Journal of Clinical and Nursing Research, 2021, Volume 5, Issue 5
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

The Causes of Individual Differences in Autism Spectrum Disorder

Yufei Jin*

Institute of Psychiatry, Psychology and Neuroscience, King's College London, London SE5 8AF, United Kingdom

***Corresponding author:** Yufei Jin, yufei.jin@kcl.ac.uk

Abstract: Autism spectrum disorder (ASD) is characterized by various symptoms including impaired social interactions, unusually repetitive behaviors, and highly restricted interests etc. People with ASD differ significantly on their clinical profiles and the causes of such individual differences are not yet fully understood. The present paper provides an overview of the causes of individual differences in ASD from three different perspectives: genetic, environmental, and neurobiological perspectives. The present paper also describes one study design in detail within each perspective (i.e., classical twin design, epidemiological case-control design, and magnetic resonance imaging), and explains how each study design is informative about the causes of ASD.

Keywords: Autism spectrum disorder; Causes; Individual differences

Publication date: September 2021; ***Online publication:*** September 30, 2021

1. Introduction

Autism spectrum disorder (ASD), also known as autism, is a complex neurodevelopmental disorder that emerges early in life and is associated with long-term disabilities [1]. Symptoms of ASD include impaired social communication and interaction, highly restricted interests, unusually repetitive behaviours, and varying degrees of intellectual disability [2]. Manifestation of autism symptoms can be highly heterogeneous. Affected individuals may differ significantly on their clinical profiles [3]. The causes of individual differences in vulnerability to ASD are not yet fully understood. To provide a comprehensive overview of the aetiology of ASD to date, the present essay aims to draw evidence from three different perspectives: genetic perspective, environmental perspective, and neurobiological perspective. Within each perspective, the present essay will outline one specific study design that is used to investigate the respective perspective. The study designs include classical twin study, epidemiological case-control study, and magnetic resonance imaging (MRI).

2. Genetic perspective

Twin studies of autism conducted from 1970s onwards have revolutionized the way people understand the determinants of ASD [4]. Results from twin studies were the first clear evidence that genes play a substantial role in the aetiology of ASD [5]. One of the most extensively used study design in behavioural genetics is the classical twin study [6]. The classical twin method draws a comparison between two types of twin pairs, monozygotic (MZ) and dizygotic (DZ) twins. MZ twins are derived from the same fertilised egg and therefore are genetically identical, whereas DZ twins are derived from two separate fertilised eggs and thus share 50% of their genetic material [6]. By comparing MZ and DZ twins reared together, the classical twin design can untangle the relative contribution of genes from environmental effects in ASD [6].

In a pioneering twin study, Folstein and Rutter [7] analyzed 21 twin pairs. They reported that the MZ twins were 36% concordant for autism, while the concordance rate for DZ twins was 0% – that is, one met the criteria for autism diagnosis, the other did not. Such result illustrates the importance of genetic influences in the causes of autism [7]. However, the sample size of this early twin study was rather small. In a more recent twin study, researchers recruited 277 twin pairs and the concordance rate for ASD was significantly higher in MZ twins – 88% in MZ twins compared to 31% in DZ twins [8]. In addition, in a population-based twin study, 37570 twin pairs were analyzed, and it was reported that the heritability rate of ASD was estimated as 87% [9]. Taken altogether, the results from classical twin studies demonstrated a strong genetic influence in the causes of ASD, suggesting that autism is a highly heritable disorder.

Nonetheless, like any other study design, the potential limitations of the classical twin study should be noted when interpreting its findings. One major limitation is the generalizability of twin studies. It is important to consider whether the samples drawn from twins are representative of the general population [4]. However, apart from twin studies, studies using other designs such as family study also support the important role of genes in ASD by demonstrating that increased genetic relatedness associates with increased risk for ASD [10].

3. Environmental perspective

Since the concordance rate for ASD in MZ twins was never 100%, it suggests that some other factors other than genetics were also involved in the development of autism. Studies of ASD have shown that environmental risk factors play a small to moderate but potentially causal role [4]. One study design that is often used to investigate environmental factors of ASD is epidemiological case-control design, which assesses the association between an exposure to risk factors and an outcome [11]. By comparing frequency of exposure in case participants to control participants, researchers seek to determine whether the exposure to risk factors may have contributed to the onset of the condition [12].

Evidence have indicated that individual vulnerability to ASD may be increased through environmental factors such as maternal diabetes and advanced paternal age. In a recent case-control study, Connolly et al. [13] compared mothers of children with diagnosed ASD to mothers of children without any developmental disorder. The results showed that maternal diabetes was significantly associated with an approximately 1.5-fold increased likelihood of ASD in the offspring [13]. Another risk factor associated with increased vulnerability to ASD is advanced paternal age. Frans et al. [14] conducted a population-based case-control study with 5936 individuals affected with ASD and 30923 unaffected individuals. The results suggested that paternal age over 35 years at birth was associated with significant risk increase of ASD in offspring, and the highest risk was found in paternal age 50 years or older [14]. A possible explanation behind the paternal age effect is that the association may be explained by an increased rate of *de novo* mutation in older father's sperm, and such genetic mutations were found to increase the risk for autism [14].

However, findings from epidemiological case-control studies should be interpreted with caution due to limitations in the design. A major limitation of case-control studies is that they may suggest an association, but they do not illustrate causation [11]. Further studies are needed to demonstrate the cause-effect relationship between exposures to environmental risk factors and increased risk of ASD.

4. Neurobiological perspective

The causes of ASD could also be discussed from a neurobiological perspective, where the individual differences in vulnerability to autism are observed in the brain. One study design that is often used to investigate brain-based differences is MRI. MRI is a type of non-invasive imaging technique that can yield detailed three-dimensional images of the brain by using strong magnetic fields and radio waves [15]. It can aid our understanding of the individual vulnerability to autism by showing how the brain develops

structurally different in people with ASD, and thus providing insight into the underlying neural mechanisms of autism [2].

In a longitudinal MRI study, Langen et al. [3] scanned participants with ASD and control participants at the mean age of 9.9 years and 12.3 years. The results indicated that, compared to the controls, participants with ASD showed an increased growth rate of striatal structures, and repetitive behavior – a core symptom of ASD – was correlated with faster growth rate of striatal structures. These findings demonstrate how altered neural development is associated with autism. However, this MRI study is retrospective in nature since autism can often be diagnosed at age of 2. Thus, it is not clear whether it is change in brain development that is driving the repetitive behavior or the other way around [3]. In a prospective MRI study, MRI scans were obtained from infants who are at high risk of developing ASD, that is, those with an older sibling diagnosed with ASD [1]. The infants were scanned multiple times during the first 24 months of their life, and the behavioral assessments for ASD was carried out at age 24 months. It was found that the development pathways for white matter fiber tracts differed significantly between infants who received a diagnosis of ASD at 24 months compared with infants not diagnosed. Such finding suggests a neurobiological foundation of ASD since the altered white matter pathways began before the onset of core behavioral symptoms in autism [1].

However, MRI studies should also be interpreted in mind with its limitations. First, ASD participants recruited for MRI studies are often those without intellectual disability so that they can complete MRI scans successfully. This might make the results less generalizable to the broader population of individuals with autism [16]. Additionally, to date, findings from MRI are not definitive and since MRI studies have been particularly difficult to replicate, more work needs to be done before findings from MRI studies can be reliably used as biomarkers of ASD [2].

5. Conclusion

In conclusion, taken the aforementioned genetic, environmental and neurobiological perspectives together, the causes of individual differences in vulnerability to ASD are not yet clear-cut. Each perspective has contributed to the underlying mechanisms of autism to a certain extent as shown by twin studies, epidemiological case-control studies and MRI studies in the present essay. It will be of importance for future research to continue deepening our understanding of the causes of ASD.

Disclosure statement

The author declares no conflict of interest.

References

[1] Wolff JJ, Gu H, Gerig G, et al., 2012, Differences in White Matter Fiber Tract Development Present from 6 to 24 Months in Infants with Autism. The American Journal of Psychiatry, 169(2): 589–600.

[2] Lord C, Brugha TS, Charman T, et al., 2020, Autism Spectrum Disorder. Nature Reviews, Disease Primers, 6(1): 5.

[3] Langen M, Bos D, Noordermeer SD, et al. 2014, Changes in the Development of Striatum are Involved in Repetitive Behavior in Autism. Biological Psychiatry, 76(5): 405–411.

[4] Ronald A, Hoekstra RA, 2011, Autism Spectrum Disorders and Autistic Traits: A Decade of New Twin Studies. American Journal of Medical Genetics, 156B(3): 255–274.

[5] Colvert E, Tick B, McEwen F, et al., 2015, Heritability of Autism Spectrum Disorder in a UK Population-Based Twin Sample. JAMA Psychiatry, 72(5): 415–423.

[6] Tick B, Bolton P, Happé F, et al., 2016, Heritability of Autism Spectrum Disorders: A Meta-Analysis of Twin Studies. Journal of Child Psychology and Psychiatry, and Allied Disciplines, 57(5): 585–595.

[7] Folstein S, Rutter M, 1977, Genetic Influences and Infantile Autism. Nature, 265(5596): 726–728.

[8] Rosenberg RE, Law JK, Yenokyan G, et al., 2009, Characteristics and Concordance of Autism Spectrum Disorders Among 277 Twin Pairs. Archives of Pediatrics & Adolescent Medicine, 163(10): 907–914.

[9] Sandin S, Lichtenstein P, Kuja-Halkola R, et al., 2017, The Heritability of Autism Spectrum Disorder. JAMA, 318(12): 1182–1184.

[10] Sandin S, Lichtenstein P, Kuja-Halkola R, et al., 2014, The Familial Risk of Autism. JAMA, 311(17): 1770–1777.

[11] Lewallen S, Courtright P, 1998, Epidemiology in Practice: Case-Control Studies. Community Eye Health, 11(28): 57–58.

[12] Buka SL, Rosenthal SR, Lacy ME, 2017, Epidemiological Study Designs: Traditional and Novel Approaches to Advance Life Course Health Development Research. Handbook of Life Course Health Development, 541–560.

[13] Connolly N, Anixt J, Manning P, et al., 2016, Maternal Metabolic Risk Factors for Autism Spectrum Disorder-An Analysis of Electronic Medical Records and Linked Birth Data. Autism Research: Official Journal of the International Society for Autism Research, 9(8): 829–837.

[14] Frans EM, Sandin S, Reichenberg A, et al., 2013, Autism Risk Across Generations: A Population-Based Study of Advancing Grandpaternal and Paternal Age. JAMA Psychiatry, 70(5): 516–521.

[15] MRI Scan, Available: https://www.nhs.uk/conditions/mri-scan/.

[16] Uddin LQ, Dajani DR, Voorhies W, et al., 2017, Progress and Roadblocks in the Search for Brain-based Biomarkers of Autism and Attention-Deficit/Hyperactivity Disorder. Translational Psychiatry, 7(8): e1218-2017.