Early Intervention in Schizophrenia: The Role of Adolescent Brain Development and Genetic-Environmental Risk Interactions

Rice D. Areepitak

ABSTRACT

Schizophrenia is a complex psychiatric disorder that often emerges during adolescence, a critical period of brain development marked by significant structural and functional changes. Changes in the adolescent brain, particularly in regions like the prefrontal cortex and hippocampus, interact with genetic predispositions and environmental stressors to increase the risk of schizophrenia. By examining prior work in this space, this review demonstrates that excessive synaptic pruning, altered dopamine signaling, disrupted connectivity, and epigenetic modifications can interact with risk genes and life experiences, increasing the development of schizophrenia. Current diagnostic gaps in capturing the pre-psychotic phase are from an overreliance on retrospective data and a lack of a holistic analysis. Diagnostics and treatments mostly focus on people who already have psychosis, rather than those in the early stages before psychosis develops, which limits the opportunities for prevention during the critical pre-psychotic phase. Additionally, much of the existing research relies on asking patients about pre-illness behaviors, which may lead to inaccurate or incomplete reporting of early experiences. The main objective of this paper is to present how the complex interplay between adolescent brain development and genetic-environmental interactions contribute to schizophrenia vulnerability and explore how these insights can guide earlier, more personalized intervention and treatment strategies for at-risk youth.

Keywords: Schizophrenia, Adolescent Brain Development, Neurodevelopment, Genetic-Environmental Interactions, Epigenetics, Pre-Psychotic Phase

INTRODUCTION

Schizophrenia (SZ) is a serious mental health condition characterized by how a person thinks, feels, and behaves, involving hallmark symptoms such as hallucinations, delusions, and disorganized thinking. It affects approximately over 23.6 million people worldwide(1), with nearly 75% of the individuals beginning showing onset of this disease before the age of 25(2). Despite this early onset, SZ in adolescents often remains undiagnosed and untreated, contributing to greater clinical severity and worse outcomes compared to the adult-onset disorder(3).
Early onset schizophrenia (EOS) is usually diagnosed using the same criteria as adult-onset schizophrenia (AOS), which may limit identification of SZ in younger populations and delay treatment(3). Since the duration of untreated psychosis significantly influences the disease course, early intervention is critical(4).
Nevertheless, it is difficult to detect symptoms in the initial stage that occurs before the first acute psychotic episode, as they develop months or years before the onset of schizophrenia. This includes altered mood, nonspecific anxiety, or relational mistrust that do not meet DSM-5-TR diagnostic criteria for SZ(5).
To increase the accuracy of EOS identification and inform more effective early-stage treatment

strategies, we need to first understand how the brain develops and reacts to genetic and environmental risk factors of SZ, as disruptions in brain development can contribute to biological changes associated with SZ. The purpose of the paper is to evaluate major risks for SZ, covering epidemiology, gene-environmental interactions, and environmental risk factors. In addition, this paper will propose feasible early treatment plans, consisting of pharmacological interventions, cognitive therapies, and psychosocial & behavioral interventions.

ADOLESCENT BRAIN DEVELOPMENT

In adolescent brain development, the growth of white matter—the part of the brain that's mainly made up of myelinated axons which act as communication pathways connecting different gray-matter regions—is crucial. Changes in white-matter pathways and emotion-related brain development have been examined using diffusion tenor imaging (DTI), which measures white-matter integrity. Imaging studies using DTI suggest that white-matter networks keep strengthening throughout the teenage years(6). Fractional anisotropy—a measurement used in DTI that reflects how directionally water moves along white-matter fibers in the brain—tends to rise slowly, around 1-2% per year in regions like the corpus callosum, mirroring the steady improvements seen in processing speed and executive functioning as adolescents mature(7). Gray matter, which contains neuronal cell bodies, dendrites, and synapses and forms the cortex and other brain regions, undergoes substantial structural changes during adolescence, including synaptic pruning.(8). This process removes unused neural connections and strengthens frequently used pathways(9,10). MRI studies have shown that the balance of gray and white matter strengthening are crucial for normative brain maturation during adolescence (**Figure 1**)(11,12).

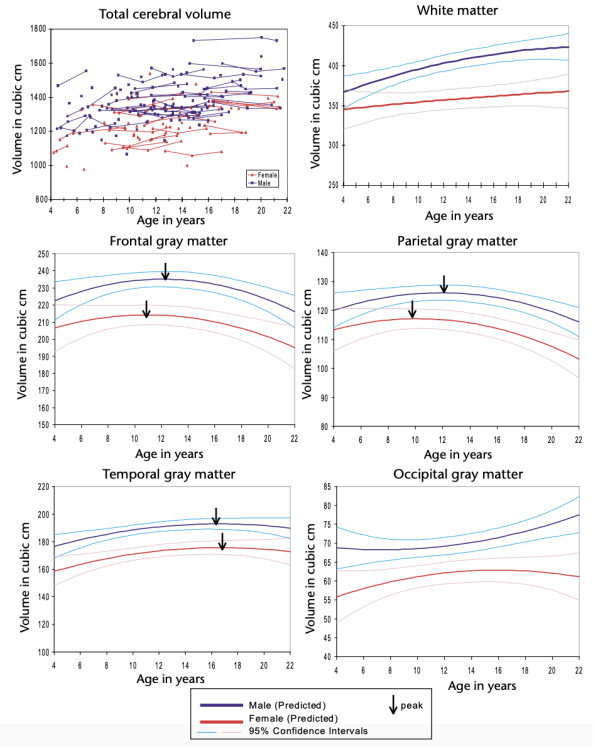

Figure 1. Developmental Trajectories for Total Brain Tissue Volume, Gray Matter Volume and White Matter Volume in Males and Females[13]
Sex-specific group level trajectories (blue = males, red-females) for each volume (bold lines with shaded 95% confidence intervals) are shown with underlying raw data (points = scans, lines link scans from the same person). Gray matter peaks in early adolescence and declines due to synaptic pruning, whereas white matter increases steadily. The figure emphasizes adolescence as a sensitive developmental period during which abnormal pruning may increase vulnerability to schizophrenia.

In SZ, the maturation process deviates: pruning may be excessive or mistimed, and white-matter development becomes disrupted, especially in the prefrontal cortex. Disrupted white-matter integrity weakens communication between brain regions involved in memory, planning, and emotional regulation. An MRI study shows that EOS patients indicate abnormally accelerated cortical pruning and reduction in gray-matter volume in key areas such as the hippocampus, temporal lobe, cerebellum, corpus callosum, and ventricles(13). Longitudinal MRI studies found an ~8% decline in cortical gray matter volume in childhood-onset SZ compared with ~2% in healthy controls, particularly in the frontal and temporal lobes(14) . At the cellular level, abnormal synaptic pruning may involve excessive microglial elimination of synapses, as demonstrated in the schizophrenia patient-derived cellular model shown in **Figure 2**.

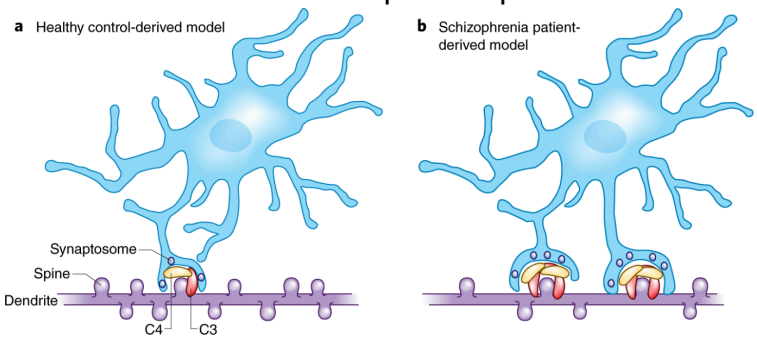

Figure 2. Increased synapse engulfment by iMGs in a schizophrenia patient-derived cellular model(15)**.**
This figure illustrates that in schizophrenia, microglia excessively eliminate synaptic connections compared to healthy brains, driven by increased tagging of synapses for removal. This overpruning leads to a loss of neural connections that are important for normal brain communication. Synaptosomes are tiny pieces of nerve endings that contain the parts of a synapse used to send and receive signals between brain cells. C3 and C4 are immune signaling proteins that help tag cells or debris for removal.

GENETIC RISK FACTORS

The genetic components play a substantial role in SZ, with an estimated heritability of 80%(16). Having a first degree relative—such as a parent, sibling, or child—with schizophrenia is one of the most significant predictors of this disorder, increasing an individual's likelihood of developing it by roughly seven- to ninefold (7.0-9.3) compared to the general population(17). This increased risk is partly due to inherited genetic differences that make a person more likely to develop SZ. Additionally, the inheritance of schizophrenia does not follow a simple single-gene pattern. Instead, a significant portion of its genetic liability is polygenic, arising from the combined effects

of many common genetic variants that individually contribute small amounts of risk but collectively increase vulnerability to the disorder(18). In 2014, The Psychiatric Genomic Consortium studied the DNA of nearly 36,989 people with SZ and 113,075 healthy controls, identifying 128 significant genetic associations across 108 locations in the genome (called loci) that were linked to the disorder ($p \leq 5\times10^{-8}$), 83 of which were newly discovered loci(19). However, these common risk alleles each only cause small increases in risk (often odds ratios near 1.1–1.2), meaning that carrying one variant alone has little impact and that risk builds only when many such variants are combined(20).

Genome-wide association studies (GWAS) have helped identify many of the common variants that contribute to the polygenic risk. In 2009, large genetic collaborations, including the International Schizophrenia Consortium (ISC), SGENE, and the Molecular Genetics of Schizophrenia (MGS) project, identified the first genome-wide significant genetic risk factors for SZ. One major finding was the Major Histocompatibility Complex (MHC) region on chromosome 6 (6p21.3), which contains genes involved in immune system function(21). The association between this region and schizophrenia suggests that immune-related processes may contribute to disease susceptibility, providing a potential link between genetic risk and immune dysfunction. It was also found that the TCF4 gene also helps regulate gene expression during brain development(22). Alterations in TCF4-related pathways may therefore influence neurodevelopmental processes relevant to SZ. Because adolescence is a period when synaptic pruning, calcium signaling, and immune pathways are rapidly reorganizing(23), disruptions in genes like TCF4 and NRGN may interfere with normal neutral maturation, increasing the likelihood that abnormal connectivity forms, a process associated with EOS(24).

Table 1. Key Schizophrenia-Associated Genes and Their Neurodevelopmental Roles
This table summarizes key schizophrenia-associated genes, highlighting their biological functions, roles in neurodevelopment, and proposed mechanisms through which genetic variation may disrupt adolescent brain maturation and contribute to early-onset schizophrenia.

Gene / Genomic Region	Major Histocompatibility Complex (MHC) region (chromosome 6p21.3)	TCF4 (Transcription Factor 4)	NRGN (Neurogranin)
Chromosomal Location	6p21.3	18q21.2	11q24.2
Primary Biological Function	Antigen presentation to T lymphocytes and immune regulation(25)	Acts as a transcription factor that regulates gene expression critical for neurodevelopment, neuronal differentiation, and synaptic function(26).	Modulates intracellular calcium signaling by regulating calmodulin availability, supporting synaptic plasticity, learning, and memory(27).

Neurodevelopmental / Neural Role	Regulates synaptic pruning and neural circuit refinement through complement-mediated signaling between neurons and microglia during brain development(28,29).	Regulates neuronal differentiation, cortical development, and synaptic plasticity by controlling gene expression during brain maturation(30,31).	Supports synaptic plasticity and activity-dependent circuit refinement by regulating calcium–calmodulin signaling in developing and mature neurons(32,33).
Relevance to Schizophrenia (SZ)	Linked to abnormal synaptic pruning and increased disease susceptibility(34,35).	Linked to altered cortical development, synaptic plasticity, and cognitive function(30,36).	linked to altered calcium-dependent synaptic signaling and cognitive dysfunction, particularly affecting learning and memory(32,36).
Proposed Mechanism in EOS/SZ	Promotes excessive microglia-mediated synaptic pruning during adolescence, leading to abnormal cortical thinning and connectivity in EOS(15).	Alters transcriptional regulation of genes involved in cortical development and synaptic plasticity, increasing vulnerability to abnormal neural circuit maturation in EOS(37).	Disrupts calcium-dependent synaptic signaling, impairing activity-dependent synaptic refinement and contributing to cognitive dysfunction in EOS(27,32,33).

Polygenic risk scores and variants within the MHC region have been linked to altered white matter development and reduced brain connectivity, suggesting that genetic risk factors may directly influence neural network formation during adolescence(38).

ENVIRONMENTAL RISK FACTORS

Although schizophrenia is highly heritable, environmental factors account for an estimated 15–40% of disease risk and contribute to variation in susceptibility across populations(39). Epidemiology studies show higher incidence rates in SZ among males, urban populations, and migrants than native-born populations.(40)
Premature rupture of membranes, gestational ages shorter than 37 weeks, and use of resuscitation or incubators were identified as significant risk factors for the subsequent

development of SZ(41). In the United States Collaborative Perinatal Project, individuals with 3+ hypoxia-related obstetric complications were over 5 times more likely to develop SZ compared to those with no hypoxia-related obstetric complications. One of the most replicated findings in the research of SZ is the association between winter and early spring births. Subjects born during this period have a 5–15% increase in risk of SZ(42), while on the other hand there is a decline in SZ risks for autumn births(43). One explanation is increased exposure to nutritional deficiencies or maternal infections during critical stages of pregnancy(44). For example, respiratory infections such as influenza are more prevalent during the winter, potentially increasing maternal immune activation and inflammatory signaling that may affect the developing fetal brain(45).

Dopamine dysregulation is considered a final common pathway in schizophrenia(46). In adolescence or early adulthood, stresses such as substance use or social hardship may push a person with underlying neurodevelopmental vulnerabilities past a critical point, leading to the onset of full psychosis(47). Drugs such as cannabis, cocaine, and amphetamines increase the risk of SZ because of how much it induces dopamine(48).Meta-analyses indicate that 25–36% of individuals with substance-induced or brief psychosis later transition to schizophrenia-spectrum disorders.(49)

Several studies have demonstrated that being born and raised in an urban area increases the risk of psychosis compared to a rural birth and upbringing. Between the years 1999 to 2020, The total number of deaths due to SZ was higher in urban areas (7,253 deaths) than rural areas (2,106 deaths)(50). However, urban morality may also be rising due to factors like limited continuity of care, homelessness, substance use, pollution, and urban medical systems, so this trend is most likely to be caused by multiple factors.

Social disadvantage is associated with increased psychosis risk across development. Researchers found that up to 19 years before the first hospitalization, the odds of being single and unemployed were higher for people with schizophrenia than the controls of healthy patients(51).

During adolescence, social exclusion more commonly manifests as bullying, peer rejection, and social withdrawal. In a longitudinal study of over 1.4 million Swedish residents followed for up to 15 years, greater neighborhood-level personal trust (an indicator of social capital) was associated with reduced incidence of non-affective psychotic disorders (hazard ratio ~0.89; 95% CI, 0.83–0.96) and bipolar disorder without psychosis, independent of socioeconomic and demographic confounders(52). However, the direction of this association remains uncertain. Social adversity may increase the risk of psychosis, but social withdrawal can also appear before schizophrenia develops and may be partly linked to genetic risk(53). This means the relationship may work in both directions.

GENE-ENVIRONMENT INTERACTIONS

Gene-environment interactions (G x E) are crucial and very widespread in SZ. However, identifying these interactions remains challenging because environmental effects often depend on exposure timing, genetic background, and the large number of possible gene–environment combinations, increasing the risk of false-positive findings, and reducing statistical power. Epidemiological studies had shown that individuals who were homozygous for the Met allele at the Catechol-O-Methyltransferase (COMT) Val158Met were more sensitive to stress(54). People who possess the same two alleles for Met have increased dopamine activity in the prefrontal

cortex, making them more sensitive to stress and potentially increasing SZ risk under high-dopamine conditions.

SNAP-25 is a gene involved in neurotransmitter release, and the mice used in the experiment carried a reduced-function (mutant) version of this gene, making them genetically vulnerable. A study on mice showed that mutation in the SNAP-25 gene displays several SZ-associated endophenotypes, including hyperactivity and increased behavioural sensitivity to psychostimulants, a class of drugs that increase alertness(55). SNAP-25 mutants are more susceptible to the negative effects of prenatal stress, particularly in terms of social behavior and sensory processing. In one study, both the SNAP-25 mutation and prenatal stress independently disrupted prepulse inhibition (PPI), a measure of sensory gating(55) found in SZ. Another experiment found that prenatal nicotine exposure in mice with reduced SNAP-25 function led to hyperactivity, impaired social interaction, and weakened long-term synaptic plasticity. Although either factor alone caused only mild abnormalities, combining the mutation with prenatal nicotine exposure produced greater hyperactivity, social deficits, and impaired long-term synaptic plasticity, a process essential for learning and memory.(55)

Interestingly, while many prenatal stressors tend to worsen SZ-related outcomes in certain genetic models, they appear to alleviate some SZ-like behaviors in mice carrying mutations in the RELN gene (reeler mice). RELN (Reelin) is a gene that makes a protein important for brain development, helping neuronal migration and synapse formation(56). Reduced Reelin disrupts these processes, contributing to abnormal brain organization(56). Reduced Reelin has been linked to SZ-like features including impaired social behavior, cognitive deficits, motor abnormalities, and altered GABA signaling(57),(58). However, mild prenatal stress surprisingly improved social interaction and reduced anxiety-like behavior in heterozygous reeler mice, suggesting that the effects of prenatal stress vary depending on genetic background(59). While RELN dysfunction has also been observed in humans with schizophrenia, the stress-induced behavioral improvement reported here has only been demonstrated in mice, not humans(60).

How to Spot Risk Early

Early intervention approaches that focus on recognizing individuals at elevated risk for psychosis may delay or prevent the first episode, reduce illness severity, and improve long-term outcomes. On detecting early syndromes, there are three criteria that indicate being at-risk: showing attenuated psychotic symptoms (APS), which are psychotic-like experiences that occur with reduced frequency or intensity; having brief, limited intermittent psychotic symptoms (BLIPS), episodes of psychosis that appear suddenly but subside on their own within a week; and possessing a genetic predisposition that increases susceptibility to developing a psychotic disorder(61). All three groups require evidence of a decline in functioning lasting at least one month within the past year.

Recent interest in early identification in this field has led to the development of various assessment tools. Examples of these tools include an interview for retrospective assessment of onset of schizophrenia (IRAOS), a structured interview used to look back and figure out when and how symptoms first started in a person's life, and a scale of prodromal symptoms, a rating scale that clinicians score on how severe each early symptom is(62). Although these assessments improve risk stratification compared to population baseline rates, they are not definitive diagnostic tools and are primarily used in specialized clinical settings rather than universal screening. Because early schizophrenia symptoms can overlap with autism spectrum

disorder, mood disorders, trauma-related conditions, and substance-related symptoms, clinicians consider developmental history, symptom course, substance use, and changes in functioning when ruling out alternative diagnoses(63,64).

Individuals with At-Risk Mental State (ARMS) may be identified through school-based screening, primary care, or specialized mental health services, although most cases are still detected only after help-seeking or first-episode psychosis(65). To improve early detection, we need approaches that catch symptoms before they become severe. Teaching mental health awareness in schools and families can help people recognize early warning signs(66). Finally, reducing stigma through education and peer support encourages young people to seek help earlier(67) . However, the limitations are early-detection strategies that face financial, logistical, and ethical challenges. Universal screening remains limited by those challenges, including false positives caused by overlap with normal adolescent development.

Clinical interviews alone may not fully capture the underlying neurobiological changes that precede psychosis. Neuroimaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI) have therefore been explored as complementary tools to detect structural brain alterations during the high-risk stage. The most frequently reported findings included enlargement of the ventricular system and reduced gray matter volume, particularly within the cortical and subcortical regions of the frontal and temporal lobes, as well as the limbic system(68). While structural MRI focuses on the brain's anatomy, functional MRI (fMRI) may offer greater potential for exploring the dysconnectivity hypothesis(69). The dysconnectivity hypothesis is the idea that schizophrenia is not caused by damage to just one brain region, but by poor communication between different brain regions(70). fMRI studies have identified abnormal activity and connectivity in frontal, temporal, and parietal regions before psychosis onset, supporting the dysconnectivity hypothesis (71).

Although MRI findings are promising, measures such as gray matter volume remain susceptible to confounding factors including head motion, limiting their use as standalone predictive biomarkers.(72)

Table 3. Neuroimaging Modalities Used in Schizophrenia Research

These imaging tools demonstrate that schizophrenia is associated with both structural brain changes and disrupted functional connectivity. However, while neuroimaging provides valuable insight into underlying neurobiology, it is not currently sufficient for diagnosis or routine early screening.

Imaging Modality	**What It Measures**	**What It Shows in SZ / High-Risk Individuals**
Structural MRI	Brain anatomy (gray matter, white matter, ventricles)	Reduced gray matter in frontal and temporal lobes; ventricular enlargement(73)
Functional MRI (fMRI)	Brain activity and functional connectivity	Aberrant activation in regions including the left inferior prefrontal cortex and hippocampus(74)
CT scan	Brain structure	Modest enlargement of sulci

		and ventricles(75)
Diffusion Tensor Imaging (DTI)	White-matter microstructure	Reduced integrity in tracts such as the corpus callosum(76)

EARLY TREATMENTS

The goal of early treatments for people with First-Episode Psychosis (FEP) is to reduce symptom severity, delay progression, lower the risk of transition to psychosis, and improve quality of life(77). Current treatment guidelines for individuals at clinical high risk and FEP recommend cognitive behavioral therapy (CBT), family-focused therapy, and other psychological approaches(78,79). In addition to these, needs-based and pharmacological interventions such as antipsychotics and Omega-3 fatty acids are also employed to reduce the likelihood of transition to psychosis(80).

CBT helps individuals recognize and modify distorted thinking patterns, promoting healthier emotional responses and behaviors(81). Studies show that CBT for SZ can reduce both positive and negative symptoms, and the effects often remain even after therapy ends(82). Once patients describe their thoughts and interpretations of their symptoms, CBT helps them develop strategies to manage symptoms, such as reducing distress from auditory hallucinations or challenging paranoid thoughts(83). These methods are preferred as they are well-tolerated and pose no risk of side effects compared to pharmacological interventions(64).

Early treatment for schizophrenia usually begins with antipsychotic medication. For individuals who are newly diagnosed, second-generation (atypical) antipsychotics (SGA) are generally preferred over first-generation options[92]. They balance dopamine antagonism, compounds that block dopamine receptors, with serotonin effects, they tend to have broader symptom coverage (positive and negative) and better tolerability for many patients, making them preferred as first-line. Common examples include aripiprazole, risperidone, and olanzapine(84).

First-generation antipsychotics (typical) (FGA) are used for rapid control of severe psychotic symptoms, violent behavior, or severe agitation. In short, they are more commonly used for acute psychosis(85). Examples include chlorpromazine (thorazine) and haloperiod (Halod)(84).

Family-focused therapy (FFT) combines psychoeducation with communication and problem-solving training to reduce relapse, lower hospitalization rates, and improve quality of life for patients and their families(86),(87). A meta-analysis found that FFT reduces relapse risk by 50–60% reduction compared with usual care(88). Family members would finally experience the reduced burden of care, improved relationships, and better mental and physical health outcomes overall.

FUTURE DIRECTIONS AND CONCLUSION

Future directions in schizophrenia care should move toward precision psychiatry, which integrates biological, genetic, environmental, and digital biomarkers to predict risk and personalize early interventions(89). By moving beyond symptom-based diagnosis, this approach seeks to identify high-risk individuals before full psychosis onset and deliver targeted, individualized treatment strategies. For precision psychiatry to work clinically, multiple data types

must be combined, including genetic profiles, multi-omics data, brain imaging, lab biomarkers, and electronic/digital health records(90). This big data alone must be high quality and interpreted through the lens of brain biology to make it clinically meaningful. However, even with these technologies, many prediction models can act like a “black box”, giving answers without meaningful reasoning. This is difficult in psychiatry, where decisions still depend heavily on conversations, observations, and clinical experience(91). However, even if predictive models are found to work, the “black box” problem remains important because clinicians must understand how predictions are made before making high-stakes decisions. Poor interpretability can lead to difficulty in detecting bias and determining whether a prediction is realistically possible. The goal of precision psychiatry is to merge data-drive tools with human judgement and improve care without replacing the patient-clinician connection.

One of the key areas within precision psychiatry is pharmacogenomics, the science studying the influence of genes on an individual‘s response to medications(92). While early single-gene approaches, such as CYP450 testing, showed limited predictive value (93), newer multigene tests incorporating machine-learning approaches have demonstrated improved ability to predict treatment response(94),(95). Similar strategies could eventually help antipsychotic selection and reduce trial and error prescribing SZ. Future advances will likely come from integrating genetic information with neuroimaging, molecular biomarkers, and clinical data to develop more accurate and individualized approaches to prevention and treatment(96),(97).

This review examined how adolescent brain development interacts with genetic and environmental risk factors to shape vulnerability to schizophrenia, highlighting early intervention as a critical window for prevention and treatment. Research shows that adolescence is a period of increased brain adaptability, during which changes in brain connections, dopamine activity, and stress responses can combine with inherited risk and environmental factors to increase the chances of developing psychosis. Understanding these processes is not just important for science, but also because it demonstrates that SZ does not happen suddenly, but instead develops gradually, providing opportunities for early recognition and support.

AI DISCLOSURE STATEMENT

The author used ChatGPT to assist with grammar, clarity, and sentence structure. All research, analysis, ideas, and conclusions presented in this work are the author’s own.

ACKNOWLEDGEMENTS

The author sincerely thanks her mentor, Dr. Laura Price, for her thoughtful insight, patience, and unwavering support in helping transform her passion into this work. The author would also like to thank her publication specialist, Dr. Sophie K., for her invaluable guidance throughout the publication process. A special thank you goes to her AP Psychology teacher, Dr. Jenna Rosen, for recognizing and encouraging her passion for psychology and schizophrenia, providing meaningful research opportunities, and supporting her aspiration to become a psychiatrist. Above all, the author expresses her deepest gratitude to her mother, Hongyan Duan, for supporting her through every step of this journey and encouraging her through the moments when she felt like giving up. This work would not have been possible without her.

References

1. Feng Z, Shan X, Fan B, Yang L, Gong F. Global burden of schizophrenia in 204 countries and regions from 1990 to 2021 and machine learning-based projections to 2036: an analysis of the 2021 global burden of disease study. Front Psychiatry. 2026 Jan 27;16:1684168. doi:10.3389/fpsyt.2025.1684168

2. Kahn RS, Sommer IE, Murray RM, Meyer-Lindenberg A, Weinberger DR, Cannon TD, et al. Schizophrenia. Nat Rev Dis Primer. 2015 Nov 12;1(1):15067. doi:10.1038/nrdp.2015.67

3. Childhood-Onset Schizophrenia and Early-onset Schizophrenia Spectrum Disorders: An Update. Child Adolesc Psychiatr Clin N Am. 2020 Jan 1;29(1):71–90. doi:10.1016/j.chc.2019.08.017

4. Marshall M, Lewis S, Lockwood A, Drake R, Jones P, Croudace T. Association Between Duration of Untreated Psychosis and Outcome in Cohorts of First-Episode Patients. ARCH GEN PSYCHIATRY. 2005;62.

5. Substance Abuse and Mental Health Services Administration. Impact of the DSM-IV to DSM-5 Changes on the National Survey on Drug Use and Health [Internet]. Rockville (MD): Substance Abuse and Mental Health Services Administration (US); 2016 [cited 2026 Mar 13]. (CBHSQ Methodology Report). Available from: http://www.ncbi.nlm.nih.gov/books/NBK519697/ PubMed PMID: 30199183.

6. Asato MR, Terwilliger R, Woo J, Luna B. White Matter Development in Adolescence: A DTI Study. Cereb Cortex. 2010 Sep 1;20(9):2122–31. doi:10.1093/cercor/bhp282

7. Krogsrud SK, Fjell AM, Tamnes CK, Grydeland H, Mork L, Due-Tønnessen P, et al. Changes in white matter microstructure in the developing brain—A longitudinal diffusion tensor imaging study of children from 4 to 11 years of age. NeuroImage. 2016 Jan;124:473–86. doi:10.1016/j.neuroimage.2015.09.017

8. Gogtay N, Giedd JN, Lusk L, Hayashi KM, Greenstein D, Vaituzis AC, et al. Dynamic mapping of human cortical development during childhood through early adulthood. Proc Natl Acad Sci U S A. 2004 May 25;101(21):8174–9. doi:10.1073/pnas.0402680101 PubMed PMID: 15148381; PubMed Central PMCID: PMC419576.

9. Gogtay N, Giedd JN, Lusk L, Hayashi KM, Greenstein D, Vaituzis AC, et al. Dynamic mapping of human cortical development during childhood through early adulthood. Proc Natl Acad Sci U S A. 2004 May 25;101(21):8174–9. doi:10.1073/pnas.0402680101 PubMed PMID: 15148381; PubMed Central PMCID: PMC419576.

10. Selemon LD. A role for synaptic plasticity in the adolescent development of executive function. Transl Psychiatry. 2013 Mar 5;3(3):e238. doi:10.1038/tp.2013.7 PubMed PMID: 23462989; PubMed Central PMCID: PMC3625918.

11. Giedd JN, Blumenthal J, Jeffries NO, Castellanos FX, Liu H, Zijdenbos A, et al. Brain development during childhood and adolescence: a longitudinal MRI study. Nat Neurosci. 1999 Oct;2(10):861–3. doi:10.1038/13158

12. Paus T. Mapping brain maturation and cognitive development during adolescence. Trends Cogn Sci. 2005 Feb;9(2):60–8. doi:10.1016/j.tics.2004.12.008 PubMed PMID: 15668098.

13. Levman J, Kabaria P, Nangaku M, Takahashi E. Morphological Abnormalities in Early-Onset Schizophrenia Revealed by Structural Magnetic Resonance Imaging. Biology. 2023 Feb 23;12(3):353. doi:10.3390/biology12030353

14. Gogtay N, Giedd JN, Lusk L, Hayashi KM, Greenstein D, Vaituzis AC, et al. Dynamic mapping of human cortical development during childhood through early adulthood. Proc Natl Acad Sci U S A. 2004 May 25;101(21):8174–9. doi:10.1073/pnas.0402680101 PubMed PMID: 15148381; PubMed Central PMCID: PMC419576.

15. Wang M, Zhang L, Gage FH. Microglia, complement and schizophrenia. Nat Neurosci. 2019 Mar 1;22(3):333–4. doi:10.1038/s41593-019-0343-1

16. Merikangas AK, Shelly M, Knighton A, Kotler N, Tanenbaum N, Almasy L. What genes are differentially expressed in individuals with schizophrenia? A systematic review. Mol Psychiatry. 2022 Mar;27(3):1373–83. doi:10.1038/s41380-021-01420-7

17. Chou IJ, Kuo CF, Huang YS, Grainge MJ, Valdes AM, See LC, et al. Familial Aggregation and Heritability of Schizophrenia and Co-aggregation of Psychiatric Illnesses in Affected Families. Schizophr Bull. 2017 Sep;43(5):1070–8. doi:10.1093/schbul/sbw159

18. Salleh MR. THE GENETICS OF SCHIZOPHRENIA.

19. Schizophrenia Working Group of the Psychiatric Genomics Consortium. Biological insights from 108 schizophrenia-associated genetic loci. Nature. 2014 Jul;511(7510):421–7. doi:10.1038/nature13595

20. Owen MJ, Legge SE, Rees E, Walters JTR, O'Donovan MC. Genomic findings in schizophrenia and their implications. Mol Psychiatry. 2023 Sep;28(9):3638–47. doi:10.1038/s41380-023-02293-8

21. Shi J, Levinson DF, Duan J, Sanders AR, Zheng Y, Pe'er I, et al. Common variants on chromosome 6p22.1 are associated with schizophrenia. Nature. 2009 Aug;460(7256):753–7. doi:10.1038/nature08192

22. Chen T, Wu Q, Zhang Y, Lu T, Yue W, Zhang D. Tcf4 Controls Neuronal Migration of the Cerebral Cortex through Regulation of Bmp7. Front Mol Neurosci. 2016 Oct 3;9. doi:10.3389/fnmol.2016.00094

23. Brenhouse HC, Schwarz JM. Immunoadolescence: Neuroimmune development and adolescent behavior. Neurosci Biobehav Rev. 2016 Nov;70:288–99. doi:10.1016/j.neubiorev.2016.05.035

24. Li H, Zhu Y, Morozov YM, Chen X, Page SC, Rannals MD, et al. Disruption of TCF4 regulatory networks leads to abnormal cortical development and mental disabilities. Mol Psychiatry. 2019 Aug;24(8):1235–46. doi:10.1038/s41380-019-0353-0

25. Bookshelf_NBK459447.

26. Savchenko RR, Skryabin NA. Transcription factor TCF4: structure, function, and associated diseases. Vavilov J Genet Breed. 2024 Nov 22;28(7):770–9. doi:10.18699/vjgb-24-85

27. Huang KP, Huang FL, Jäger T, Li J, Reymann KG, Balschun D. Neurogranin/RC3 Enhances Long-Term Potentiation and Learning by Promoting Calcium-Mediated Signaling. J Neurosci. 2004 Nov 24;24(47):10660–9. doi:10.1523/JNEUROSCI.2213-04.2004

28. Gomez-Arboledas A, Acharya MM, Tenner AJ. The Role of Complement in Synaptic Pruning and Neurodegeneration. ImmunoTargets Ther. 2021 Sep;Volume 10:373–86. doi:10.2147/ITT.S305420

29. Sekar A, Bialas AR, De Rivera H, Davis A, Hammond TR, Kamitaki N, et al. Schizophrenia risk from complex variation of complement component 4. Nature. 2016 Feb 11;530(7589):177–83. doi:10.1038/nature16549

30. Forrest MP, Hill MJ, Kavanagh DH, Tansey KE, Waite AJ, Blake DJ. The Psychiatric Risk Gene Transcription Factor 4 (TCF4) Regulates Neurodevelopmental Pathways Associated With Schizophrenia, Autism, and Intellectual Disability. Schizophr Bull. 2018 Aug 20;44(5):1100–10. doi:10.1093/schbul/sbx164

31. Hill MJ, Killick R, Navarrete K, Maruszak A, McLaughlin GM, Williams BP, et al. Knockdown of the schizophrenia susceptibility gene TCF4 alters gene expression and proliferation of progenitor cells from the developing human neocortex. J Psychiatry Neurosci. 2017 May 1;42(3):181–8. doi:10.1503/jpn.160073

32. Pak JH, Huang FL, Li J, Balschun D, Reymann KG, Chiang C, et al. Involvement of neurogranin in the modulation of calciumycalmodulin-dependent protein kinase II, synaptic plasticity, and spatial learning: A study with knockout mice.

33. Zhong L, Cherry T, Bies CE, Florence MA, Gerges NZ. Neurogranin enhances synaptic strength through its interaction with calmodulin. EMBO J. 2009 Oct 7;28(19):3027–39. doi:10.1038/emboj.2009.236

34. Sinkus ML, Adams CE, Logel J, Freedman R, Leonard S. Expression of immune genes on chromosome 6p21.3–22.1 in schizophrenia. Brain Behav Immun. 2013 Aug;32:51–62. doi:10.1016/j.bbi.2013.01.087

35. Mokhtari R, Lachman HM. The Major Histocompatibility Complex (MHC) in Schizophrenia: A Review. J Clin Cell Immunol. 2016;07(06). doi:10.4172/2155-9899.1000479

36. Steinberg S, de Jong S, Andreassen OA, Werge T, Børglum AD, Mors O, et al. Common variants at VRK2 and TCF4 conferring risk of schizophrenia. Hum Mol Genet. 2011 Oct 15;20(20):4076–81. doi:10.1093/hmg/ddr325

37. Li H, Zhu Y, Morozov YM, Chen X, Page SC, Rannals MD, et al. Disruption of TCF4 regulatory networks leads to abnormal cortical development and mental disabilities. Mol Psychiatry. 2019 Aug;24(8):1235–46. doi:10.1038/s41380-019-0353-0

38. Caseras X, Simmonds E, Pardiñas AF, Anney R, Legge SE, Walters JTR, et al. Common risk alleles for schizophrenia within the major histocompatibility complex predict white matter microstructure. Transl Psychiatry. 2024 Apr 22;14(1):194. doi:10.1038/s41398-024-02910-2

39. Robinson N, Bergen SE. Environmental Risk Factors for Schizophrenia and Bipolar Disorder and Their Relationship to Genetic Risk: Current Knowledge and Future Directions. Front Genet. 2021 Jun 28;12:686666. doi:10.3389/fgene.2021.686666

40. McGrath J, Saha S, Welham J, El Saadi O, MacCauley C, Chant D. A systematic review of the incidence of schizophrenia: the distribution of rates and the influence of sex, urbanicity, migrant status and methodology. BMC Med. 2004 Apr 28;2(1):13. doi:10.1186/1741-7015-2-13

41. Review: schizophrenia is associated with premature rupture of membranes, gestational age <37 weeks, and use of an incubator or resuscitation. Evid Based Ment Health. 2000 Feb;3(1):30–30. doi:10.1136/ebmh.3.1.30

42. Davies G, Welham J, Chant D, Torrey EF, McGrath J. A Systematic Review and Meta-analysis of Northern Hemisphere Season of Birth Studies in Schizophrenia. Schizophr Bull. 2003 Jan 1;29(3):587–93. doi:10.1093/oxfordjournals.schbul.a007030

43. Krueger RF. The Structure of Common Mental Disorders. Arch Gen Psychiatry. 1999 Oct 1;56(10):921. doi:10.1001/archpsyc.56.10.921

44. Aylward EH, Harris GJ, Hoehn-Saric R, Barta PE, Machlin SR, Pearlson GD. Normal Caudate Nucleus in Obsessive-compulsive Disorder Assessed by Quantitative Neuroimaging. Arch Gen Psychiatry. 1996 Jul 1;53(7):577–84. doi:10.1001/archpsyc.1996.01830070021006

45. Egorova M, Egorov V, Zabrodskaya Y. Maternal Influenza and Offspring Neurodevelopment. Curr Issues Mol Biol. 2024 Jan 2;46(1):355–66. doi:10.3390/cimb46010023

46. Howes OD, Kapur S. The Dopamine Hypothesis of Schizophrenia: Version III—The Final Common Pathway. Schizophr Bull. 2009 May 1;35(3):549–62. doi:10.1093/schbul/sbp006

47. O'Brien KJ, Huque ZM, Pike MR, Smith EC, Davies NL, Ellman LM. Synergistic pathways to psychosis: understanding developmental risk and resilience factors. Neuropsychopharmacology. 2026 Jan 1;51(1):273–92. doi:10.1038/s41386-025-02261-6

48. Kohno M, Dennis LE, McCready H, Hoffman WF. Dopamine dysfunction in stimulant use disorders: mechanistic comparisons and implications for treatment. Mol Psychiatry. 2022 Jan;27(1):220–9. doi:10.1038/s41380-021-01180-4

49. Abouzed M, Gabr A, Elsheikh M, Elag KA, Zeid MY, Barakat M, et al. Transition rates to schizophrenia and early intervention effectiveness in substance-induced and brief psychotic disorders: a randomized controlled trial. Sci Rep. 2025 Nov 18;15(1):40386. doi:10.1038/s41598-025-24785-z

50. Bote SK, Hamid AAAM, Chunarova A. Assessment of Urban-Rural Differences in Schizophrenia Mortality in the United States Using the CDC-WONDER Database: A Retrospective Study. Cureus. 2025 Aug 2. doi:10.7759/cureus.89257

51. Agerbo E, Byrne M, Eaton WW, Mortensen PB. Marital and Labor Market Status in the Long Run in Schizophrenia. Arch Gen Psychiatry. 2004 Jan 1;61(1):28. doi:10.1001/archpsyc.61.1.28

52. Song-Chase A, Dykxhoorn J, Hollander AC, Magnusson C, Dalman C, Kirkbride JB. Longitudinal association between neighborhood-level social capital and incidence of major psychiatric disorders in a cohort of 1.4 million people in Sweden. Nat Ment Health. 2025 Oct 20;3(11):1425–37. doi:10.1038/s44220-025-00518-z

53. Cornblatt B. The schizophrenia prodrome: promise for prevention. Dialogues Clin Neurosci. 2001 Jun 30;3(2):93–8. doi:10.31887/DCNS.2001.3.2/bcornblatt

54. Serrano JM, Banks JB, Fagan TJ, Tartar JL. The influence of Val158Met COMT on physiological stress responsivity. Stress. 2019 Mar 4;22(2):276–9. doi:10.1080/10253890.2018.1553949

55. Oliver PL, Davies KE. Interaction between environmental and genetic factors modulates schizophrenic endophenotypes in the Snap-25 mouse mutant blind-drunk. Hum Mol Genet. 2009 Dec 1;18(23):4576–89. doi:10.1093/hmg/ddp425

56. Impagnatiello F, Guidotti AR, Pesold C, Dwivedi Y, Caruncho H, Pisu MG, et al. A decrease of reelin expression as a putative vulnerability factor in schizophrenia. Proc Natl Acad Sci. 1998 Dec 22;95(26):15718–23. doi:10.1073/pnas.95.26.15718

57. Guidotti A, Auta J, Davis JM, Gerevini VD, Dwivedi Y, Grayson DR, et al. Decrease in Reelin and Glutamic Acid Decarboxylase67 (GAD67) Expression in Schizophrenia and Bipolar Disorder: A Postmortem Brain Study. Arch Gen Psychiatry. 2000 Nov 1;57(11):1061. doi:10.1001/archpsyc.57.11.1061

58. Barr AM, Fish KN, Markou A. The reelin receptors VLDLR and ApoER2 regulate sensorimotor gating in mice. Neuropharmacology. 2007 Mar;52(4):1114–23. doi:10.1016/j.neuropharm.2006.11.011

59. Boersma GJ, Tamashiro KL. Individual differences in the effects of prenatal stress exposure in rodents. Neurobiol Stress. 2015 Jan;1:100–8. doi:10.1016/j.ynstr.2014.10.006

60. Impagnatiello F, Guidotti AR, Pesold C, Dwivedi Y, Caruncho H, Pisu MG, et al. A decrease of reelin expression as a putative vulnerability factor in schizophrenia. Proc Natl Acad Sci. 1998 Dec 22;95(26):15718–23. doi:10.1073/pnas.95.26.15718

61. Radez J, Waite F, Izon E, Johns L. Identifying individuals at risk of developing psychosis: A systematic review of the literature in primary care services. Early Interv Psychiatry. 2023 May;17(5):429–46. doi:10.1111/eip.13365

62. Häfner H, Riecher-Rössler A, Hambrecht M, Maurer K, Meissner S, Schmidtke A, et al. IRAOS: an instrument for the assessment of onset and early course of schizophrenia. Schizophr Res. 1992 Mar 1;6(3):209–23. doi:10.1016/0920-9964(92)90004-O

63. Recommendations | Psychosis and schizophrenia in children and young people: recognition and management | Guidance | NICE [Internet]. NICE; 2013 [cited 2026 Sep 12]. Available from: https://www.nice.org.uk/guidance/CG155/chapter/recommendations

64. Psychosis and schizophrenia in adults: treatment and management. London: NICE; 2014.

65. Fusar-Poli P, McGorry PD, Kane JM. Improving outcomes of first-episode psychosis: an overview. World Psychiatry. 2017 Oct;16(3):251–65. doi:10.1002/wps.20446

66. Kelly ME, Duff H, Kelly S, McHugh Power JE, Brennan S, Lawlor BA, et al. The impact of social activities, social networks, social support and social relationships on the cognitive functioning of healthy older adults: a systematic review. Syst Rev. 2017 Dec;6(1):259. doi:10.1186/s13643-017-0632-2

67. Gulliver A, Griffiths KM, Christensen H. Perceived barriers and facilitators to mental health help-seeking in young people: a systematic review. BMC Psychiatry. 2010 Dec;10(1):113. doi:10.1186/1471-244X-10-113

68. Keshavan MS, Collin G, Guimond S, Kelly S, Prasad KM, Lizano P. Neuroimaging in Schizophrenia. Neuroimaging Clin N Am. 2020 Feb;30(1):73–83. doi:10.1016/j.nic.2019.09.007

69. Koc NA, Rakowski M, Dębska A, Szmyd B, Zawadzka A, Zaczkowski K, et al. Theoretical, Technical, and Analytical Foundations of Task-Based and Resting-State Functional Magnetic Resonance Imaging (fMRI)—A Narrative Review. Biomedicines. 2026 Jan 31;14(2):333. doi:10.3390/biomedicines14020333

70. Zhou Y, Fan L, Qiu C, Jiang T. Prefrontal cortex and the dysconnectivity hypothesis of schizophrenia. Neurosci Bull. 2015 Apr;31(2):207–19. doi:10.1007/s12264-014-1502-8

71. Whalley HC, Simonotto E, Flett S, Marshall I, Ebmeier KP, Owens DGC, et al. fMRI correlates of state and trait effects in subjects at genetically enhanced risk of schizophrenia. Brain. 2004 Mar 1;127(3):478–90. doi:10.1093/brain/awh070

72. Reuter M, Tisdall MD, Qureshi A, Buckner RL, Van Der Kouwe AJW, Fischl B. Head motion during MRI acquisition reduces gray matter volume and thickness estimates. NeuroImage. 2015 Feb;107:107–15. doi:10.1016/j.neuroimage.2014.12.006

73. Haijma SV, Van Haren N, Cahn W, Koolschijn PCMP, Hulshoff Pol HE, Kahn RS. Brain Volumes in Schizophrenia: A Meta-Analysis in Over 18 000 Subjects. Schizophr Bull. 2013 Sep;39(5):1129–38. doi:10.1093/schbul/sbs118

74. Achim AM, Lepage M. Episodic memory-related activation in schizophrenia: meta-analysis. Br J Psychiatry. 2005 Dec;187(6):500–9. doi:10.1192/bjp.187.6.500

75. Malla AK, Bs M, Mittal C, Lee M, Scholten DJ, Assis L, et al. Computed tomography of the brain morphology of patients with first-episode schizophrenic psychosis.

76. Kubicki M, Mccarley R, Westin C, Park H, Maier S, Kikinis R, et al. A review of diffusion tensor imaging studies in schizophrenia. J Psychiatr Res. 2007 Jan;41(1–2):15–30. doi:10.1016/j.jpsychires.2005.05.005

77. Mcgorry PD, Killackey E, Yung A. Early intervention in psychosis: concepts, evidence and future directions. World Psychiatry. 2008 Oct;7(3):148–56. doi:10.1002/j.2051-5545.2008.tb00182.x

78. Morrison AP, French P, Walford L, Lewis SW, Kilcommons A, Green J, et al. Cognitive therapy for the prevention of psychosis in people at ultra-high risk: Randomised controlled trial. Br J Psychiatry. 2004 Oct;185(4):291–7. doi:10.1192/bjp.185.4.291

79. Miklowitz DJ, O'Brien MP, Schlosser DA, Addington J, Candan KA, Marshall C, et al. Family-Focused Treatment for Adolescents and Young Adults at High Risk for Psychosis: Results of a Randomized Trial. J Am Acad Child Adolesc Psychiatry. 2014 Aug;53(8):848–58. doi:10.1016/j.jaac.2014.04.020

80. Kane JM, Robinson DG, Schooler NR, Mueser KT, Penn DL, Rosenheck RA, et al. Comprehensive Versus Usual Community Care for First-Episode Psychosis: 2-Year Outcomes From the NIMH RAISE Early Treatment Program. Am J Psychiatry. 2016 Apr 1;173(4):362–72. doi:10.1176/appi.ajp.2015.15050632

81. Simos G, editor. Cognitive behaviour therapy. 2: Cognitive behaviour therapy: a guide for the practising clinician / ed. by Gregoris Simos. 1. publ. In. London: Routledge; 2009.

82. Wykes T, Steel C, Everitt B, Tarrier N. Cognitive Behavior Therapy for Schizophrenia: Effect Sizes, Clinical Models, and Methodological Rigor. Schizophr Bull. 2007 May 4;34(3):523–37. doi:10.1093/schbul/sbm114

83. Turkington D, Dudley R, Warman DM, Beck AT. Cognitive-Behavioral Therapy for Schizophrenia: A Review. P U B C O N S.

84. Keepers GA, Fochtmann LJ, Anzia JM, Benjamin S, Lyness JM, Mojtabai R, et al. The American Psychiatric Association Practice Guideline for the Treatment of Patients With

Schizophrenia. Am J Psychiatry. 2020 Sep 1;177(9):868–72. doi:10.1176/appi.ajp.2020.177901

85. Lieberman JA, Rosenheck RA, Davis SM, Hsiao JK. Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia. N Engl J Med. 2005.

86. Miklowitz DJ, Chung B. Family-Focused Therapy for Bipolar Disorder: Reflections on 30 Years of Research. Fam Process. 2016 Sep;55(3):483–99. doi:10.1111/famp.12237

87. Miklowitz DJ, George EL, Axelson DA, Kim EY, Birmaher B, Schneck C, et al. Family-focused treatment for adolescents with bipolar disorder. J Affect Disord. 2004 Oct;82:S113–28. doi:10.1016/j.jad.2004.05.020

88. Horigian VE, Anderson AR, Szapocznik J. Family-Based Treatments for Adolescent Substance Use. Child Adolesc Psychiatr Clin N Am. 2016 Oct;25(4):603–28. doi:10.1016/j.chc.2016.06.001

89. Comai S, Manchia M, Bosia M, Miola A, Poletti S, Benedetti F, et al. Moving toward precision and personalized treatment strategies in psychiatry. Int J Neuropsychopharmacol. 2025 May 9;28(5):pyaf025. doi:10.1093/ijnp/pyaf025

90. Williams LM. Precision psychiatry: a neural circuit taxonomy for depression and anxiety. Lancet Psychiatry. 2016 May;3(5):472–80. doi:10.1016/S2215-0366(15)00579-9

91. Fernandes BS, Williams LM, Steiner J, Leboyer M, Carvalho AF, Berk M. The new field of 'precision psychiatry.' BMC Med. 2017 Dec;15(1):80. doi:10.1186/s12916-017-0849-x

92. Bousman CA, Bengesser SA, Aitchison KJ, Amare AT, Aschauer H, Baune BT, et al. Review and Consensus on Pharmacogenomic Testing in Psychiatry. Pharmacopsychiatry. 2021 Jan;54(01):5–17. doi:10.1055/a-1288-1061

93. Hicks J, Bishop J, Sangkuhl K, Müller D, Ji Y, Leckband S, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for *CYP2D6* and *CYP2C19* Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors. Clin Pharmacol Ther. 2015 Aug;98(2):127–34. doi:10.1002/cpt.147

94. Thase ME, Parikh SV, Rothschild AJ, Dunlop BW, DeBattista C, Conway CR, et al. Impact of Pharmacogenomics on Clinical Outcomes for Patients Taking Medications With Gene-Drug Interactions in a Randomized Controlled Trial. J Clin Psychiatry. 2019 Oct 31;80(6). doi:10.4088/JCP.19m12910

95. Hicks J, Bishop J, Sangkuhl K, Müller D, Ji Y, Leckband S, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for *CYP2D6* and *CYP2C19* Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors. Clin Pharmacol Ther. 2015 Aug;98(2):127–34. doi:10.1002/cpt.147

96. Le-Niculescu H, Roseberry K, Gill SS, Levey DF, Phalen PL, Mullen J, et al. Precision medicine for mood disorders: objective assessment, risk prediction, pharmacogenomics, and

repurposed drugs. Mol Psychiatry. 2021 Jul;26(7):2776–804. doi:10.1038/s41380-021-01061-w

97. Češková E, Šilhán P. From Personalized Medicine to Precision Psychiatry? Neuropsychiatr Dis Treat. 2021 Dec;Volume 17:3663–8. doi:10.2147/NDT.S337814