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The Dual Role of Microglial Synaptic Pruning in Autism Spectrum Disorder and Schizophrenia: A Literature Review

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Abstract

This review investigates the dual roles of microglial synaptic pruning dysfunction in Autism Spectrum Disorder (ASD) and schizophrenia. While ASD is characterized by insufficient synaptic pruning leading to synaptic overabundance, schizophrenia exhibits excessive pruning and synaptic loss. This review aims to synthesize current knowledge on these distinct roles and clarify their associations with divergent behavioral phenotypes, ultimately contributing to identifying new research questions and potential therapeutic targets. Peer-reviewed literature from 2000-2025 was identified and analyzed using open-access databases such as PubMed, Scopus, and Google Scholar. Articles were selected based on relevance to microglial synaptic pruning in mammalian models of ASD and schizophrenia, focusing on synaptic markers, electrophysiological recordings, and complement cascade expression. Exclusion criteria included non-mammalian models, primary focus on other disorders, opinion articles and editorials, and use of purely *in vitro* evidence. In ASD, findings consistently indicate increased synaptic density and immature dendritic spines, particularly in the prefrontal cortex (PFC), temporal lobe, and cingulate cortex, linked to sensory hypersensitivity and social deficits. Electrophysiological studies show network hyperexcitability and excitation/inhibition imbalance. The classical complement cascade's role is less clear, with evidence pointing to dysfunction in the CX3CR1-CX3CL1 signaling axis impairing pruning instead. Conversely, schizophrenia exhibits reduced synaptic density in regions like the PFC and hippocampus. Electrophysiological recordings reveal decreased excitatory postsynaptic currents and widespread hypoconnectivity. Strong evidence implicates excessive classical complement cascade activation, especially C4 gene variants, in driving synaptic loss in schizophrenia. These findings highlight a striking neurobiological opposition: ASD appears to involve too little pruning leading to overconnectivity, while schizophrenia involves too much, resulting in synaptic loss. These structural and functional disparities underlie distinct behavioral phenotypes. Crucially, this suggests that a "one-size-fits-all" approach to neurodevelopmental disorder treatment is likely ineffective. Therapies must be tailored to address the specific pruning imbalance present in each condition. Understanding these precise mechanisms is crucial for developing targeted therapeutic strategies and diagnostic biomarkers. Future research should investigate regional specificity of pruning dysfunction, explore the heterogeneity of microglial phenotypes, and develop human-relevant translational models to uncover novel treatments.

Keywords: autism spectrum disorder; schizophrenia; microglia; synaptic plasticity; neurodevelopment

Introduction

Neurodevelopmental disorders (NDDs) represent a group of conditions that profoundly influence brain function and neurological development, leading to challenges in social, cognitive, and emotional domains. While NDDs typically manifest in childhood or adolescence, their impact can extend throughout an individual's life or even go undiagnosed until adulthood [1].

Among the most extensively studied NDDs are Autism Spectrum Disorder (ASD) and schizophrenia. ASD is characterized by deficits in social communication and interaction, coupled with restricted, repetitive patterns of behaviors [2]. The disorder has an estimated prevalence rate of 0.76% and is diagnosed using various screening tools such as the Survey of Wellbeing of Young Children. Common behavioral phenotypes include impaired eye contact, difficulties understanding social cues, heightened sensitivity to sensory input, and repetitive motor behaviors. These symptoms emerge in early childhood and exhibit variability in their presentation and severity [3–7]. In contrast, schizophrenia is a psychiatric disorder characterized by delusions, hallucinations, disorganized speech, alterations in drive and volition, and impaired cognition [8]. The disorder's prevalence rate was estimated as 0.75% in 2018 and can be diagnosed based on the *Diagnostic and Statistical Manual for Mental Disorders*, which assesses and scores the severity of symptoms and the duration of these symptoms to determine whether the

individual meets schizophrenia criteria [9, 10]. Individuals with schizophrenia often experience a profound sense of being "disconnected" from reality. Behavioral phenotypes in schizophrenia include social withdrawal, flattened affect, reduced motivation, disorganized behavior, and disturbances in episodic and working memory. These symptoms emerge in late adolescence [11, 12]. These neurodevelopmental disorders are also frequently viewed through the lens of excitation/inhibition (E/I) imbalance, deficits in neuroimmune development, and improper timing within critical developmental periods [13–15].

One of the most important cells that contribute to neurodevelopment is microglia. Microglia regulate neurogenesis, guide synapse formation, and support neuronal survival (or elimination, in the case of abnormal neurons) to shape neuronal networks in the brain and maintain CNS homeostasis in healthy individuals [6, 7, 16–18]. One of these functions is synaptic pruning. During normal early brain development, there is an initial overproduction of neurons and synaptic connections; synaptic pruning refines these synapses and sculpts neural circuits to optimize their efficiency [8, 16, 19].

This intricate process involves the phagocytosis of dendritic spines via the classical complement cascade [19–21]. The cascade initiates synaptic removal when the C1q protein secreted by microglia and astrocytes selectively binds to and tags apoptotic, immature, or weakly-developing synapses. This tagging then recruits C3. Subsequently, microglia recognize and bind to the C3-tagged synapses via Complement Receptor 3 (CR3), triggering their engulfment and elimination [22, 23]. Dysregulation of synaptic pruning can lead to synaptic dysfunction and is implicated in various neurological and mental disorders, including ASD and schizophrenia [19, 23]. ASD is often characterized by insufficient pruning, whereas schizophrenia may be characterized by excessive pruning [8, 11, 12]. In ASD, insufficient pruning may lead to hyperconnectivity and excessive synaptic density, particularly in areas governing sensory processing and social cognition. This may result in sensory overload and other characteristic phenotypes. In schizophrenia, excessive synaptic pruning during adolescence is thought to result in hypoconnectivity, especially in the prefrontal cortex (PFC) and hippocampus - regions critical for executive function and working memory. This synaptic loss disrupts normal communication between brain regions, potentially explaining the cognitive deficits observed in schizophrenia [3, 7, 9, 24–26].

Despite these associations, many questions remain about how pruning dysfunction gives rise to behavioral phenotypes in each disorder. The precise circuits affected—and how they result in specific behavioral symptoms—aren't well understood. Additionally, molecular mechanisms underlying pruning dysfunction differ across the two disorders. In schizophrenia, variants in complement component genes (particularly C4) have been linked to overactivation of the complement cascade and increased synapse elimination. However, in ASD, the role of the complement pathway is less clear. Pruning deficits may instead result from alterations in other pathways involving microglial receptors such as CX3CR1 or TREM2, or in genes like MEF2C and PTEN that modulate synaptic development. For instance, disruption of CX3CR1 signaling in mouse models of ASD have been shown to delay microglial colonization of the brain and impairs synaptic pruning during critical developmental windows, resulting in long-term social deficits [18]. Environmental factors such as maternal immune activation and early-life inflammation are also known to influence microglial function, but their timing, specificity, and behavioral consequences are still unclear [26–30].

This review synthesizes current knowledge on the shared and distinct roles of microglia in ASD and schizophrenia, with a focus on how differences in synaptic pruning may lead to divergent behavioral phenotypes. By comparing molecular mechanisms (e.g., complement cascade activation), structural consequences (e.g., synaptic density), and functional outcomes (e.g., electrophysiological and behavioral changes) in ASD and schizophrenia, this paper seeks to clarify the associations between microglia-mediated synaptic pruning dysfunction and behavioral phenotypes. In doing so, this review aims to contribute to key unanswered questions and identify targets for future therapeutic intervention or early diagnosis.

Methods

This systematic review utilized peer-reviewed literature on microglial roles in synaptic homeostasis in neurodevelopmental disorders. Open-access databases (e.g., PubMed, Scopus, Google Scholar, Medline) were utilized to access studies published from 2000-2025. Papers published earlier than 2000 were selected only if they were landmark papers on the subject for background information. Searches were limited to English-language articles that included combinations of the following keywords: ("microglia" OR "microglial cells") AND ("synaptic pruning" OR "synapse elimination") AND ("autism spectrum disorder" OR "ASD") AND ("schizophrenia" OR "psychosis") AND ("behavior" OR "behavioral phenotype" OR "cognition") AND ("complement system" OR "C1q" OR "C3" OR "CR3"). Reference lists of papers were also searched to identify additional relevant literature.

Studies were excluded if (1) they used only non-mammalian models, (2) they focus primarily on other disorders, (3) they do not contain experimental evidence, and (4) they only contain in vitro evidence. These exclusions were enforced to ensure the findings were the most relevant to human brain function and behavior, which may not be well-represented by the findings of purely non-mammalian or *in vitro* studies.

Results

This review synthesizes findings from prominent literature on microglial synaptic pruning dysfunction in ASD and schizophrenia, focusing on experiments pertaining to synaptic markers, electrophysiological recordings, and complement cascade expression.

Autism Spectrum Disorder (ASD)

Synaptic Markers

Studies utilizing synaptic markers in ASD animal models and post-mortem brain tissue indicate an increased density of synapses and immature dendritic spines. Immunohistochemical analyses often reveal elevated levels of certain pre-synaptic markers and spine types like synaptophysin and post-synaptic density protein 95 (PSD-95), and insufficiency of the synapse scaffold protein Shank3 (an important component of the post-synaptic density of glutamatergic synapses in the cortex), in specific brain regions of individuals and animal models of ASD [7, 24]. These findings on aberrant synaptic distributions provide evidence for the excitation/inhibition imbalance that is hypothesized to contribute to ASD [31].

In humans, post-mortem studies of cortical tissue from ASD individuals have reported increased dendritic spine density on pyramidal neurons in the PFC, temporal lobe, and cingulate cortex [7, 24, 32]. The excess synapses in areas that are critical for executive functions, social cognition, language processing and attention, may lead to hyper or hypoconnectivity, e.g., hypoactivation in the PFC, amygdala, and fusiform gyrus, and hyperactivation in the medial and right frontal regions of the brain. This has been shown to contribute to the social difficulties that characterize ASD [33–35]. For example, a study conducted in people with autism demonstrates functional underconnectivity (and thus hypoactivity) in the cortical network that allows for Theory of Mind (processing the mental states of other people) [35].

In mouse models of ASD, similar findings of persistent immature spines, higher total spine density, and increased synaptic protein expression (except *Shank3*, which shows the decreased expression mentioned previously, and *Pten*) have been observed across various brain regions, including the cortex, hippocampus, and striatum [36–38]. The synaptic overabundance in these regions is thought to contribute to sensory overload and difficulties processing social information [39]. Increased synaptophysin and PSD-95 levels in sensory cortices, such as the somatosensory cortex, have been correlated with hypersensitivity to sensory stimuli observed in ASD [7].

Electrophysiology

Electrophysiological recordings in ASD models demonstrate alterations in excitatory postsynaptic currents (EPSCs) and network hyperexcitability, consistent with increased synaptic density. ASD model mice have increased miniature EPSC (mEPSC) frequency and amplitude, reflecting a higher number of functional synapses or increased synaptic strength [40]. This elevated excitatory activity isn't uniform across all brain regions; for instance, hyperexcitability is often noted in the hippocampus, leading to an imbalance in the excitation/inhibition (E/I) ratio [39, 41]. This E/I imbalance, specifically a relative excess of excitation resulting from insufficient pruning, is now considered a core pathogenic mechanism in ASD [39]. This imbalance can manifest as atypical network oscillations (e.g., increased gamma-band power) or an increased susceptibility to seizures [42, 43].

This enhanced synaptic excitation and E/I imbalance are hypothesized to contribute to sensory processing abnormalities (e.g., tactile or auditory hypersensitivity) by causing plastic changes in the primary somatosensory cortex that make it difficult to filter stimuli [44, 45]. Further, altered long-term potentiation (LTP) and long-term depression (LTD), reflecting impaired synaptic plasticity, potentially contributes to learning and memory difficulties [46]. Guang et al. reports deficiencies in spatial memory, contextual fear memory, and object recognition in animal models of ASD with mutated *Shank* [46].

Complement Cascade Expression

The classical complement cascade hasn't been well-studied in ASD-related synaptic pruning dysfunction. Instead, other microglial pathways and intrinsic neural mechanisms have received more attention. In particular, dysfunction in the CX3CR1-CX3CL1 signaling axis, a crucial pathway for microglial maturation, motility, and direct interaction with neurons, has been extensively studied [47]. CX3CL1 (also known as fractalkine) is a chemokine released by neurons, and its receptor CX3CR1 is expressed on microglia. This signaling pathway is critical for guiding microglial processes to survey synapses and mediate their pruning activity during development. When this signaling is disrupted, as shown in mouse models with deleted or dysfunctional CX3CR1, microglia exhibit impaired synaptic pruning and this is directly linked to abnormal neural connectivity during development, including in disorders like ASD [47]. Dysfunction of the CX3CR1-CX3CL1 signaling axis, which helps to regulate immune processes of the microglia, is an example of a deficit in neuroimmune development that might lead to NDDs [15]. This leads to a higher density of persistent, often immature, dendritic spines (which indicates insufficient synaptic pruning) in regions such as the hippocampus [48]. Behaviorally, this impaired pruning stemming from CX3CR1 dysfunction is consistently correlated with social behavioral deficits in animal models, including reduced social interaction and increased repetitive behaviors, mirroring core characteristics of ASD phenotypes [49].

Schizophrenia

Synaptic Markers

Investigations into synaptic markers in schizophrenia patients and animal models frequently demonstrate reduced

synaptic density and lower expression of synaptic proteins. Post-mortem studies of individuals with schizophrenia have consistently reported decreased levels of pre-synaptic markers like synaptophysin on pyramidal neurons in the PFC and superior temporal gyrus [50, 51]. This reduction is often significant, reaching up to about 20% in cortical layer 3 [51]. This loss of synapses and synaptic proteins such as receptors provides a foundation for network hypoconnectivity and excitation/inhibition imbalance that could result in NDDs [52, 53]. The timing of this synaptic loss is crucial, with evidence suggesting that it largely occurs during late adolescence and early adulthood, coinciding with the typical onset of schizophrenic symptoms and a period of intense synaptic reorganization in the healthy brain [54].

Animal models of schizophrenia (e.g., those exposed to early-life stressors, viral infections, or genetic risk factors like DISC1 mutations) also show decreased synaptic protein expression and reduced dendritic spine density during adolescence, primarily in the PFC and hippocampus [55]. This structural synaptic loss is strongly correlated with the severity of negative symptoms (e.g., social withdrawal, anhedonia) and cognitive impairments, including working memory deficits, attention deficits, and executive dysfunction, as a reduced number of synapses directly impacts the efficiency and integrity of neural circuits supporting these functions [56].

Electrophysiology

Electrophysiological studies in schizophrenia models and, where possible, human-derived neural systems, consistently show reduced EPSCs, reflecting the overall decrease in synaptic number or strength and leading to network hypoconnectivity. In schizophrenia animal models, decreased mEPSC frequency and amplitude are commonly observed, indicating fewer functional synapses and possibly weaker synaptic transmission, particularly in the PFC [57]. This reduction in excitatory synaptic drive leads to widespread hypoconnectivity within neural networks, measured via reduced functional connectivity in fMRI studies [58]. This is another example of how an excitation/inhibition imbalance can lead to long-lasting deficits, and potentially NDDs [59]. Studies often report reduced long-range functional connectivity, particularly within the default mode network and between frontal and parietal regions, reflecting breakdown in information processing [60]. This underconnectivity can manifest as disorganized thought and fragmented perceptions, as well as cognitive deficits characteristic of schizophrenia (e.g., impaired working memory, attention deficits) [61].

Complement Cascade Expression

A growing body of evidence in schizophrenia points to upregulation of the classical complement cascade as causing excessive synaptic pruning. Genetic studies have identified associations between common variants in the *C4* gene (specifically *C4A* alleles) and increased risk for schizophrenia, with these variants correlating with higher C4 protein expression in the brain [3]. This leads to increased tagging of synapses by complement components. Post-mortem brain tissue from schizophrenia patients have demonstrated elevated levels of C1q, C3 and C4 localized to synapses, particularly in the PFC, midbrain and hippocampus, indicating increased synaptic tagging for removal [3, 62].

Microglia in schizophrenia models and post-mortem brains also show altered morphology (e.g., more active, amoeboid-like states, or dystrophic features) and crucially, increased expression of CR3, suggesting heightened phagocytic activity necessary for synaptic pruning [63]. PET studies have also shown increased microglial activity, potentially linked to their pruning function, in those with high risk of psychosis and those with schizophrenia [64]. This excessive complement-mediated tagging and subsequent microglial engulfment of synapses, particularly during the critical period of adolescent brain development, is linked to synaptic loss in schizophrenia and is hypothesized to drive the emergence of psychotic symptoms [11, 65].

A summary comparing the differences in synaptic markers, electrophysiology and complement cascade, as well as the relevant symptoms of ASD and schizophrenia, can be found in Table 1.

Table 1. Summary of Research Findings on Synaptic Markers, Electrophysiology, and Complement Cascades (Rows) in ASD Versus Schizophrenia (Columns), Along With a Comparison of Behavioral Phenotypes

Feature	ASD	Schizophrenia
Synaptic Markers	Increased dendritic spine density and synaptic overabundance (e.g., high synaptophysin, PSD-95). Basis for excessive excitation.	Decreased dendritic spine density and synaptic loss (e.g., low synaptophysin). Basis for network hypoactivity.
Electrophysiology	Network hyperexcitability; E/I imbalance skewed toward excitation (high mEPSC frequency and amplitude).	Network hypoconnectivity; E/I imbalance skewed toward inhibition (low mEPSC frequency and amplitude).
Complement Cascade	Focus is on non-complement pathways like CX3CR1-CX3CL1 dysfunction, leading to insufficient tagging.	Upregulation and overactivation (e.g., of C4 variants), leading to excessive synaptic tagging and removal.
Relevant Behavioral Phenotypes	Sensory hypersensitivity, repetitive behaviors, difficulties with social communication and cues.	Cognitive deficits (e.g., in working memory and attention), psychotic symptoms (delusions, hallucinations), social withdrawal.

Discussion

The distinct roles of microglial synaptic pruning dysfunction in ASD and schizophrenia present unique neurobiological opposites: while one disorder appears to have too little synaptic pruning, the other appears to have too much.

One difference between the two disorders is the structural integrity of neural circuits, as shown in synaptic marker studies. In ASD, the persistent overabundance of synapses, particularly in the PFC, temporal lobe, and cingulate cortex, suggests insufficient pruning. This overconnectivity in areas crucial for executive functions, social cognition, and attention likely underlies ASD traits like sensory hypersensitivity, rigid behaviors, and difficulties processing social information. Conversely, schizophrenia is marked by profound loss of synapses, observed in the PFC, hippocampus, and superior temporal gyrus. This results in neuroanatomical "thinning" that is associated with severe cognitive deficits. This excessive synaptic pruning, which occurs during adolescent brain development, is one example of how brain dysfunction during critical periods can lead to NDDs. The reason these brain regions are differentially affected remains unknown. Future research should investigate the mechanisms for regional specificity of pruning dysfunction, exploring factors such as unique developmental trajectories of microglial-neuronal interactions across different cortical areas, or susceptibility of specific neuron populations to pruning signals. From a clinical perspective, identifying distinct structural abnormalities offers promising diagnostic and therapeutic avenues. Meanwhile, research on potential treatments has shown that in preclinical ASD models, interventions that restore proper protein levels or function may be able to ameliorate synaptic overabundance and associated behavioral deficits [36, 37]. Repetitive grooming behavior was previously rescued by using hM3Dq to enhance striatopallidal medium spiny neuron activity [37]. In schizophrenia models, reducing the activity of complement components, particularly C4, mitigated synaptic loss and improve behavioral outcomes [3, 11, 57]. However, these studies were conducted primarily in animal models. Future clinical research testing the efficacy and safety of these interventions in humans is necessary before treatment development based on this research can proceed.

Structural disparities between ASD and schizophrenia impact functional brain activity and connectivity. Electrophysiological recordings in ASD models mostly demonstrate network hyperexcitability – that is, an E/I imbalance that is skewed towards excitation. This excitatory drive may impede information processing, resulting in sensory overload. In contrast, schizophrenia models have been previously shown to exhibit reduced excitatory drive and widespread network hypoconnectivity, particularly across frontal-parietal circuits. This contributes to working memory deficits and disorganized thought. These findings emphasize the potential for E/I imbalance to contribute to brain dysfunction, including NDDs. Treatments that reduce neural excitability, such as benzodiazepines and anticonvulsants, could potentially rebalance the E/I ratio and alleviate these symptoms; however, research in this area is still developing [39, 66]. In schizophrenia preclinical models, rescuing C4 circuit alterations by increasing levels of its interaction partner SNX27 reduced hypoconnectivity and mitigated behavioral deficits [56, 57]. These links between synaptic dysfunction and behavioral outcomes underscore the importance of understanding the precise circuits involved in dysfunctional pruning. Future research should focus on identifying specific circuits to understand how particular neuronal and glial populations are affected, and whether the observed behavioral phenotypes might recursively affect the synapses themselves; for example, if processing excessive amounts of sensory stimuli in ASD could possibly lead to the strengthening of synapses to cope with increased neural activity in a positive feedback loop.

Interventions that restore proper functioning of these circuits could be a potential treatment for these disorders; however, given that much of the research has been primarily in preclinical animal models, it is important to first investigate the affected circuits in humans before considering any development of treatments.

Another neurobiological distinction between ASD and schizophrenia is the molecular drivers of aberrant pruning. Previous research implicates excessive complement cascade activation involving C4 gene variants and heightened C1q/C3 tagging of synapses as potentially contributing to the pathological removal of healthy synapses and the emergence of psychotic symptoms in schizophrenia. Conversely, the evidence for a primary role of the complement cascade in insufficient pruning in ASD is less robust. Instead, dysfunction in other microglial-neuronal communication pathways, such as the CX3CR1-CX3CL1 signaling axis that is a central component of neuroimmune development, is what is hypothesized to lead to persistent immature spines and associated social deficits. Targeting these distinct molecular pathways has shown therapeutic promise in preclinical animal models. Minocycline, an antibiotic that suppresses the C1q/C3-CR3 complement signaling pathway, has been shown to prevent excessive synapse uptake by microglia and reduce psychosis in adolescents with schizophrenia [3, 11, 67]. (Research on the effects of restoring proper CX3CR1 signaling in ASD could not be found; however, based on related research, it is expected to normalize synaptic pruning and ameliorate social and behavioral deficits [47, 49].) This suggests potentially new avenues for precision medicine. For schizophrenia, genetic screening for C4 risk variants could identify individuals at high risk, possibly allowing for prophylactic interventions using complement cascade modulators. For ASD, CX3CR1 agonists or other targeted immunomodulatory approaches might promote healthy pruning instead. However, this research was conducted primarily in animals. Developing human-relevant translational models, such as induced pluripotent stem cell (iPSC)-derived brain organoids containing microglia, will be vital to better understand these complex molecular pathways and screen for targeted therapeutics so that the growing research in this field may be translated into real improvements in healthcare for ASD and schizophrenia.

Despite the opposite outcomes of synaptic pruning (insufficient in ASD versus excessive in schizophrenia), both disorders do share underlying microglial and immune-related pathologies, suggesting a common vulnerability in neuroimmune development. For instance, while excessive activation of the complement cascade drives excessive synaptic pruning in schizophrenia (as established previously), the complement system's initial tagging component C1q specifically has been implicated in ASD pathology [68]. C1q is integral to the proper formation and maintenance of synapses during early life. Its dysfunction, whether manifesting as insufficient activity (contributing to hypo-pruning in ASD) or hyperactivation (driving excess pruning in schizophrenia), suggests that a fundamental vulnerability lies in the complement system's ability to discriminate between healthy and pathological synapses.

Another instance of shared pathology can be found in the CX3CR1-CX3CL1 axis. Rare genetic variants in the microglial receptor CX3CR1 have been found to increase the susceptibility risk for *both* ASD and schizophrenia [69].

These commonalities in the pathology of ASD and schizophrenia highlight that fundamental disruptions in microglia and neuroimmune functioning can predispose an individual to either disorder, with the final phenotype likely determined by the specific type of disruption.

Conclusions

This review reveals the opposing roles of microglial synaptic pruning dysfunction in ASD and schizophrenia, with ASD characterized by insufficient pruning and schizophrenia by excessive pruning. This distinction is vital for developing targeted treatments and diagnostic biomarkers, allowing for personalized interventions. Future research should pinpoint which brain areas are most affected, understand the specific microglial dysfunctions involved, and investigate the bidirectional relationships between behavior and synaptic changes to further advance our understanding of these two disorders and identify new potential therapies.

List of Abbreviations

ASD: autism spectrum disorder
CNS: central nervous system
CR3: complement receptor 3
E/I: excitation/inhibition
EPSCs: excitatory postsynaptic currents
mEPSC: miniature excitatory postsynaptic current
fMRI: functional magnetic resonance imaging
iPSC: induced pluripotent stem cell
LTD: long-term depression
LTP: long-term potentiation
NDD: neurodevelopmental disorder
PFC: prefrontal cortex
PET: positron emission tomography
PSD-95: post-synaptic density protein 95
SWYC: survey of wellbeing of young children

Conflicts of Interest

The authors declare that they have no conflict of interests.

Ethics Approval and/or Participant Consent

No approval or consent was needed to complete this review study.

Authors' Contributions
HW: designed the study, collected and analysed literature, drafted the manuscript, and gave final approval of the version to be published.

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