

Review Article

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Artificial Intelligence-Driven Transcranial Magnetic Stimulation (TMS) for Autism Spectrum Disorder

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ABSTRACT

Autism Spectrum Disorder (ASD) is a complex neurodevelopmental condition characterized by impairments in social communication, repetitive behaviors, sensory processing abnormalities, and variable cognitive deficits. Despite significant advances in behavioral therapies and pharmacological interventions, effective treatments capable of directly modulating dysfunctional neural networks remain limited. Transcranial Magnetic Stimulation (TMS) has emerged as a promising non-invasive neuromodulation technique that can alter cortical excitability, enhance neuroplasticity, and potentially improve cognitive and behavioral outcomes. Simultaneously, recent developments in Artificial Intelligence (AI), Machine Learning (ML), Deep Learning (DL), Explainable Artificial Intelligence (XAI), Reinforcement Learning (RL), and Digital Twin technologies have created new opportunities to personalize TMS protocols using multimodal patient data, including structural and functional neuroimaging, electroencephalography (EEG), behavioral assessments, genetic information, and longitudinal clinical outcomes.

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Introduction

This review presents a comprehensive interdisciplinary examination of AI-assisted TMS for ASD, emphasizing the integration of neuroscience, biomedical engineering, computational intelligence, and precision medicine. The manuscript reviews the electromagnetic principles governing TMS-induced electric fields, mathematical and finite-element models of brain stimulation, and the neurobiological mechanisms underlying ASD. It further examines state-of-the-art AI methodologies for optimizing stimulation parameters, identifying treatment-responsive biomarkers, and implementing adaptive closed-loop neuromodulation systems. Current clinical evidence regarding cognitive enhancement, executive function, language development, social behavior, and pediatric safety is critically evaluated. Finally, emerging technologies—including digital twins, multimodal biomarker fusion, federated learning, wearable biosensors, and foundation AI models are discussed as enabling components of next-generation precision neuromodulation. By integrating established clinical knowledge with advanced computational methodologies, this review provides a forward-looking framework for individualized, evidence-based TMS interventions that may improve cognitive function and quality of life for children and adolescents with Autism Spectrum Disorder while identifying key research priorities for future clinical translation. See Figure-1 [1-4].

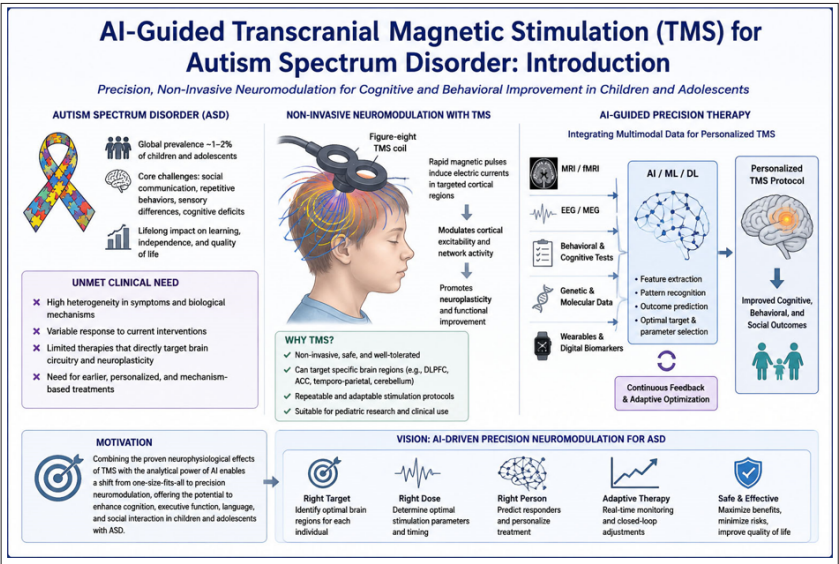


Figure 1: Artificial Intelligence-Guided Precision Transcranial Magnetic Stimulation (TMS) for Autism Spectrum Disorder: A Framework for Personalized Non-Invasive Neuromodulation (**Source:** Image Generation Model DALL·E-class)

This depiction in Figure-1 illustrates the integration of Artificial Intelligence (AI) with Transcranial Magnetic Stimulation (TMS) to provide personalized, non-invasive neuromodulation for Autism Spectrum Disorder (ASD). It highlights how multimodal clinical data are analyzed using AI to optimize stimulation parameters, improve cognitive and behavioral outcomes, and support precision medicine in children and adolescents.

Transcranial Magnetic Stimulation (TMS) activates neural tissue by generating a rapidly changing magnetic field that induces an electric field within the brain. A single magnetic pulse can produce sufficient electrical stimulation to depolarize cortical neurons and initiate action potentials. The extent of neuronal activation depends on the spatial orientation of the induced electric field relative to neuronal structures, particularly axons, which largely determines whether depolarization occurs. The magnitude and distribution of the induced electric field are influenced by the electrical conductivity of different tissue layers, including the scalp, skull, cerebrospinal fluid, gray matter, and white matter. As a result, the strongest electric fields are typically generated in the superficial cortical gyri and the adjacent subcortical white matter.

Both excitatory and inhibitory neuronal pathways are believed to be affected by TMS. The likelihood that an individual axon will generate an action potential depends on several factors, including its geometric orientation, degree of myelination, proximity to the induced electric field, and the neuron’s physiological condition. Neuronal excitability is further influenced by synaptic inputs, intrinsic membrane properties, resting membrane potential, and ongoing firing activity. Computational and biophysical models indicate that TMS preferentially stimulates axonal terminals located around the crowns, lips, and upper surfaces of cortical gyri. In addition, bends and branching points of myelinated axons within the juxtacortical white matter beneath these cortical regions may also be directly activated.

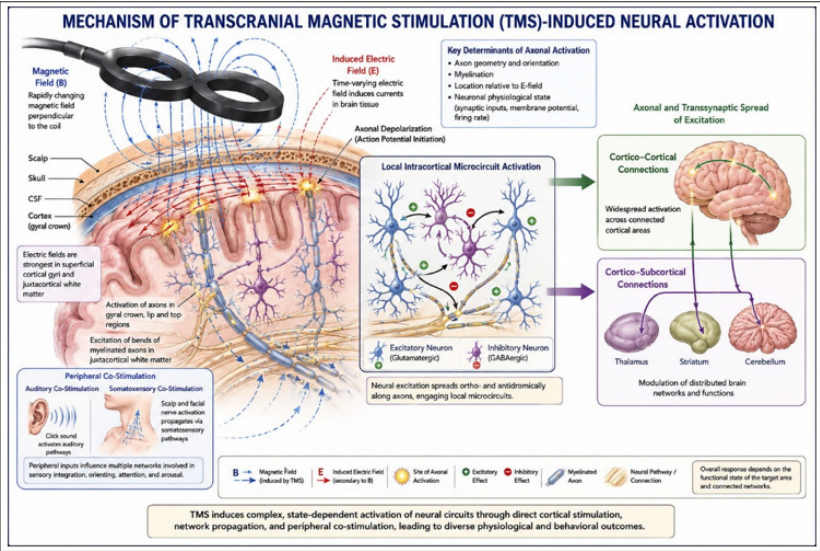


Figure 2: Mechanism of Transcranial Magnetic Stimulation (TMS)-Induced Neural Activation and Network Propagation in the Human Brain (**Source:** Image Generation Model DALL·E-class)

Figure-2 illustrates the fundamental mechanisms of Transcranial Magnetic Stimulation (TMS), showing how a rapidly changing magnetic field induces electric currents that depolarize cortical neurons, activate local microcircuits, and propagate neural activity through cortico-cortical and cortico-subcortical networks. It also highlights the influence of tissue properties, neuronal characteristics, and peripheral co-stimulation on the physiological and functional responses to TMS, providing a comprehensive overview of its neuromodulator effects.

Following the initial excitation, neural signals propagate in both orthodromic and antidromic directions along stimulated axons, triggering secondary activation of interconnected neurons within local cortical microcircuits. This excitation subsequently spreads through cortico-cortical and cortico-subcortical pathways, influencing activity across distributed functional brain networks. The overall neural response depends not only on the physical characteristics of the induced electric field but also on the functional state and excitability of the targeted cortical network at the time of stimulation.

In addition to its effects on the central nervous system, TMS also directly stimulates components of the peripheral nervous system. This peripheral activation generates auditory, tactile, and somatosensory inputs that are transmitted to the brain and can influence multiple neural systems involved in sensory integration, attention, orientation, and arousal. Consequently, the physiological and behavioral effects observed following TMS reflect a complex interaction between direct cortical stimulation, network-level neural dynamics, and peripheral sensory co-activation. A comprehensive understanding of these mechanisms is essential for optimizing TMS protocols, accurately interpreting experimental findings, and further advancing TMS as both a powerful neuroscience research technique and an effective therapeutic modality [5-7].

In summary, Autism spectrum disorder (ASD) is a heterogeneous neurodevelopmental disorder characterized by impairments in social interaction and communication, as well as restricted and repetitive patterns of behavior, interests, and activities. Because ASD manifests differently across individuals, there is considerable variation in symptom severity, cognitive profiles, sensory processing, neural connectivity, and treatment response.

This heterogeneity highlights the need for a more comprehensive and individualized therapeutic framework that considers the clinical, behavioral, sensory, and neurophysiological complexity of the disorder. Transcranial magnetic stimulation (TMS) is a non-invasive neuromodulation technique that has gained considerable attention because of its ability to modulate cortical excitability, promote neuroplasticity, and influence functional brain networks through the application of rapidly changing magnetic fields. However, the substantial variability in ASD presentation and treatment response makes it challenging to apply a single standardized TMS protocol across all individuals. Artificial Intelligence (AI) and Machine Learning (ML) offer promising approaches to address this challenge by analyzing multimodal clinical, behavioral, neuroimaging, and neurophysiological data to support personalized TMS-based interventions. This review examines how AI and ML can be integrated with TMS to identify altered neural circuitry, optimize stimulation targets and treatment parameters, classify patient subgroups, and improve the prediction of individualized therapeutic responses in individuals with ASD.

Fundamentals of TMS

Electromagnetic induction, pulse generators, coil geometries, neuron activation, repetitive TMS, theta burst stimulation, pediatric considerations.

Transcranial Magnetic Stimulation (TMS) is a non-invasive brain stimulation technique that modulates neuronal activity through the principle of electromagnetic induction. A high-current pulse generated by a capacitor-discharge pulse generator flows through a stimulation coil positioned over the scalp, producing a rapidly changing magnetic field. According to Faraday’s law of electromagnetic induction, this time-varying magnetic field penetrates the skull with minimal attenuation and induces an electric field within the underlying cortical tissue. When the induced electric field exceeds the activation threshold of neuronal membranes, it depolarizes cortical axons and initiates action potentials, thereby modulating the excitability of local neural circuits and distributed functional brain networks. The magnitude and spatial distribution of the induced electric field depend on several factors, including coil geometry, stimulation intensity, pulse waveform, tissue conductivity, and the orientation of neuronal fibers relative to the applied magnetic field.

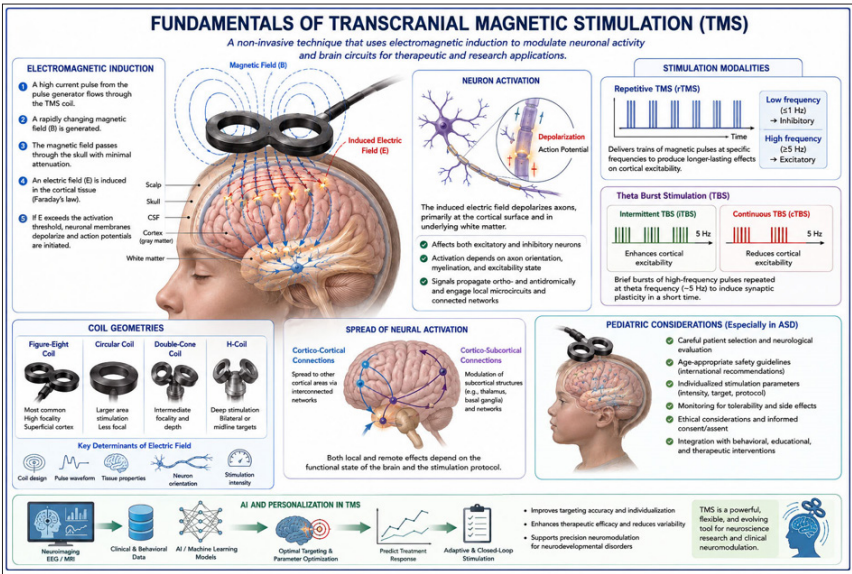


Figure 3: Fundamentals of Transcranial Magnetic Stimulation (TMS): Electromagnetic Principles, Neuronal Activation, Stimulation Modalities, and AI-Guided Precision Neuromodulation (Source: Image Generation Model DALL·E-class)

The application of TMS in pediatric populations, particularly for children and adolescents with Autism Spectrum Disorder (ASD), requires careful attention to safety, ethical considerations, and individualized treatment planning. Appropriate patient selection, comprehensive neurological evaluation, adherence to internationally accepted stimulation guidelines, and continuous monitoring are essential to minimize adverse events while maximizing therapeutic benefit. Recent advances in Artificial Intelligence (AI), Machine Learning (ML), and computational modeling further support personalized TMS by optimizing stimulation targets, predicting treatment response, and adapting stimulation parameters according to each patient's neurophysiological characteristics, thereby advancing TMS toward a precision neuromodulation platform for neurodevelopmental disorders [2,5,6].

Mathematical Model of TMS-Induced Electric Fields

The therapeutic effects of Transcranial Magnetic Stimulation (TMS) are governed by the principles of classical electromagnetism and are commonly analyzed using mathematical and computational models. A rapidly changing current flowing through a figure-eight stimulation coil generates a transient magnetic field that penetrates the scalp and skull with minimal attenuation. According to Faraday's law of electromagnetic induction, the time-varying magnetic field induces an electric field within the brain that is capable of depolarizing cortical neurons when the induced field exceeds the neuronal activation threshold. The relationship is expressed by $\nabla \times \mathbf{E} = -\partial \mathbf{B} / \partial t$, where $\mathbf{E}$ represents the induced electric field and $\mathbf{B}$ denotes the magnetic flux density. The induced current density within biological tissue follows $\mathbf{J} = \sigma \mathbf{E}$, where $\mathbf{J}$ is the current density and σ represents the electrical conductivity of the tissue. These equations form the physical basis for predicting the spatial distribution of electric fields and the resulting neural activation during TMS, as illustrated in Figure-4 [5-8].

Because the human head consists of multiple tissue layers - including the scalp, skull, cerebrospinal fluid, gray matter, and white matter—with different electrical conductivities, accurate prediction of the induced electric field requires advanced Finite-Element Modeling (FEM). Modern computational models employ patient-specific anatomical data obtained from magnetic resonance imaging (MRI) together with anisotropic conductivity tensors derived from Diffusion Tensor Imaging (DTI) to simulate current flow throughout the brain. These personalized head models enable precise estimation of electric field magnitude, current density, and cortical activation patterns, allowing optimization of coil placement, stimulation intensity, and pulse orientation for individual patients. Consequently, computational electromagnetic modeling has become an essential component of AI-assisted precision neuromodulation, supporting individualized TMS treatment planning and improving the accuracy, safety, and therapeutic effectiveness of interventions for Autism Spectrum Disorder [5-8].

Neurobiology of ASD

Excitation/inhibition imbalance, cortical connectivity, DLPFC, anterior cingulate cortex, cerebellum, mirror neuron system, executive dysfunction [3,4,9].

Autism Spectrum Disorder (ASD) is increasingly recognized as a disorder of altered brain network organization rather than a localized structural abnormality. One of the most widely accepted neurobiological hypotheses is an imbalance between excitatory glutamatergic and inhibitory Gamma-Aminobutyric Acid (GABA)-mediated neurotransmission, commonly referred to as the excitation/inhibition (E/I) imbalance. This disruption contributes to abnormal cortical excitability, impaired synaptic plasticity, atypical neural oscillations, and altered information processing, which collectively influence cognition, attention, sensory integration, and social behavior. Functional neuroimaging studies have demonstrated

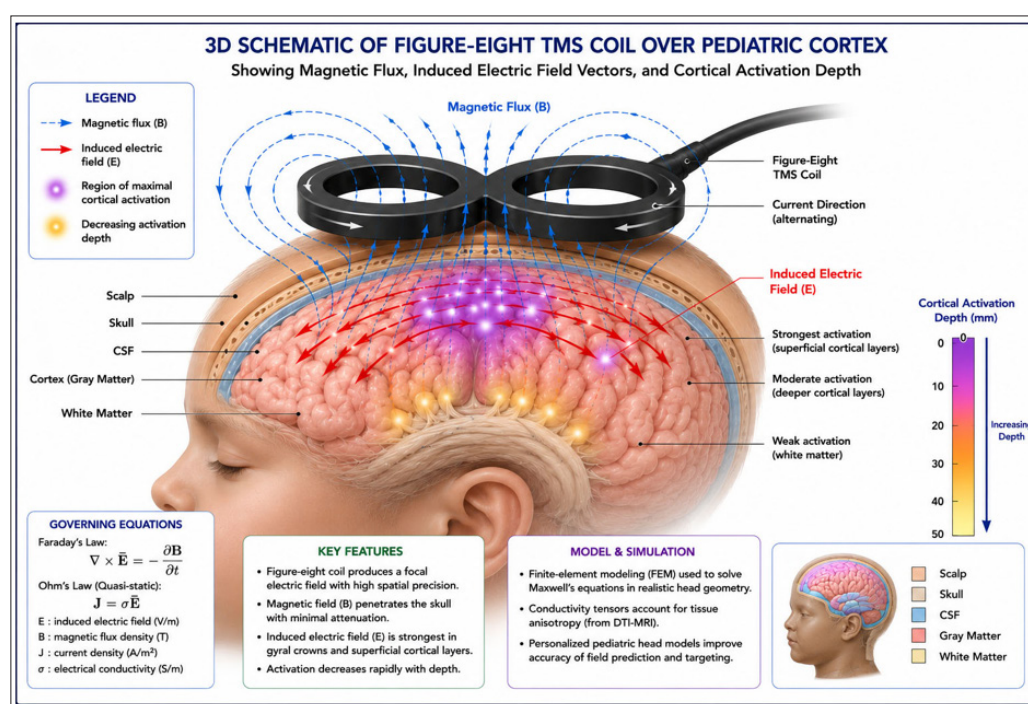


Figure 4: Three-Dimensional Schematic of Figure-Eight Transcranial Magnetic Stimulation (TMS): Magnetic Flux Distribution, Induced Electric Field, and Cortical Activation in the Pediatric Brain (**Source:** Image Generation Model DALL·E-class)

widespread abnormalities in cortical connectivity, characterized by reduced long-range communication between brain regions and excessive local connectivity, resulting in inefficient neural network integration.

Several brain regions play critical roles in the pathophysiology of ASD. The dorsolateral prefrontal cortex (DLPFC) is associated with executive function, working memory, attention, and cognitive flexibility, while the anterior cingulate cortex (ACC) contributes to emotional regulation, conflict monitoring, and decision-making. Altered activity within the cerebellum, traditionally recognized for motor coordination, has also been linked to cognitive processing, language development, and social interaction. Furthermore, dysfunction of the mirror neuron system, particularly within the inferior frontal and parietal cortices, has been proposed as a contributing factor to impaired imitation, empathy, and social communication. Together, these neurobiological abnormalities contribute to the executive dysfunction commonly observed in individuals with ASD, including deficits in planning, behavioral flexibility, inhibitory control, problem-solving, and adaptive decision-making. Understanding these interconnected neural mechanisms provides the scientific foundation for targeted neuromodulation approaches, such as Transcranial Magnetic Stimulation (TMS), aimed at restoring functional brain connectivity and improving cognitive and behavioral outcomes [3,4,9].

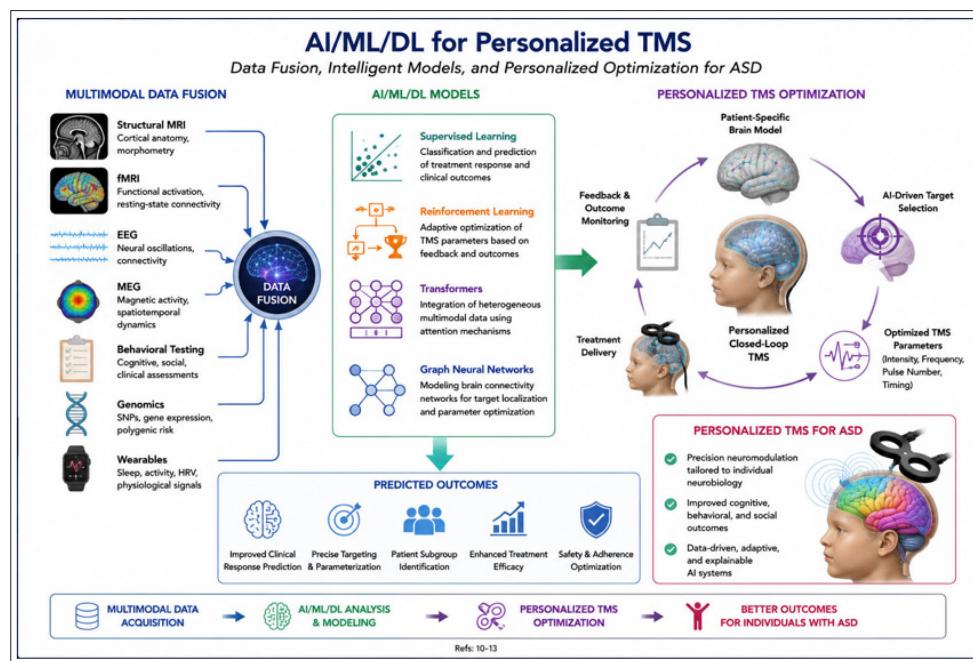


Figure 5: Artificial Intelligence, Machine Learning, and Deep Learning Framework for Personalized Transcranial Magnetic Stimulation (TMS) in Autism Spectrum Disorder
(Source: Image Generation Model DALL·E-class)

Artificial Intelligence, Machine Learning, and Deep Learning for Personalized TMS

Artificial Intelligence (AI), Machine Learning (ML), and Deep Learning (DL) are transforming Transcranial Magnetic Stimulation (TMS) from a standardized neuromodulation technique into a precision medicine approach tailored to the unique neurophysiological characteristics of each individual with Autism Spectrum Disorder (ASD). Modern AI frameworks integrate multimodal data acquired from structural magnetic resonance imaging (MRI), functional MRI (fMRI), electroencephalography (EEG), magnetoencephalography (MEG), behavioral and cognitive assessments, genomic profiles, and wearable biosensors to provide a comprehensive representation of brain structure, function, and clinical status. This data fusion enables the identification of patient-specific biomarkers, characterization of altered neural circuitry, and prediction of treatment response, thereby supporting individualized therapeutic planning [10-13].

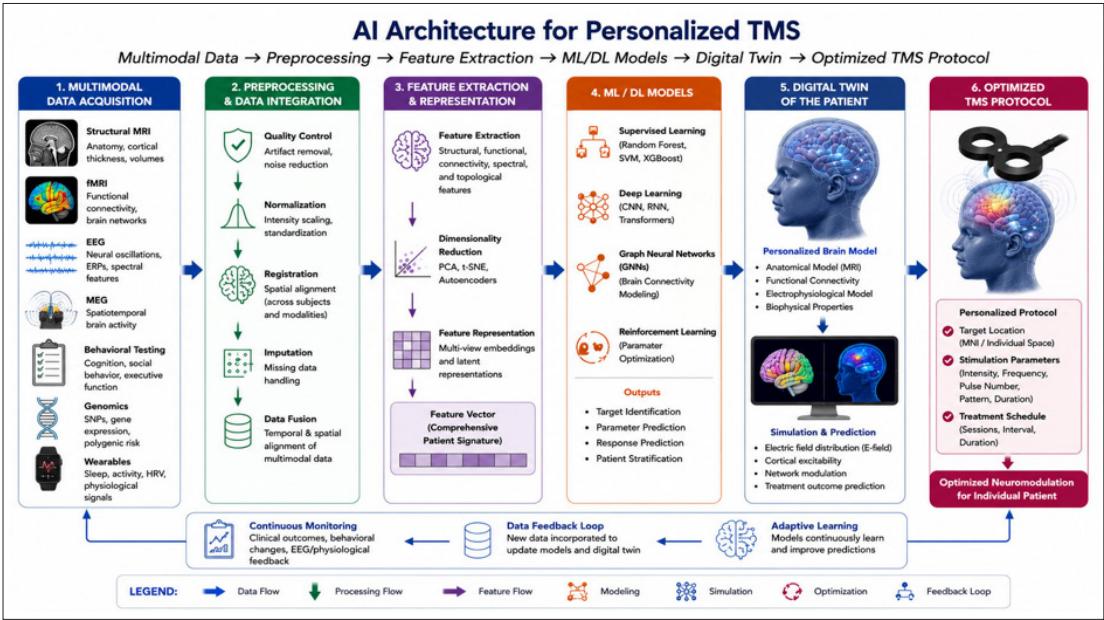


Figure 6: Artificial Intelligence Architecture for Personalized Transcranial Magnetic Stimulation: Multimodal Data Fusion, Machine Learning, Digital Twin Modeling, and Optimized Neuromodulation (Source: Image Generation Model DALL·E-class)

Utilizing Figure-5 and Figure-6, which is depicting advanced ML and DL algorithms play complementary roles in optimizing TMS treatment. Supervised learning models, including Random Forests, Support Vector Machines (SVMs), and Gradient Boosting methods, classify patients and predict clinical outcomes using labeled datasets. Reinforcement learning continuously refines stimulation parameters by adapting to real-time neurophysiological and behavioral feedback, facilitating closed-loop neuromodulation. More recently, Transformer architectures have demonstrated exceptional capability in integrating heterogeneous multimodal data through attention mechanisms, while Graph Neural Networks (GNNs) model the complex functional and structural connectivity of the brain, enabling accurate localization of stimulation targets and optimization of treatment protocols. Together, these AI-driven computational approaches support personalized TMS by improving target selection, stimulation intensity, pulse frequency, and treatment scheduling, ultimately advancing precision neuromodulation and enhancing cognitive, behavioral, and social outcomes for individuals with ASD [10-13].

Comparative ML/DL Algorithms

Selecting the most appropriate Artificial Intelligence (AI) algorithm is critical for optimizing personalized Transcranial

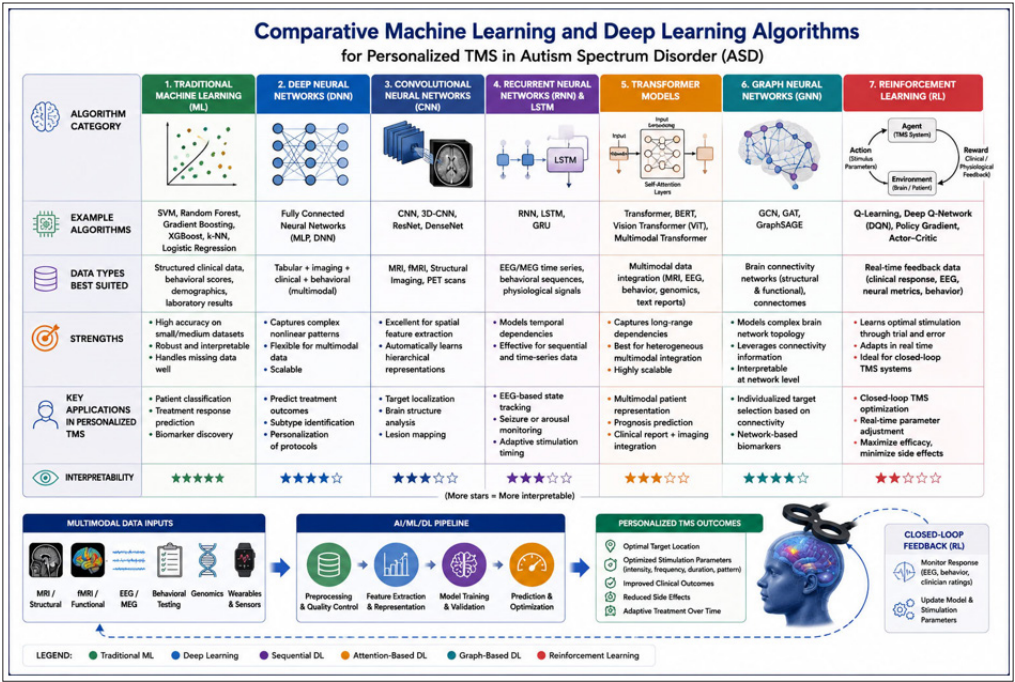


Figure 7: Comparative Analysis of Machine Learning and Deep Learning Algorithms for Personalized Transcranial Magnetic Stimulation in Autism Spectrum Disorder (Source: Image Generation Model DALL·E-class)

Magnetic Stimulation (TMS) in individuals with Autism Spectrum Disorder (ASD). Different Machine Learning (ML) and Deep Learning (DL) techniques offer distinct advantages depending on the type, complexity, and dimensionality of the available data. Conventional supervised learning algorithms, such as Support Vector Machines (SVMs), Random Forests (RFs), Gradient Boosting Machines (GBMs), and Extreme Gradient Boosting (XGBoost), are widely used for patient classification, biomarker identification, and prediction of treatment response because of their high accuracy, robustness, and interpretability when applied to structured clinical datasets. In contrast, Deep Neural Networks (DNNs) and Convolutional Neural Networks (CNNs) are particularly effective for analyzing high-dimensional neuroimaging data, including MRI and fMRI, by automatically extracting hierarchical spatial features associated with altered brain morphology and functional connectivity.

More advanced DL architectures have expanded the capabilities of personalized neuromodulation. Recurrent Neural Networks (RNNs) and Long Short-Term Memory (LSTM) networks effectively model temporal EEG and behavioral data, while Transformer models employ self-attention mechanisms to integrate heterogeneous multimodal datasets with improved contextual understanding. Graph Neural Networks (GNNs) are especially well suited for representing structural and functional brain connectivity, enabling individualized stimulation target selection based on network topology. Furthermore, Reinforcement Learning (RL) continuously adapts stimulation parameters by learning from real-time clinical and neurophysiological feedback, making it particularly valuable for closed-loop TMS systems.

Consequently, combining multiple AI algorithms within a multimodal framework provides the greatest potential for improving patient stratification, optimizing stimulation protocols, predicting therapeutic outcomes, and advancing precision neuromodulation for individuals with ASD. See Figure-7 for holistic and conceptual image for this section.

Closed-Loop Adaptive Transcranial Magnetic Stimulation (TMS)
Closed-loop adaptive Transcranial Magnetic Stimulation (TMS) represents the next generation of precision neuromodulation by continuously adjusting stimulation parameters in response to real-time neurophysiological feedback. Unlike conventional open-loop TMS protocols that use predetermined stimulation settings, closed-loop systems integrate Electroencephalography (EEG) with Artificial Intelligence (AI) to monitor ongoing brain activity and dynamically modify stimulation intensity, frequency, pulse timing, and cortical target selection. This adaptive approach

enables treatment to respond to moment-to-moment changes in cortical excitability and functional brain states, thereby improving therapeutic precision while minimizing unnecessary stimulation. Real-time EEG-driven TMS is particularly promising for individuals with Autism Spectrum Disorder (ASD), where neural activity and cognitive responses can vary considerably across patients and throughout treatment sessions [11-21].

Advanced computational techniques further enhance the performance of adaptive TMS systems. Bayesian optimization efficiently identifies optimal stimulation parameters by balancing exploration of new parameter combinations with exploitation of previously successful treatment responses, thereby reducing the number of experimental trials required. Explainable Artificial Intelligence (XAI) provides transparent decision-making by allowing clinicians to understand the factors influencing AI-generated recommendations, increasing confidence in personalized treatment planning. In parallel, digital twin technology creates a patient-specific virtual model that integrates multimodal imaging, electrophysiological, and clinical data to simulate treatment outcomes before stimulation is delivered. Continuous safety monitoring, including EEG surveillance, physiological measurements, and automated detection of adverse events, further ensures that stimulation remains within clinically acceptable limits. Together, these technologies establish a robust framework for individualized, adaptive, and safe neuromodulation, advancing TMS toward precision medicine for ASD and other neurodevelopmental disorders [11-21].

Clinical Evidence

An increasing body of clinical evidence suggests that Transcranial Magnetic Stimulation (TMS) is a promising non-invasive neuromodulation therapy for improving cognitive, behavioral, and social functioning in individuals with Autism Spectrum Disorder (ASD). Numerous pilot studies randomized controlled trials, and systematic reviews have demonstrated that repetitive TMS (rTMS), particularly when applied to the Dorsolateral Prefrontal Cortex (DLPFC), can reduce repetitive behaviors, enhance executive function, improve attention, and facilitate social communication. These therapeutic effects are believed to result from modulation of cortical excitability, restoration of the excitation/inhibition (E/I) balance, enhancement of synaptic plasticity, and normalization of functional connectivity within distributed brain networks. Although treatment outcomes vary among individuals, many studies have reported significant improvements in cognitive flexibility, working memory, emotional regulation, and adaptive behavior following repeated TMS sessions.

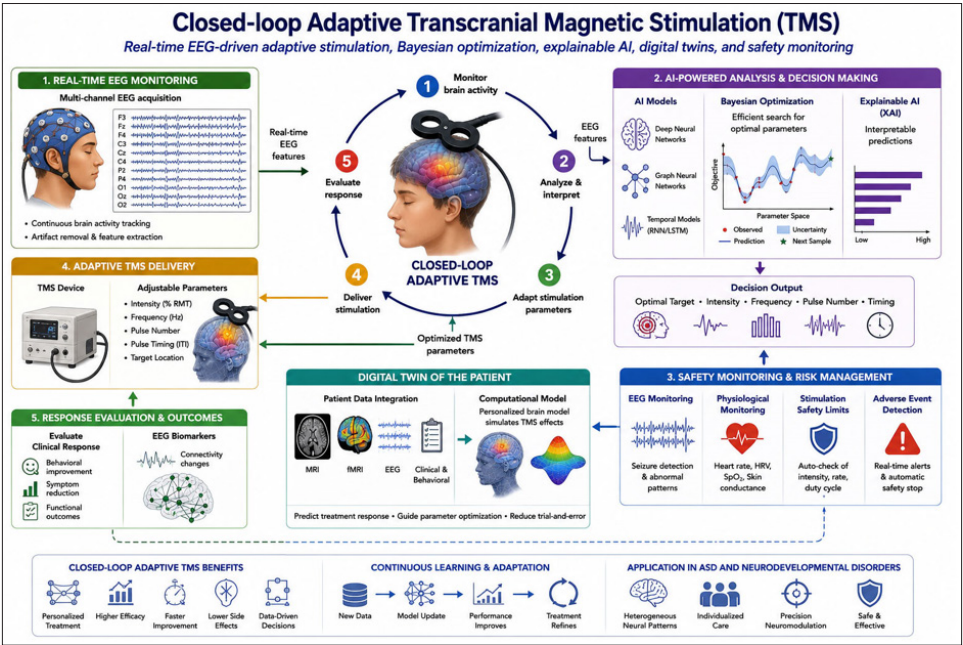


Figure 8: Closed-Loop Adaptive Transcranial Magnetic Stimulation (TMS): AI-Driven Real-Time Neuromodulation, Digital Twin Modeling, and Safety Monitoring
(Source: Image Generation Model DALL·E-class)

The integration of Artificial Intelligence (AI) and Machine Learning (ML) has further strengthened the clinical potential of TMS by enabling personalized treatment planning and response prediction. AI algorithms can analyze multimodal datasets—including structural and functional MRI, electroencephalography (EEG), behavioral assessments, neuropsychological testing, genomic information, and wearable sensor data to identify patient-specific biomarkers and optimize stimulation targets and parameters. Emerging closed-loop TMS systems continuously adapt stimulation based on real-time EEG feedback, while digital twin models simulate individualized treatment responses before therapy is administered, thereby improving precision and reducing trial-and-error optimization. Clinical studies indicate that AI-assisted personalized TMS protocols may achieve greater therapeutic efficacy, fewer adverse effects, and more durable clinical improvements than conventional fixed-parameter stimulation approaches. Nevertheless, larger multicenter randomized controlled trials with standardized protocols, longer follow-up periods, and diverse patient populations are still needed to validate these promising findings and establish AI-guided TMS as a routine precision medicine strategy for ASD.

Future Directions

The future of Artificial Intelligence (AI)-guided Transcranial Magnetic Stimulation (TMS) lies in the development of highly personalized, adaptive, and predictive neuromodulation systems capable of delivering precision therapy for individuals with Autism Spectrum Disorder (ASD). Advances in multimodal neuroimaging, wearable biosensors, high-density electroencephalography (EEG), and continuous physiological monitoring will enable the collection of comprehensive patient-specific data throughout the treatment process. The integration of these heterogeneous datasets with sophisticated AI algorithms, including deep learning, transformer models, and graph neural networks, will improve the identification of neural biomarkers, optimize stimulation targets, and predict individualized therapeutic responses with greater accuracy. In addition, digital twin technology is expected to revolutionize treatment planning by creating virtual patient-specific brain models

that simulate cortical activation, network dynamics, and clinical outcomes before stimulation is administered, thereby reducing trial-and-error approaches and improving treatment safety.

Another important direction is the implementation of fully closed-loop adaptive TMS systems that continuously adjust stimulation parameters based on real-time neurophysiological feedback. Reinforcement learning, Bayesian optimization, and explainable AI (XAI) will enable intelligent decision-making while providing transparent and clinically interpretable recommendations for physicians. Future research should also emphasize multicenter clinical trials, standardized stimulation protocols, long-term safety evaluations, and the development of regulatory frameworks for AI-assisted neuromodulation. Furthermore, the integration of cloud computing, federated learning, and secure digital health platforms will facilitate collaborative research while preserving patient privacy and data security. As computational neuroscience, biomedical engineering, and artificial intelligence continue to evolve, AI-driven precision TMS has the potential to transform the management of ASD by providing individualized, evidence-based therapies that improve cognition, social communication, executive function, and overall quality of life. Continued interdisciplinary collaboration among neuroscientists, engineers, clinicians, and regulatory agencies will be essential for translating these emerging technologies into routine clinical practice.

Conclusion

Artificial Intelligence (AI), Machine Learning (ML), and Deep Learning (DL) are transforming Transcranial Magnetic Stimulation (TMS) into a highly personalized and adaptive neuromodulation therapy for Autism Spectrum Disorder (ASD). By integrating multimodal data from structural and functional neuroimaging, electroencephalography (EEG), behavioral assessments, genomics, and wearable sensors, AI-driven computational models can identify patient-specific neural biomarkers, optimize stimulation targets, and predict individualized treatment responses with greater accuracy than conventional fixed-parameter approaches. Emerging technologies, including digital twins, closed-loop adaptive

TMS, Bayesian optimization, and explainable AI (XAI), further enhance treatment precision by continuously adjusting stimulation protocols according to real-time neurophysiological feedback while maintaining safety and clinical transparency.

Although encouraging clinical studies have demonstrated improvements in cognition, executive function, attention, social communication, and behavioral regulation following personalized TMS interventions, additional large-scale multicenter clinical trials are required to establish standardized treatment protocols and validate long-term efficacy. Future progress will depend on continued collaboration among neuroscientists, clinicians, biomedical engineers, computer scientists, and regulatory agencies to develop robust, interpretable, and ethically responsible AI systems. As computational neuroscience and precision medicine continue to advance, AI-guided TMS has the potential to become a transformative, non-invasive therapeutic platform that significantly improves the quality of life for children and adolescents with ASD while establishing a new paradigm for personalized neurorehabilitation and brain health.

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