International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2025: 7.089

Association of CNTNAP2 rs7794745 Polymorphism with Autism Spectrum Disorder in South Indian Children: A Case-Control Study

Pushkala S,[1] Valarmathi S,[2] Kiruthiga A[3]

[1]Department of Immunology, The T.N. Dr. M.G.R. Medical University, Guindy, Chennai – 32, India
Email: *pushkala66[at]gmail.com*

[2]Department of Epidemiology, The T.N. Dr. M.G.R. Medical University, Guindy, Chennai – 32, India
Corresponding Author Email: *Valarsrini[at]gmail.com*

[3]Department of Immunology, The T.N. Dr. M.G.R. Medical University, Guindy, Chennai – 32, India
Email: *kiruthigaalexander[at]gmail.com*

Abstract: ***Autism Spectrum Disorder (ASD) is a complex neurodevelopmental disorder characterized by impairments in social communication and interaction, with restricted and repetitive behaviours. Genetic factors contribute to ASD susceptibility and polymorphisms in the Contactin-Associated Protein-Like 2 (CNTNAP2) gene have been implicated in its pathogenesis. Aim: This study investigated the association between the CNTNAP2 rs7794745 (A/T) polymorphism and ASD susceptibility in South Indian children. Materials and Methods: A case–control study was conducted among 72 children aged 4–11 years, including 32 clinically diagnosed ASD cases and 40 healthy controls. Genomic DNA was extracted from EDTA-anticoagulated blood samples and genotyping of the CNTNAP2 rs7794745 polymorphism was performed using Polymerase Chain Reaction–Restriction Fragment Length Polymorphism (PCR-RFLP). Genotype and allele frequencies were compared using chi-square analysis and odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Results: Genotype distribution differed significantly between ASD cases and controls ($\chi^2 = 8.22$, $p < 0.02$), with the TT genotype more frequent among ASD cases. The T allele was enriched in ASD cases ($\chi^2 = 7.05$, $p < 0.05$) and carriers showed increased ASD risk (OR = 1.91, 95% CI: 0.76–4.79). Male sex and delayed cry after birth were associated with ASD. Conclusion: Consistent with earlier studies, the CNTNAP2 rs7794745 polymorphism may contribute to ASD susceptibility in South Indian children, warranting further multicenter validation studies.***

Keywords: Autism Spectrum Disorder, CNTNAP2, rs7794745, polymorphism, PCR-RFLP.

1. Introduction

Autism Spectrum Disorder (ASD), formerly classified under pervasive developmental disorders (PDDs), is a multifaceted neurodevelopmental disorder of global public health importance. [1-3] It is characterised by deficits in social communication and interaction, along with restricted and repetitive patterns (DSM-5) of behaviour, interests, or activities, with a substantial impact on affected individuals and their families. [4-6]

The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), published by the American Psychiatric Association in 2013 and revised in 2022 as DSM-5-TR, serves as the standard diagnostic framework for classifying and diagnosing mental disorders in clinical practice and research settings. [4,5]

According to the World Health Organization (WHO, 2025), it was estimated that approximately 1 in 127 individuals worldwide were living with autism in 2021, representing an average estimate of 61.8 million people globally. [1] Nevertheless, reliable epidemiological data from many low- and middle-income countries, including India, remain scarce.[1,2] In India, increasing awareness, improved diagnostic practices and expanding research have brought greater attention to the growing burden of ASD. [7,8]

The reported prevalence of ASD varies considerably across studies owing to differences in sex and age distribution, geographic location, study population characteristics and the screening and diagnostic criteria used, [2,9,10] highlighting the need for further research into its genetic and environmental determinants. [11,12]

Though the aetiology and pathogenesis of ASD are not yet fully understood, it seems to involve a complex interplay between genetic, environmental and neurobiological factors. [11] Apart from genetic predisposition, several prenatal and perinatal factors have been associated with the development of ASD. [12,13] These include advanced parental age, maternal infections, gestational complications, exposure to environmental toxins, preterm birth and low birth weight.[3,14] In addition, immune dysregulation, altered neurotransmitter activity, epigenetic modifications and abnormalities in brain development and connectivity have also been implicated in ASD pathogenesis. [3, 15-18]

Current evidence indicates that ASD has a complex and heterogeneous genetic architecture involving both common and rare genetic variants. [19-21] Common variants are thought to contribute to ASD risk through cumulative polygenic effects, [22] while rare genetic alterations, including de novo mutations and copy number variations (CNVs),[21]may have a greater individual impact.[23]

Several genes involved in synaptic development, neuronal signalling, and neurodevelopmental processes, such as *SHANK3, NRXN1, NLGN3, NLGN4,* and *CHD8*, have been identified as significant contributors to ASD.[19] Furthermore, ASD has been associated with various chromosomal abnormalities and genetic syndromes, including Fragile X syndrome and Rett syndrome. [24] Although substantial progress has been made in genetic research of ASD, the precise molecular pathways and mechanisms responsible for its development remain unclear. [25]

Studies on syndromic disorders such as Williams syndrome, Prader–Willi syndrome, Angelman syndrome and DiGeorge syndrome have provided valuable insights into the genetic and neurobiological basis of ASD, owing to their overlapping neurodevelopmental and behavioural characteristics. [21,26,27]

Among the candidate genes implicated in ASD, *CNTNAP2* (*Contactin-Associated Protein-Like 2*) has attracted significant research interest. [28-30] Located on chromosome 7q35–q36, *CNTNAP2* encodes the Caspr2 protein, a member of the neurexin superfamily that plays a critical role in neuronal development, synaptic organisation and neural communication.[30] Several single-nucleotide polymorphisms (SNPs) within CNTNAP2, particularly rs7794745 (A/T) located in intron 2, have been investigated for their association with ASD and related neurodevelopmental disorders. [28] Variations in the *CNTNAP2* expression or function may disrupt neuronal connectivity and signalling, contributing to deficits in language, cognitive skills and social behaviour, which are hallmark features of ASD. [29, 31,32]

Therefore, we conducted a hospital-based case–control study to examine the association between the CNTNAP2 rs7794745 polymorphism and Autism Spectrum Disorder in South Indian children.

This study was undertaken to evaluate the association of the CNTNAP2 rs7794745 (A/T) polymorphism with the risk of autism spectrum disorder (ASD). Additionally, the study examined the association between ASD and selected demographic and clinical variables, namely age, sex and seizure occurrence.

2. Materials and Methods

This hospital-based case–control study, including sample processing, genomic DNA extraction, PCR amplification and PCR-RFLP analysis, was carried out in the Department of Immunology, The Tamil Nadu Dr. M.G.R. Medical University, Guindy, India, after obtaining approval from the Institutional Ethics Committee.

Study population:

Inclusion Criteria: 72 children aged 4–11 years, comprising 32 children diagnosed with autism spectrum disorder (ASD) according to ICD-10 criteria and 40 healthy controls. ASD cases were recruited from the outpatient and inpatient departments of Government Chengalpattu Medical College and Hospital. Controls were children without neuropsychiatric disorders and with no reported family history of neuropsychiatric disorders across three generations.

Exclusion Criteria: Children with hearing disorders were excluded from the study.

Sample collection:
Two millilitres of venous blood were collected under aseptic conditions from the study participants into EDTA-containing tubes

Genomic DNA extraction:
Genomic DNA extraction was done from EDTA - anticoagulated whole blood using the HEINI Purefast Human Blood DNA Minispin Kit (HELINI BIOMOLCULES, Chennai, Tamil Nadu, India) according to the manufacturer's instructions. Briefly, blood samples were subjected to proteinase K digestion and lysis, followed by ethanol precipitation and purification using silica-based spin columns. The purified DNA was eluted in elution buffer and stored at −20°C until further analysis. The extracted DNA was subsequently used for polymerase chain reaction (PCR)-based genotyping of the *CNTNAP2* rs7794745 polymorphism.

PCR Amplification of CNTNAP2 rs7794745 Polymorphism
Genotyping of the CNTNAP2 rs7794745 (A/T) polymorphism was performed by polymerase chain reaction (PCR) using the following primers flanking the polymorphic site: Forward 5′-GAGGTGAAATACGACCAAGA-3′ and Reverse 5′-ACCAGTGTGCTTCAGACCAA-3′. PCR amplification was carried out in a final reaction volume of 25 µL containing genomic DNA, forward and reverse primers, master mix and nuclease-free water. The amplification conditions included an initial denaturation at 95°C for 5 minutes, followed by 35 cycles of denaturation at 95°C for 30 seconds, annealing at 58°C for 30 seconds, extension at 72°C for 30 seconds and a final extension at 72°C for 5 minutes.

Restriction Fragment Length Polymorphism (RFLP) Analysis
The amplified PCR products were subjected to Restriction Fragment Length Polymorphism using TasI restriction enzyme for the rs7794745 polymorphic site according to the manufacturer's protocol. The digestion reaction was prepared in a total volume of 30 µL containing PCR product, 10X Buffer B, TasI Restriction enzyme and PCR-grade water. The reaction mixture was incubated at 65°C for 1 hour and 30 minutes in a thermal cycler. The digested products were subsequently analysed by agarose gel electrophoresis for genotype determination. The genotypes were identified based on the characteristic banding patterns generated after TasI digestion and subsequent agarose gel electrophoresis

Agarose Gel Electrophoresis
PCR and PCR-RFLP products were analysed by horizontal agarose gel electrophoresis for the separation and identification of DNA fragments. A 2% agarose gel was prepared in 1X TAE buffer and stained with ethidium bromide. The molten agarose was poured into a gel casting

tray fitted with combs and allowed to solidify at room temperature.

Following solidification, the gel was placed in an electrophoresis tank containing 1X TAE running buffer. PCR products and restriction-digested PCR-RFLP products were mixed with gel loading dye and loaded into the wells along with a DNA ladder. Electrophoresis was performed at 100 V until adequate separation of DNA fragments was achieved. The separated bands were visualised under ultraviolet illumination using a gel documentation system, and the fragment patterns were analysed for SNP genotype determination.

Statistical analysis

The Statistical analysis was done with the help of SPSS software (Version 21) and Microsoft Excel.

1) Allele frequency was estimated by allele counting
2) Hardy- Weinberg equilibrium was assessed by the Chi-Square test
3) Genotype frequency and Allele frequency between the cases and controls were compared with the help of the chi-square test.
4) Odds ratio is used for the assessment of the distribution of the T allele in the study population
5) Parameters such as seizure history, age, family history of autism, associated neurological conditions are tabulated and a statistical analysis is done.

3. Results

A total of 72 participants were included in the present study to investigate the association between the rs7794745 (A/T) polymorphism in the CNTNAP2 gene and autism spectrum disorder (ASD). The mean age of the participants was 6.93 ± 2.20 years, with ages ranging from 4 to 11 years. The highest proportion of participants belonged to the 6-year age group (25.0%), as presented in Figure 1. Among the participants, 53 (73.6%) were males and 19 (26.4%) were females.

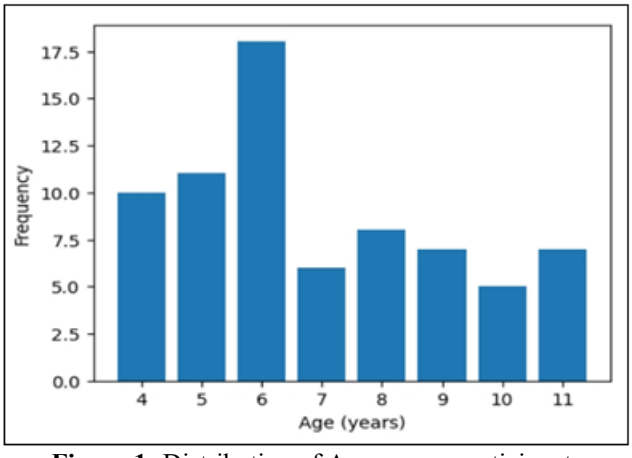

Figure 1: Distribution of Age among participants

The sex distribution among cases and controls demonstrated a statistically significant association with ASD ($\chi^2 = 8.584$, $p = 0.003$), indicating a higher prevalence among males. The distribution of sex among participants is shown in Figure 2.

Delayed cry after birth was observed in 6 participants (8.3%), all of whom belonged to the ASD group. Fisher's Exact test demonstrated a statistically significant association between delayed cry after birth and ASD ($p = 0.006$). The distribution of cry after birth among the participants is shown in Table 1. The genotype distribution among controls was tested for Hardy–Weinberg equilibrium.

Table 1: Distribution of cry after birth among participants

Cry after birth	Frequency	Percentage
Normal	66	91.7
Delayed	6	8.3

The frequency of the wild allele (A) was 0.55, while the frequency of the risk allele (T) was 0.45. The observed genotype frequencies did not significantly deviate from the expected genotype frequencies under Hardy–Weinberg equilibrium **($\chi^2 = 4.8$, $p > 0.05$),** indicating that the control population was genetically stable. The observed and expected genotype frequencies are summarized in Table 2.

Table 2: Hardy–Weinberg equilibrium analysis among controls

Genotype	Observed	Expected
AA	18	12
AT	8	8
TT	14	20

The genotype distribution among ASD cases and controls demonstrated a statistically significant association with ASD status ($\chi^2 = 8.22$, $p < 0.02$). TT genotype shows a strong association (OR = 5.40, CI = 1.72–16.93). Although the AT genotype showed an odds ratio above 1, its 95% confidence interval (0.78–9.34) crossed unity, indicating that this association is statistically non-significant AT genotype shows a weaker, non-significant association (OR = 2.70, CI = 0.78–9.34).

Table 3: Genotype distribution among ASD cases and controls

Genotype	Cases (n=32)	Controls (n=40)	χ^2 Value	p-value	OR (95% CI)
AA	5 (15.6%)	18 (45.0%)	8.22	–	Reference
AT	6 (18.8%)	8 (20.0%)		0.34	2.70 (0.78–9.34)
TT	21 (65.6%)	14 (35.0%)		0.016	5.40 (1.72–16.93)

The genotype distribution among cases and controls is presented in Table 3 and Figure 3.

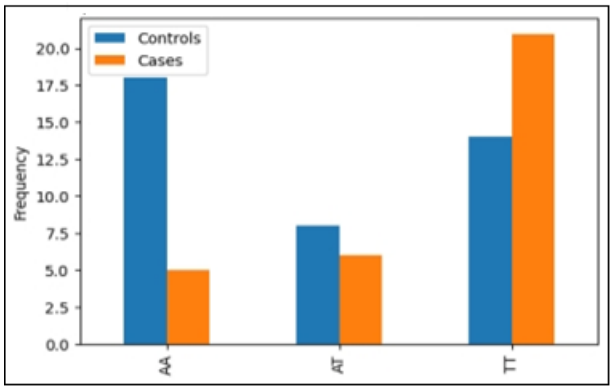

Figure 3: Genotype Distribution among cases and controls

Carriers of the T allele (AT+TT) was more frequent among ASD cases compared to controls ($\chi^2 = 7.05$, $p = 0.008$), with an odds ratio of 1.91 (95% CI: 0.76–4.79). There is a borderline association since the confidence interval crossed unity.

Table 4: Allele distribution among ASD cases and controls

Allele Group	ASD Cases	Controls	χ^2 Value	p-value	Odds Ratio (95% CI)
T^+	27(84%)	22(55%)	7.05	0.008	1.91 (0.76–4.79)
T^-	5(16%)	18(45%)			Reference

The allele distribution among cases and controls is summarized in Table 4 and illustrated in Figure 4.

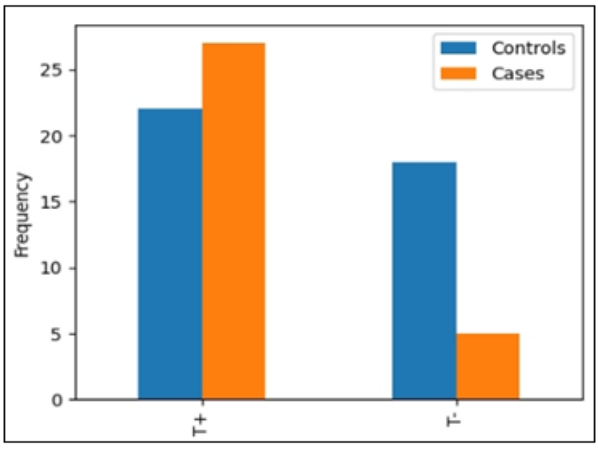

Figure 4: Allele Distribution among cases and Controls

Individuals carrying the T allele demonstrated a 1.91-fold increased risk of developing ASD compared to individuals carrying the A allele (95% CI: 0.76–4.79).

To summarize, the overall findings indicate that carriers of the T allele of rs7794745 in CNTNAP2 face a markedly higher risk of ASD, establishing this variant as a significant genetic susceptibility factor.

4. Discussion

Autism Spectrum Disorder (ASD) is a complex neurodevelopmental disorder characterized by diverse clinical manifestations and varying degrees of severity. The core symptoms typically become apparent within the first two years of life and primarily affect social communication and interaction, accompanied by restricted, repetitive patterns of behaviour, interests, or activities. [33]

Since Leo Kanner's initial description of autism as autistic disturbances of affective contact' in 1943, extensive efforts have been made to identify the factors contributing to ASD. Growing evidence supports a substantial genetic component in its pathogenesis, with numerous candidate genes and genetic variants being implicated in susceptibility to the disorder. [34]

ASD is widely recognized as a multifactorial disorder arising from a complex interplay between genetic susceptibility and environmental exposures, such as dietary factors, pesticides and infections, that influence neurodevelopment and contribute to the characteristic behavioural features of the disorder. [35-37]

CNTNAP2 (Contactin-Associated Protein-Like 2), the candidate gene investigated in this study, is located on **chromosome 7** and has been closely linked to ASD in addition to other neurological disorders such as epilepsy, intellectual disability, and ADHD. [29,30,34] It encodes the protein **Caspr2** (Contactin-Associated Protein-like 2), which functions as a cell adhesion molecule in the nervous system. [30, 38] The gene is highly expressed during early brain development, particularly in cortical regions involved in language and social processing [29,30] Dysfunction in the production or function of Caspr2 is thought to result in autism-related phenotypes [29,32]

Located in intron 2 of the CNTNAP2 gene, the rs7794745 TT genotype has been associated with altered CNTNAP2 expression and impaired Caspr2 function, potentially affecting neuronal signalling and neurodevelopment through its role in neural network formation and synaptic organization. [29,30,39]

In the present study, the A allele was significantly more frequent among healthy controls than among individuals with ASD ($\chi^2 = 7.05$, $p < 0.05$). Conversely, the homozygous TT genotype was associated with a significantly increased risk of ASD compared with the AT and AA genotypes ($\chi^2 = 8.22$, $p < 0.02$). Furthermore, carriers of the T allele exhibited a 1.91-fold higher risk of developing ASD than carriers of the A allele.

The findings of the present study are in agreement with earlier reports that have implicated the CNTNAP2 rs7794745 polymorphism in ASD susceptibility. Nascimento et al. (2015) reported a higher frequency of the homozygous TT genotype among individuals with ASD.[40] Furthermore, Whalley et al. (2011) demonstrated that CNTNAP2 risk variants are associated with altered activation of language-processing regions of the brain. [41]

However, the association between CNTNAP2 rs7794745 and ASD has not been consistently replicated across all populations. Murdoch et al. reported that the observed association was not confirmed in larger datasets, suggesting the variant's contribution to ASD susceptibility may be

limited. Such discrepancies may reflect differences in ethnicity, sample size, study design, diagnostic criteria and gene–environment interactions. [42]

CNTNAP2 has been implicated as an autism susceptibility gene, and its protein product, Caspr2, is essential for potassium channel localization and normal neuronal communication in myelinated axons. [43,38]

Issa et al. (2018) reported a similar significant association between the CNTNAP2 rs7794745 polymorphism and ASD in an Iraqi population, with genotype frequencies differing significantly between ASD patients and controls. [44]

The structural study by Lu et al. revealed the unique architecture of CNTNAP2 and its specific interaction with Contactin-2, highlighting the protein's crucial role in neuronal adhesion, neural network development and cellular communication within the nervous system. [45]

The present findings indicate an increased risk of ASD among individuals carrying the TT and AT genotypes compared with the AA genotype. This association may reflect altered CNTNAP2 expression and Caspr2-related neurodevelopmental pathways, as suggested by previous studies, leading to disruptions in neural network development and neuronal communication [29,30,39]

5. Conclusion

The present study assessed only a single genetic variant, rs7794745, in the CNTNAP2 gene, whereas ASD is a multifactorial disorder influenced by multiple genetic and environmental factors. The relatively small sample size may limit the statistical power and generalizability of the findings. Although the T allele appeared more frequent among ASD cases, the confidence interval crossed unity, indicating only a borderline association. Larger studies are required to confirm whether CNTNAP2 rs7794745 contributes significantly to ASD susceptibility in this population. Furthermore, the association of this polymorphism with disease severity, clinical phenotype, and prognosis was not investigated.

References

[1] World Health Organization. Autism [Internet]. Geneva: World Health Organization; 2025 [cited 2026 Jun 2]. Available from: https://www.who.int/news-room/fact-sheets/detail/autism-spectrum-disorders
[2] Zeidan J, Fombonne E, Scorah J, et al. Global prevalence of autism: A systematic review update. Autism Res. 2022;15(5):778-790. doi:10.1002/aur.2696
[3] Lord C, Brugha TS, Charman T, et al. Autism spectrum disorder. Nat Rev Dis Primers. 2020;6(1):5. Published 2020 Jan 16. doi:10.1038/s41572-019-0138-4
[4] American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. Washington (DC): American Psychiatric Association; 2013.
[5] American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed., text rev. Washington (DC): American Psychiatric Association; 2022. doi:10.1176/appi.books.9780890425596
[6] Sánchez Amate JJ, Luque de la Rosa A. The Effect of Autism Spectrum Disorder on Family Mental Health: Challenges, Emotional Impact, and Coping Strategies. Brain Sci. 2024;14(11):1116. Published 2024 Nov 1. doi:10.3390/brainsci14111116.
[7] Chauhan A, Sahu JK, Jaiswal N, et al. Prevalence of autism spectrum disorder in Indian children: A systematic review and meta-analysis. Neurol India. 2019;67(1):100-104. doi:10.4103/0028-3886.253970.
[8] Uke P, Gaikwad S, Vagha K, et al. Unraveling the Spectrum: A Comprehensive Review of Autism Spectrum Disorder in India. Cureus. 2024;16(6):e62753. Published 2024 Jun 20. doi:10.7759/cureus.62753.
[9] Williams JG, Higgins JP, Brayne CE. Systematic review of prevalence studies of autism spectrum disorders. Arch Dis Child. 2006;91(1):8-15. doi:10.1136/adc.2004.062083.
[10] Chiarotti F, Venerosi A. Epidemiology of Autism Spectrum Disorders: A Review of Worldwide Prevalence Estimates Since 2014. Brain Sci. 2020;10(5):274. Published 2020 May 1. doi:10.3390/brainsci10050274.
[11] Lai MC, Lombardo MV, Baron-Cohen S. Autism. Lancet. 2014;383(9920):896-910. doi:10.1016/S0140-6736(13)61539-1.
[12] Modabbernia A, Velthorst E, Reichenberg A. Environmental risk factors for autism: an evidence-based review of systematic reviews and meta-analyses. Mol Autism. 2017;8:13. doi:10.1186/s13229-017-0121-4.
[13] Gardener H, Spiegelman D, Buka SL. Prenatal risk factors for autism: comprehensive meta-analysis. Br J Psychiatry. 2009;195(1):7-14. doi:10.1192/bjp.bp.108.051672.
[14] Sandin S, Hultman CM, Kolevzon A, et al. Advancing maternal age is associated with increasing risk for autism: a review and meta-analysis. J Am Acad Child Adolesc Psychiatry. 2012;51(5):477-486.e1. doi:10.1016/j.jaac.2012.02.018
[15] Estes ML, McAllister AK. Immune mediators in the brain and peripheral tissues in autism spectrum disorder. Nat Rev Neurosci. 2015;16(8):469-486. doi:10.1038/nrn3978
[16] Ecker C, Bookheimer SY, Murphy DG. Neuroimaging in autism spectrum disorder: brain structure and function across the lifespan. Lancet Neurol. 2015;14(11):1121-1134. doi:10.1016/S1474-4422(15)00050-2
[17] Frye RE, Casanova MF, Fatemi SH et al. Neuropathological mechanisms of seizures in autism spectrum disorder. Front Neurosci. 2016; 10: 192. doi:10.3389/fnins.2016.00192.
[18] Loke YJ, Hannan AJ, Craig JM. The Role of Epigenetic Change in Autism Spectrum Disorders. Front Neurol. 2015; 6: 107. doi:10.3389/fneur.2015.00107

[19] Persico AM, Napolioni V. Autism genetics. Behav Brain Res. 2013;251:95-112. doi:10.1016/j.bbr.2013.06.012
[20] Tick B, Bolton P, Happé F, et al. Genetic contributions to autism spectrum disorder. Psychol Med. 2016;46(16):3421-3432. doi:10.1017/S0033291716002368.
[21] Vorstman JAS, Parr JR, Moreno-De-Luca D, et al. Autism genetics: opportunities and challenges for clinical translation. Nat Rev Genet. 2017;18(6):362-376. doi:10.1038/nrg.2017.4.
[22] Gaugler T, Klei L, Sanders SJ, et al. Most genetic risk for autism resides with common variation. Nat Genet. 2014;46(8):881-885. doi:10.1038/ng.3039
[23] Sanders SJ, He X, Willsey AJ, et al. Insights into autism spectrum disorder genomic architecture and biology from 71 risk loci. Neuron. 2015;87(6):1215-1233. doi:10.1016/j.neuron.2015.09.016.
[24] Betancur C. Etiological heterogeneity in autism spectrum disorders: more than 100 genetic and genomic disorders and still counting. Brain Res. 2011; 1380: 42-77. doi:10.1016/j.brainres.2010.11.078
[25] de la Torre-Ubieta L, Won H, Stein JL, Geschwind DH. Advancing the understanding of autism disease mechanisms through genetics. Nat Med. 2016;22(4):345-361. doi:10.1038/nm.4071.
[26] Abrahams BS, Geschwind DH. Advances in autism genetics: on the threshold of a new neurobiology. Nat Rev Genet. 2008;9(5):341-355. doi:10.1038/nrg2346.
[27] Moss J, Howlin P. Autism spectrum disorders in genetic syndromes: implications for diagnosis, intervention and understanding the wider autism spectrum disorder population. J Intellect Disabil Res. 2009;53(10):852-873. doi:10.1111/j.1365-2788.2009.01197.x.
[28] Alarcón M, Abrahams BS, Stone JL, et al. Linkage, association, and gene-expression analyses identify CNTNAP2 as an autism-susceptibility gene. Am J Hum Genet. 2008;82(1):150–159. doi:10.1016/j.ajhg.2007.09.005.
[29] Peñagarikano O, Geschwind DH. What does CNTNAP2 reveal about autism spectrum disorder? Trends Mol Med. 2012;18(3):156-163. doi:10.1016/j.molmed.2012.01.003.
[30] Rodenas-Cuadrado P, Ho J, Vernes SC. Shining a light on CNTNAP2: complex functions to complex disorders. Eur J Hum Genet. 2014;22(2):171-178. doi:10.1038/ejhg.2013.100.
[31] Vernes SC, Newbury DF, Abrahams BS, et al. A functional genetic link between distinct developmental language disorders. N Engl J Med. 2008;359(22):2337-2345. doi:10.1056/NEJMoa0802828.
[32] Peñagarikano O, Abrahams BS, Herman EI, et al. Absence of CNTNAP2 leads to epilepsy, neuronal migration abnormalities, and core autism-related deficits. Cell. 2011;147(1):235–246. doi:10.1016/j.cell.2011.08.040.
[33] Hodis B, Mughal S, Saadabadi A. Autism spectrum disorder. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 [cited 2026 Jun 2]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK525976/
[34] Qiu S, Qiu Y, Li Y, et al. Genetics of autism spectrum disorder: an umbrella review of systematic reviews and meta-analyses. Transl Psychiatry. 2022;12:249. doi:10.1038/s41398-022-02009-6.
[35] Yoon SH, Choi J, Lee WJ, et al. Genetic and epigenetic etiology underlying Autism Spectrum Disorder. J Clin Med. 2020;9(4):966. doi:10.3390/jcm9040966.
[36] Bölte S, Girdler S, Marschik PB. The contribution of environmental exposure to the etiology of Autism Spectrum Disorder. Cell Mol Life Sci. 2019;76(7):1275–1297. doi:10.1007/s00018-018-2988-4.
[37] Love C, Sominsky L, O'Hely M, et al. Prenatal environmental risk factors for Autism Spectrum Disorder and their potential mechanisms. BMC Med. 2024; 22: 393.doi:10.1186/s12916-024-03580-1.
[38] Poliak S, Gollan L, Martinez R, et al. Caspr2, a new member of the neurexin superfamily, is localized at the juxtaparanodes of myelinated axons and associates with K+ channels. Neuron. 1999;24(4):1037-1047. doi:10.1016/s0896-6273(00)81049-1.
[39] Poot M. Connecting the CNTNAP2 Networks with Neurodevelopmental Disorders. Mol Syndromol. 2015;6(1):7-22. doi:10.1159/000371594.
[40] Nascimento PP, Bossolani-Martins AL, Rosan DBA, et al. Association of CNTNAP2 polymorphisms with autism spectrum disorder and language-related phenotypes. Genet Mol Res. 2016;15(1):15017422.
[41] Whalley HC, O'Connell G, Sussmann JE, et al. Genetic variation in CNTNAP2 alters brain function during linguistic processing in healthy individuals. Am J Med Genet B Neuropsychiatr Genet. 2011;156B(8):941-948. doi:10.1002/ajmg.b.31241.
[42] Murdoch JD, Gupta AR, Sanders SJ, et al. Defining the role of CNTNAP2 in autism susceptibility. PLoS One. 2013;8(10):e77906. doi:10.1371/journal.pone.0077906.
[43] Arking DE, Cutler DJ, Brune CW, et al. A common genetic variant in the neurexin superfamily member CNTNAP2 increases familial risk of autism. Am J Hum Genet. 2008;82(1):160-164. doi:10.1016/j.ajhg.2007.09.015.
[44] Issa AH, Abbas FN, Manshad FA, et al. Polymorphisms of rs7794745 in the CNTNAP2 gene as a biomarker of autistic patients in Thi-Qar Province, Iraq. Int J Adv Sci Eng Technol. 2018;6(2 Suppl 1):49-54.
[45] Lu Z, Reddy MV, Liu J, et al. Molecular Architecture of Contactin-associated Protein-like 2 (CNTNAP2) and Its Interaction with Contactin 2 (CNTN2). J Biol Chem. 2016;291(46):24133-24147. doi:10.1074/jbc.M116.748236.