Neural Mechanisms of Motor Development Disorders in Children with Autism

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Abstract

Developmental motor disorders are common features of autism spectrum disorder. Through systematic review of neuroscientific research on motor development disorders in children with autism, it has been found that alterations in γ-aminobutyric acid and serotonin concentrations, as well as abnormal expression of γ-aminobutyric acid-related proteins and Shank proteins, not only impair central nervous system development but also lead to an imbalance between synaptic excitation and inhibition, thereby altering functional connectivity between the cerebellum and cerebral motor cortex in children with autism. Structural changes in the cerebellum, basal ganglia, and corpus callosum of children with autism have negatively impacted whole-brain connectivity. Abnormalities in neurochemical mechanisms and brain structure jointly lead to functional brain abnormalities, ultimately causing motor development disorders in children with autism. Furthermore, the common neural basis for motor development disorders and core symptoms of autism mainly includes mirror neuron system dysfunction, abnormalities in the thalamus, basal ganglia, and cerebellum, as well as SLC7A5 and PTEN gene mutations. Future research needs to focus on other neurotransmitters closely related to motor function, such as acetylcholine and dopamine; explore the dynamic mechanisms and formation of neural networks underlying motor development disorders; and analyze the interaction between the neural mechanisms of this disorder and those of the core symptoms of autism.

Full Text

Neural Mechanisms of Developmental Motor Disorders in Children with Autism Spectrum Disorder*

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Abstract: Developmental motor disorders represent a common feature of autism spectrum disorder (ASD). Through a systematic review of neuroscientific research, we find that alterations in the concentrations of γ-aminobutyric acid (GABA) and serotonin, along with abnormal expression of GABA-related proteins and Shank proteins, not only impair central nervous system development but also lead to synaptic excitation-inhibition imbalance, consequently altering functional connectivity between the cerebellum and motor cortex in children with ASD. Structural changes in the cerebellum, basal ganglia, and corpus callosum negatively impact whole-brain connectivity in these children. Abnormalities in neurobiochemical mechanisms and brain structure jointly produce functional brain abnormalities, ultimately resulting in developmental motor disorders. Moreover, the common neural basis shared by motor developmental disorders and core ASD symptoms primarily includes mirror neuron system dysfunction, abnormalities in the thalamus, basal ganglia, and cerebellum, as well as SLC7A5 and PTEN gene mutations. Future research should focus on other neurotransmitters closely related to motor function, such as acetylcholine and dopamine; explore the dynamic mechanisms and formation of neural networks underlying developmental motor disorders; and analyze the interactions between the neural mechanisms of motor developmental disorders and those of core ASD symptoms.

Keywords: autism spectrum disorder, children, developmental motor disorders, neural mechanism

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Autism spectrum disorder (ASD) is a neurodevelopmental condition that emerges early in childhood, with core symptoms later manifesting as social communication impairments, restricted interests, and repetitive or atypical behaviors (American Psychiatric Association, 2013). In recent years, accumulating research has revealed that beyond these core symptoms, developmental motor disorders represent a common comorbidity in children with ASD. The prevalence of these disorders ranges from 59% to 80% (Davidovitch et al., 2015; Dewey et al., 2007; Green et al., 2009; Liu & Breslin, 2013; Paquet et al., 2016). Specifically, 36% to 63% of children with ASD exhibit fine motor impairments, while 52% to 64% show gross motor deficits (Paquet et al., 2016). Despite the increasing incidence of motor developmental disorders in ASD, their developmental trajectories and neural mechanisms remain poorly understood.

Motor development is a lifelong process of continuous improvement in coordination and control, closely linked to cognitive, linguistic, emotional, and social development (董奇 & 陶沙, 2011; 原雅青 et al., 2019). Research on motor developmental disorders in ASD primarily investigates impairments in motor coordination and control, deficits in their integration, and influencing factors. Previous findings indicate: (1) Children with ASD show varying degrees of impairment in both motor coordination and control, manifesting primarily as postural control deficits and motor coordination difficulties (Bojanek et al., 2020; Fournier et al., 2010; Isenhower et al., 2012; Minshew et al., 2004; Xavier et al., 2018); (2)

These children demonstrate poor integration of motor coordination and control, limiting their ability to adapt to environmental demands, with functional motor deficits including abnormal gait and handwriting difficulties (Anzulewicz et al., 2016; Biffi et al., 2018; Johnson et al., 2013; Kindregan et al., 2015); and (3) Motor developmental disorders in ASD are mainly influenced by three factors: impaired motor learning ability, motor execution difficulties, and sensorimotor dysfunction (Marko et al., 2015; Paquet et al., 2019; Stoit et al., 2013; Whyatt & Craig, 2013).

Previous research has noted that motor developmental disorders in ASD correlate significantly with social deficits and ASD symptom severity (Fitzpatrick et al., 2017; Gong et al., 2020; Hirata et al., 2014). Moreover, these motor disorders are not merely consequences of epilepsy or developmental regression but represent an integral component of overall brain dysfunction (Ming et al., 2007). Therefore, it is essential to explore the neural mechanisms underlying motor developmental disorders in ASD and their shared pathophysiological basis with core symptoms, thereby deepening our understanding of ASD' s nature and pathogenesis while providing novel therapeutic strategies for intervention.

Prior brain lesion, neuroimaging, and animal studies have identified brain regions associated with motor developmental disorders in ASD. Motor control and coordination deficits are closely linked to structural abnormalities in the basal ganglia and corpus callosum (Barbeau et al., 2015; Hocking & Caeyenberghs, 2017; Kaur et al., 2018; Qiu et al., 2010). Abnormal gait and handwriting difficulties primarily involve cerebral functional lateralization and cerebellar circuit abnormalities (Floris et al., 2016; Mosconi et al., 2015). Impaired motor learning ability is associated with altered cerebellar microstructure (Marko et al., 2015), while motor execution difficulties are closely related to cerebellar activation and abnormal brain functional networks (Carper et al., 2015; Mostofsky et al., 2009). The neural basis of sensorimotor dysfunction lies primarily in abnormal functional connectivity between visual and motor regions (Nebel et al., 2016). However, no study has yet systematically analyzed the neural mechanisms of motor developmental disorders in ASD. This review examines these mechanisms from three perspectives—neurobiochemical mechanisms, brain structural basis, and brain functional mechanisms—while analyzing the common neural basis shared with core ASD symptoms, aiming to provide insights for future research.

2 Neurobiochemical Mechanisms of Developmental Motor Disorders in Children with ASD

Neurotransmitters are crucial neurochemicals that serve as messengers in interneuronal communication at synapses. The neurobiochemical mechanisms of motor developmental disorders in ASD primarily involve alterations in neurotransmitter concentrations and abnormal expression of related proteins.

2.1 Alterations in GABA Concentration and Parvalbumin Expression

γ-aminobutyric acid (GABA) is one of the most important inhibitory neurotransmitters in the human brain. Using magnetic resonance spectroscopy (MRS), Gaetz et al. (2014) measured GABA-to-creatine ratios in 17 children with ASD, finding significantly lower GABA+/Cr in the motor cortex compared to typically developing children. Puts et al. (2017) similarly reported reduced GABA levels in the sensorimotor cortex of children with ASD. Umesawa et al. (2020) combined behavioral and MRS studies to reveal that altered GABA concentrations in different motor areas correspond to distinct motor deficits: higher GABA in the primary motor area correlates with poorer overall motor performance, while lower GABA in the supplementary motor area relates to motor coordination difficulties. These abnormalities likely arise from GABA system dysfunction causing excitation-inhibition imbalance (El-Ansary & Al-Ayadhi, 2014; Masuda et al., 2019; Pizzarelli & Cherubini, 2011), which affects information processing and behavioral regulation (Uzunova et al., 2016). Overall, altered GABA concentrations in sensorimotor, primary motor, and supplementary motor areas may underlie deficits in cortical inhibition functions necessary for sensory information processing, motor execution regulation, and motor planning, ultimately leading to various motor developmental disorders.

Parvalbumin (PV), a marker of highly metabolically active GABAergic neuron subpopulations, plays a crucial role in cerebellar Purkinje cell synaptic plasticity (Berdel & Moryś, 2000; Schwaller et al., 2002). Soghomonian et al. (2017) used in situ hybridization histochemistry to detect altered PV gene expression in the cerebellum of individuals with ASD. This alteration profoundly affects cerebellar output fibers, causing abnormal GABA signaling between Purkinje cells and deep cerebellar nuclei, thereby altering critical motor and non-motor functions. These motor changes likely result from impaired inhibitory synaptic transmission due to abnormal PV expression, leading to delayed or disrupted cerebellar development and consequent motor dysfunction (Courchesne et al., 1988; Jaber, 2016; Wöhr et al., 2015).

2.2 Alterations in Other Neurotransmitter Concentrations and Related Protein Expression

Beyond GABA and PV abnormalities, exploratory biochemical mechanism studies have employed animal models to investigate ASD-specific mechanisms by directly measuring or pharmacologically manipulating neurotransmitter concentrations. Serotonin (5-hydroxytryptamine, 5-HT), first discovered in serum, is another important inhibitory neurotransmitter. Up to 30-40% of individuals with ASD exhibit elevated blood serotonin concentrations, potentially related to pathophysiological mechanisms (Azmitia et al., 2011). Animal models with high serotonin display social deficits characteristic of ASD (McNamara et al., 2008). Hough and Segal (2016) found that administering high levels of serotonin receptor agonists to juvenile rats significantly altered dendritic structure and synaptic features in cerebellar dentate nucleus neurons, which may under-

lie cognitive deficits such as delayed motor learning and difficulty with motor automation. During brain development, the serotonin system influences axonal growth and synapse formation while contributing to behavior and memory improvements involving higher cognitive demands (Bacqué-Cazenave et al., 2020; Bonnin & Levitt, 2011). Therefore, abnormal cerebellar neuron development caused by elevated serotonin may have lasting negative effects on motor learning ability.

Shank proteins are major scaffolding proteins in the postsynaptic density (PSD) of glutamate synapses, playing a key role in glutamatergic transmission (Boeckers et al., 2002). Shank3 mutant mice exhibit both core ASD symptoms and abnormal motor learning strategies in accelerated rotarod tasks, suggesting that Shank3 mutations may contribute to motor learning deficits in ASD (Yang et al., 2012). Additionally, Shank2 mutations in individuals with ASD are associated with motor developmental disorders and cerebellar dysfunction (Leblond et al., 2014). Peter et al. (2016) demonstrated that Shank2 deficiency impairs long-term potentiation (LTP) at parallel fiber-Purkinje cell synapses in the cerebellum, with mice showing severe motor learning deficits. This suggests that loss of Shank2 function may reduce cerebellar Purkinje cell synaptic plasticity, leading to motor learning impairments in children with ASD.

3.1 Structural Abnormalities of the Cerebellum and Basal Ganglia

The cerebellum is a critical motor control center that regulates muscle tone, maintains balance, coordinates fine movements, and participates in extensive cognitive and emotional functions including perception, learning, language, and emotion regulation (林冲宇 & 翁旭初, 2006; Adamaszek et al., 2017; Booth et al., 2007; Stoodley, 2016; Vokaer et al., 2002). Individuals with ASD commonly show cerebellar abnormalities (D' Mello & Stoodley, 2015; Jeong et al., 2014; Wang et al., 2014). Using magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI), Hanaie et al. (2013) found that children with ASD exhibited significantly reduced fractional anisotropy in the right superior cerebellar peduncle, with this microstructural abnormality negatively correlating with overall motor performance and ball skills. Marko et al. (2015) observed that children with ASD were less proficient than typically developing children at using visual information to perceive errors during motor learning, and structural imaging revealed smaller cerebellar anterior lobe volumes adjacent to cerebellar posterior lobules (VI and VIII). These findings suggest that reduced cerebellar volume may underlie deficits in visual feedback-based motor learning. Using diffusion spectrum imaging (DSI), Lin et al. (2019) assessed white matter microstructural properties across whole-brain motor circuits in boys with ASD, finding that abnormalities in white matter tracts from the left parietal lobe through the pons to the cerebellum impaired somatosensory signal transmission to the cerebellum, thereby altering motor adaptation abilities including control and error correction.

The basal ganglia, also known as the basal nuclei, play crucial roles in motor regulation, motor learning, and execution (Barter et al., 2015b; Jin & Costa, 2015; Sheng et al., 2019; Shmuelof & Krakauer, 2011). Qiu et al. (2010) demonstrated that inward deformation of the right posterior putamen, which receives projections from the primary motor cortex, serves as an important predictor of motor control deficits in children with ASD, while inward deformation of the anterior and posterior putamen receiving premotor projections predicts poor hand motor performance. Regarding gait, Nayate et al. (2005) hypothesized that head/trunk postural abnormalities in children with Asperger' s syndrome align with striatal dysfunction, while Subramanian et al. (2017) suggested that gait abnormalities in ASD may result from intrinsic basal ganglia changes.

Maturation of subcortical structures provides the material and physiological foundation for motor development, with structural changes profoundly impacting motor learning abilities. These impairments can lead to reduced motor execution accuracy, longer completion times, and difficulty acquiring flexible movement patterns or effectively integrating complex action sequences. Notably, while the cerebellum and basal ganglia each refine motor commands through distinct feedback mechanisms, their normal interaction facilitates optimal motor cortex command generation. In ASD, structural alterations in the basal ganglia likely impede information flow from the cerebellum to the cortex, negatively affecting motor learning. Currently, few studies have simultaneously examined cerebellar and basal ganglia structural abnormalities to explore their combined neural mechanisms in ASD motor developmental disorders. Future research should integrate neuroimaging techniques (MRI, fMRI, DTI) with behavioral studies to investigate these combined subcortical neural mechanisms.

3.2 Structural Abnormalities of the Corpus Callosum

The corpus callosum transmits cortical activity between hemispheres, specializing in visual, somatosensory, and motor information transfer. Located at the base of the longitudinal fissure, it is the largest commissural fiber bundle in the cerebrum (Paul et al., 2007; Valenti et al., 2020). Numerous studies have documented structural changes in the corpus callosum of children with ASD (Casanova et al., 2009; Casanova et al., 2011; Hanaie et al., 2014; Keary et al., 2009; Prigge et al., 2013). These alterations may directly affect bilateral body coordination and negatively impact interhemispheric connectivity, leading to bimanual coordination deficits (Barbeau et al., 2015; Hocking & Caeyenberghs, 2017; Kaur et al., 2018). Additionally, agenesis of the corpus callosum (ACC) represents another structural abnormality in ASD (Lau et al., 2013; Paul et al., 2007). Children with ACC exhibit motor deficits including delayed motor development, poor fine motor skills, balance difficulties, reduced muscle tone, and insensitive depth perception (Moes et al., 2009). Notably, corpus callosum abnormalities appear during infancy in ASD (Fingher et al., 2017), with abnormal fractional anisotropy in the genu at 6 months significantly predicting atypical sensory responses at 2 years (Wolff et al., 2017). These sensory abnor-

malities likely impair sensorimotor coupling, preventing individuals with ASD from appropriately adjusting movements to rapidly changing contexts (Whyatt & Craig, 2013).

However, some studies have found that macro- and microstructural features of the corpus callosum correlate only with social deficits, not motor deficits (Hanaie et al., 2014). Furthermore, corpus callosum abnormalities exhibit sex differences in ASD (Nordahl et al., 2015). While both boys and girls with ASD show reduced total corpus callosum area, girls' callosal fibers extend more toward the anterior frontal cortex, whereas boys' fibers tend toward the orbitofrontal cortex (OFC). This suggests that sex-specific structural changes may affect different brain regions, producing distinct motor deficits. Future research should continue to validate the relationship between corpus callosum structural features and motor developmental disorders in ASD, conducting comprehensive studies to characterize sex-specific developmental patterns of callosal abnormalities and their associated clinical motor symptoms.

4.1 Cerebellar Activation and Cortico-Cerebellar Circuit Abnormalities

Cerebellar dysfunction in ASD primarily involves altered cerebellar activation and cortico-cerebellar circuit abnormalities. Using functional magnetic resonance imaging, Mostofsky et al. (2009) analyzed brain activation differences during sequential finger tapping tasks in children with ASD. Results showed significantly reduced activation in the ipsilateral anterior cerebellum, which may explain motor execution difficulties. Cortico-cerebellar circuits are critical for spatial and motor information acquisition and provide feedback for movement adjustment (杨叶红 & 王树明, 2018). Mosconi et al. (2015) demonstrated that alterations in anterior cerebellar-primary motor cortex circuits disrupt feedforward control, preventing stable control of initial movement force, while posterior cerebellar-parietal cortex circuit abnormalities impair feedback control mechanisms, preventing stable maintenance of force during movement. Consequently, abnormal parieto-cerebellar circuits involved in perceptual-motor integration and primary motor-cerebellar circuits involved in spatial sequencing may prevent children with ASD from using visual information to perceive and correct errors between actual and intended movements, hindering formation of complex movement patterns during motor learning. This partially explains why children with ASD show unstable motor skills, particularly poor control, during continuous movements involving hand force and postural adjustments.

4.2 Cerebral Functional Lateralization and Connectivity Abnormalities

Atypical cerebral functional lateralization negatively impacts motor development in ASD. Research indicates that abnormal lateralization contributes to gait and postural asymmetries (Esposito et al., 2011; McCleery et al., 2009).

Floris et al. (2016) used fMRI to analyze motor cortex network connectivity in high-functioning right-handed children with ASD aged 8-12, revealing rightward lateralization of motor circuit functional connectivity that negatively correlated with gait, balance, and movement sequencing accuracy, potentially underlying gross motor deficits.

Altered connectivity within and between brain networks represents a hallmark of functional brain abnormalities in ASD (Di Martino et al., 2014). Motor execution and coordination difficulties, as well as sensorimotor dysfunction, have been linked to abnormal brain functional connectivity. Regarding motor execution and coordination, the corticospinal tract (CST) controls body regulation and manages voluntary movements, particularly fine movements of distal limbs. The precentral gyrus, where CST originates, controls contralateral body movement. Carper et al. (2015) reported that children with ASD show hyperconnectivity between CST and medial prefrontal, parietal, occipital, and cingulate cortices, along with reduced hemispheric asymmetry in precentral functional connectivity, affecting basic motor execution. Mostofsky et al. (2009) found that reduced functional connectivity in motor execution regions explains poor coordination during motor skill automation.

In sensorimotor dysfunction, numerous studies have confirmed that hyper- or hypoconnectivity between thalamus and cortex explains sensorimotor deficits in ASD (Nair et al., 2013; Woodward et al., 2017). Oldehinkel et al. (2019) suggested that abnormal connectivity between cerebellum, visual, and sensorimotor regions, influenced by connectivity abnormalities in other brain areas, may underlie visuomotor integration deficits. Nebel et al. (2016) found abnormal functional connectivity between visual and motor regions, with reduced synchrony between these systems reflecting decreased visuomotor integration. Future research should employ electroencephalography (EEG), magnetoencephalography (MEG), and fMRI to investigate dynamic connectivity among primary motor, premotor, supplementary motor, somatosensory, and primary visual areas to clarify abnormal network connectivity patterns underlying sensorimotor dysfunction.

5 Common Neural Basis of Developmental Motor Disorders and Core Symptoms of Autism

The shared neural basis between motor developmental disorders and core ASD symptoms primarily involves mirror neuron system dysfunction, abnormalities in the thalamus, basal ganglia, and cerebellum, and mutations in SLC7A5 and PTEN genes.

First, mirror neurons in the premotor cortex area F5 are sensorimotor neurons activated both during action execution and action observation, playing a fundamental role in understanding others' actions and intentions (Rizzolatti et al., 2014; Rizzolatti et al., 1996). This indicates that motor cortex functions not only as an execution system but also contributes to social domains by understanding

others' behaviors, interacting, exploring the environment, and acquiring new information. Numerous studies have confirmed atypical mirror neuron system activation in children with ASD (Dapretto et al., 2006; Martineau et al., 2008), suggesting that both social and motor deficits may stem from mirror neuron system abnormalities (Fabbri-Destro et al., 2013).

Second, thalamic, basal ganglia, and cerebellar abnormalities are implicated in both motor developmental disorders and core ASD symptoms. Specifically, hypoconnectivity between thalamus and prefrontal, parieto-occipital, and temporal lobes relates to social, cognitive, and communication deficits, while abnormal functional connectivity between thalamus and motor cortex impairs motor development (Chen et al., 2016; Nair et al., 2013; Woodward et al., 2017). Basal ganglia morphological abnormalities predict not only motor deficits but also correlate with social impairments and repetitive behaviors (Qiu et al., 2010; Schuetze et al., 2016). Reduced Purkinje cell numbers represent one of the most common pathological features in ASD (Skefos et al., 2014; Wegiel et al., 2014). Animal studies link both motor and social deficits in ASD mouse models to Purkinje cell loss, suggesting shared cerebellar substrates (Al Sagheer et al., 2018).

Finally, SLC7A5 and PTEN mutations may serve as genetic links between social deficits and motor developmental disorders. Tărlungeanu et al. (2016) found that mice lacking SLC7A5 in the blood-brain barrier exhibited abnormal gait, reduced exploration, lower movement speed, and decreased social interaction (maintaining greater distance from conspecifics). Whole exome sequencing identified SLC7A5 mutations in children with ASD and motor coordination deficits (Tărlungeanu et al., 2016), suggesting SLC7A5 mutations may cause co-occurring ASD and motor coordination disorders. PTEN mutations occur in 7.1% of individuals with ASD (McBride et al., 2010). PTEN-induced Purkinje cell structural abnormalities cause not only social deficits and repetitive behaviors but also motor coordination and learning impairments in mice (Cupolillo et al., 2016). These findings suggest interacting neural substrates for motor developmental disorders and core ASD symptoms, though the precise mechanisms require further investigation.

6.1 Interactive Model of Neurobiochemical Mechanisms, Brain Structure Basis, and Brain Function Mechanisms

The neurobiochemical mechanisms, brain structural basis, and brain functional mechanisms of motor developmental disorders in ASD do not operate independently but form an interconnected organic system. First, altered neurotransmitter concentrations and abnormal protein expression affect not only cerebellar neuron development and structural maturation but also impair effective neuronal information transmission, negatively impacting connectivity between cerebellar and cortical motor neurons. Second, structural abnormalities in cerebellum, basal ganglia, and corpus callosum are directly associated with various motor developmental disorders and likely persistently affect their connectivity

with the cerebrum, hindering appropriate motor command generation and indirectly exerting profound, lasting negative effects on motor development. Finally, functional brain abnormalities result from combined neurobiochemical and structural changes, with brain structure showing closer relationships to motor developmental disorder manifestations than neurobiochemical mechanisms alone (Figure 1 [Figure 1: see original paper]). Future research should integrate multiple neuroscience methods to validate and refine this model.

6.2 Future Directions

Investigating the neural mechanisms of motor developmental disorders in ASD enhances understanding of the disorder and its pathophysiology. Based on our analysis of existing research, future studies should prioritize the following areas.

First, expand neurotransmitter research in ASD motor developmental disorders. Current studies have focused only on GABA, glutamate, and serotonin. However, other neurotransmitters are closely related to motor function: acetylcholine participates in neuromuscular signal transmission (安楠, 2011), while dopamine regulates movement (Barter et al., 2015a; Da Silva et al., 2018). These chemicals likely constitute fundamental components of motor neural networks in ASD. Future research could employ neurotransmitter fluorescent probes to precisely detect dopamine and acetylcholine release and regulation patterns during motor deficits, deepening understanding of pathogenic mechanisms. Additionally, since motor developmental disorders may stem from excitation-inhibition imbalance caused by GABA alterations, and the neurotransmitter imbalance hypothesis posits that ASD arises from similar synaptic imbalances (Hussman, 2001), future studies could integrate investigations of ASD and motor developmental disorder pathogenesis.

Second, explore dynamic mechanisms and formation of neural networks underlying motor developmental disorders. Most current research examines single brain region structural or functional abnormalities to explain specific motor deficits. However, movement generation, maintenance, and control require coordinated participation of complex circuits involving sensory cortex, motor cortex, and basal ganglia—pathological changes in any component can cause brain dysfunction (李澄宇 et al., 2016). Single-region abnormalities cannot explain the complex manifestations of motor developmental disorders. Future research should identify core neural networks for motor developmental disorders while examining local and long-range circuit coordination to understand overall dynamic patterns from sensory input to motor output. This research direction should leverage safe, movement-tolerant neuroscientific techniques to conduct prospective studies of motor developmental disorders in high-risk infants, obtaining longitudinal developmental trajectories of core neural networks to facilitate early identification and intervention.

Third, dissect interactions between neural mechanisms of motor developmental disorders and core ASD symptoms. Some researchers propose that motor disor-

der neural mechanisms negatively impact core symptom substrates—for example, Khalil et al. (2018) suggested that mirror neuron systems involving motor regions, basal ganglia, and insula affect frontal cortex, anterior cingulate, and temporoparietal junction responsible for social reasoning. However, this hypothesis lacks empirical support, and no studies have examined whether core symptom-related brain abnormalities reciprocally affect motor disorder mechanisms. Future research should integrate these mechanisms, constructing bidirectional neural network models between the two domains.

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