthetic on people's figure to get the social conformity. By the adolescence girls completing McKnight Risk Factor Survey, which had body height and weight measured, and underwent a structured clinical interview, it was found that in the Arizona, there was a significant correlation between Hispanics' intense focus on thin body image and social pressure, and the likelihood of developing eating disorders. The study also found that an increase in negative life events contributed to the onset of these disorders (The McKnight Investigators et al., 2003).

3.2. Surroundings cause mental illnesses

Can surroundings trigger mental disorders? In specific phobias, exposure to environments perceived as risky or harmful can induce fear. This fear response could lead to changes in the brain, notably in the amygdala's fear circuits, resulting in non-associative specific phobias (Garcia, 1970). Taking nyctophobia, for example: exposure to darkness, a new environment for many children, may activate the amygdala. In children who develop nyctophobia, this amygdala response is often heightened due to changes in the brain's fear response mechanisms (Rosen et al., 2015). On the other hand, classical conditioning and its generalization could cause associative specific phobia, The famous Little Albert experiment by John Watson is a prime example. In this study, Little

Albert was conditioned to fear a white rat by pairing it with a loud, frightening noise. Eventually, Little Albert began to get specific phobia not only the white rat but also other white, fluffy objects, demonstrating the process of generalization. Furthermore, in terms of Seasonal Affective Disorder (SAD), the shorter photoperiod in winter is negatively correlated with SAD onset (Rohan et al., 1970). Reduced daylight affects melatonin release from the pineal gland, impacting emotional well-being, daily and social activities, and even pain perception during winter. (Lewy et al., 2006) (David Schlager et al., 2004)

4. Gene- environment interaction contributes to mental illnesses

Indeed, the majority of mental illnesses arise from the interaction between genetic and environmental factors. Is it simplistic to attribute certain psychological disorders solely to genetics or environmental causes? Taking Post-Traumatic Stress Disorder (PTSD) as an example, studies have shown that a significant proportion of PTSD cases do not stem from major traumas as defined by the DSM-IV. Specifically, about

40% (36 out of 103) of individuals diagnosed with PTSD reported not experiencing a major traumatic event. This suggests that the symptoms associated with PTSD may not be exclusive to experiencing terrifying events (Bodkin et al., 2006). However, it is summarized evidence for the genetic factors of the development of PTSD (Smoller, 2015). The genetic variation in the CRP gene, specifically the single nucleotide polymorphisms (SNPs), leads to an increase in CRP levels in the blood serum. This rise in CRP, indicative of heightened inflammation, contributes to hyperarousal symptoms, which in turn can precipitate the development of PTSD (Michopoulos et al., 2014).

Do we necessarily have to use either environmental or genetic factors to understand PTSD? Epigenetic scientists have put forth a new perspective. Genes are chemically modified and thus change their expression under different environmental influences, affecting gene activity by modifying the environment surrounding the DNA.For example, maternal obesity is negatively affecting the placenta's development, potentially impacting the fetus's defense against stress hormones. hindering the transfer serotonin, brain-derived neurotrophic factor (BDNF), and leptin to the fetus, increasing the rate of getting mental disorders including attention deficit hyperactivity disorder, autism, anxiety, and depression as it can disrupt in the cell cycle in development. (Grissom and Reyes,2013). Stress, an environmental factor, can lead to stable alterations in gene expression, disrupting neural circuit functionality and ultimately influencing behavior. So the interaction of stress and gene can contribute to the development of stress- related mental illnesses, including major depressive disorder (Nestler et al., 2016).

5. Summary

The relative importance of these factors depends on the type of mental illness under consideration. Moreover, the interaction between genetic and environmental factors is a key aspect of understanding mental illness, highlighting the need for a more nuanced approach to their etiology. Looking ahead, the field of epigenetic adds a layer of complexity to this narrative. This emerging area of research holds promise for a deeper understanding of the interplay between genes and the environment. In practice, recognizing the significance of both genetic and environmental factors in mental illness is crucial for effective prevention, diagnosis, and treatment. A holistic approach that considers the complex interactions between these factors will lead to better outcomes for individuals grappling with mental health challenges.

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