

Book Chapter Template**Mitochondrial Dysfunction, Neural Network Dysregulation, and Precision QEEG-Guided Photobiomodulation in Autism Spectrum Disorder**

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Abstract

Autism Spectrum Disorder (ASD) is a heterogeneous neurodevelopmental condition characterized by impairments in social communication, repetitive behaviors, sensory abnormalities, and atypical cognitive functioning. Increasing evidence suggests that ASD involves complex interactions among metabolic, neurophysiological, immunological, and electrophysiological processes, with mitochondrial dysfunction emerging as a potentially important contributor to altered cellular energy metabolism, oxidative stress, neuroinflammation, atypical neural synchronization, disrupted functional connectivity, and large-scale neural network dysregulation.

This chapter examines the relationships among mitochondrial dysfunction, neural network dysregulation, and electrophysiological abnormalities in ASD through the complementary frameworks of quantitative electroencephalography (QEEG) and transcranial photobiomodulation (tPBM). QEEG is reviewed as a non-invasive tool for evaluating cortical functioning, oscillatory regulation, functional connectivity, and large-scale brain network organization, while tPBM is explored as a neuromodulation modality that may influence mitochondrial function, cellular bioenergetics, neuroplasticity, neural synchronization, large-scale network organization, and cortical regulation through stimulation of cytochrome c oxidase within the mitochondrial electron transport chain.

By integrating findings from mitochondrial biology, neurophysiology, network neuroscience, and neuromodulation research, this chapter highlights the potential value of QEEG-guided tPBM as a biomarker-informed precision neuromodulation approach for evaluation, individualized intervention planning, and monitoring of neurophysiological change in ASD. Illustrative adolescent and adult single case studies demonstrate how QEEG biomarkers may be used to identify neurophysiological abnormalities in spectral power, coherence, phase-lag dynamics, hemispheric asymmetry, and functional connectivity while monitoring electrophysiological changes following intervention. Although preliminary findings are encouraging, further controlled research is needed to establish optimal stimulation parameters, clarify underlying biological mechanisms, and determine long-term neurophysiological and clinical outcomes.

Keywords: Autism Spectrum Disorder (ASD); Quantitative Electroencephalography (QEEG); Transcranial Photobiomodulation (tPBM); Mitochondrial Dysfunction; Neural Network Dysregulation; Functional Connectivity; Biomarker-Informed Intervention; Precision Neuromodulation

1. Introduction

Autism Spectrum Disorder (ASD) is a heterogeneous neurodevelopmental condition characterized by impairments in social communication, restricted and repetitive behaviors, sensory abnormalities, and atypical cognitive functioning, affecting approximately 1 in 36 children in the United States [1, 2, 3, 4].

Increasing evidence supports a multifactorial model of ASD involving interacting neurophysiological, metabolic, immunological, and epigenetic mechanisms that influence cortical development and functional brain organization [2, 3, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23]. Among these mechanisms, mitochondrial dysfunction, oxidative stress, neuroinflammation, and altered network organization may contribute to atypical cortical maturation and impaired large-scale neural integration observed in ASD [3, 6, 7, 8, 9, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38].

Current ASD interventions primarily emphasize behavioral and educational approaches, while growing interest has focused on biologically informed neuromodulation methods targeting dysregulated neural connectivity, cortical activity, and mitochondrial dysfunction [1, 4, 29, 30, 31, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48].

Quantitative electroencephalography (QEEG) is a non-invasive method for assessing cortical activity and network organization in ASD [27, 28, 49, 50, 51]. Measures including spectral power, coherence, phase, and phase lag may serve as biomarkers of neural dysregulation [27, 28, 49, 50, 51, 52, 53, 54, 55, 56]. Combined with source-localization methods such as standardized weighted low-resolution electromagnetic tomography (swLORETA), QEEG can identify abnormalities within large-scale functional networks implicated in ASD [24, 25, 26, 27, 28, 51, 57, 58, 59, 60, 61, 62, 63, 64, 65, 55, 56, 66, 67].

tPBM is a non-invasive neuromodulation approach under investigation for its effects on mitochondrial function, neuroplasticity, and neural regulation [29, 30, 31, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48]. Emerging evidence suggests that QEEG-guided tPBM may support individualized neuromodulation and biomarker-informed protocols. This chapter examines the interplay among mitochondrial dysfunction, neurophysiological alterations, and large-scale network dysregulation in ASD, and explores the potential application of QEEG-guided transcranial photobiomodulation (tPBM) as a biomarker-informed precision neuromodulation approach.

2. Multifactorial Pathophysiology of ASD

ASD is increasingly recognized as a multifactorial neurodevelopmental condition involving genetic, metabolic, immune, epigenetic, and environmental influences that affect neurodevelopment and functional brain organization [5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 24, 25, 26]. Mitochondrial dysfunction has emerged as a key mechanism linking altered cellular bioenergetics, oxidative stress, immune dysregulation, and atypical neural connectivity in ASD [6, 7, 8, 24, 25, 26, 54, 68, 69, 70, 57, 71, 72, 73].

2.1 Biological Foundations of ASD



ASD has a highly polygenic architecture involving genes that regulate synaptic function, neuronal excitability, neuroplasticity, and cortical development [5, 21, 22, 24]. Despite their diversity, many genetic influences converge on common mechanisms, including excitation–inhibition imbalance, mitochondrial dysfunction, oxidative stress, and altered neural connectivity [5, 21, 24]. Metabolic abnormalities involving mitochondrial bioenergetics and redox regulation, together with immune dysregulation and epigenetic alterations, may further contribute to abnormalities in neurodevelopment and functional brain organization [7, 54, 68, 11, 12, 13, 14, 15, 16, 17, 18].

2.2 Mitochondrial Dysfunction in ASD

Mitochondria generate adenosine triphosphate (ATP) through oxidative phosphorylation and provide the energy required for neuronal development, synaptic function, and neuroplasticity [6, 54, 71]. Because cortical development depends heavily on efficient energy metabolism, mitochondrial dysfunction may impair neuronal signaling, network maturation, and cortical regulation, particularly during critical developmental periods [6, 24, 70, 71].

Accumulating evidence suggests that mitochondrial abnormalities are present in a substantial subset of individuals with ASD, with estimates ranging from approximately 5% to 30% depending on diagnostic criteria and methods of assessment [6, 7, 54, 68]. Reported findings include abnormalities in electron transport chain complexes I, III, IV, and V, reduced cytochrome c oxidase (Complex IV) activity, altered mitochondrial DNA (mtDNA) copy number and integrity, impaired oxidative phosphorylation, and decreased ATP production [6, 7, 54, 68, 71, 72, 73]. These metabolic abnormalities may increase oxidative stress, reduce cellular resilience, and compromise the high energetic demands required for synaptic transmission, neuroplasticity, and large-scale neural network development [6, 7, 8, 24, 54, 68, 71].

Mitochondrial dysfunction has also been associated with neurological and systemic manifestations frequently observed in ASD, including developmental regression, motor impairment, fatigue, gastrointestinal dysfunction, and increased seizure susceptibility [54, 68]. Collectively, these findings support the view that impaired cellular bioenergetics may represent an important biological contributor to atypical neurodevelopment and altered cortical network organization in subsets of individuals with ASD [6, 7, 8, 24, 25, 26, 54, 68, 69, 70, 57, 71, 72, 73].

2.3 Oxidative Stress and Neuroinflammation

Elevated oxidative stress and impaired antioxidant defenses may contribute to cellular injury and disrupted neuronal signaling in ASD [2, 6, 7, 8]. Chronic neuroinflammation may further impair mitochondrial function and neurodevelopment, creating a self-reinforcing cycle linking metabolic dysfunction, oxidative stress, and altered cortical organization in ASD [8, 9, 10, 11, 12, 13, 14, 15].

2.4 Environmental and Toxicological Contributions



Environmental exposures may further influence neurodevelopmental vulnerability by impairing mitochondrial function, redox regulation, and immune signaling [19, 20]. Toxic metals such as lead, mercury, cadmium, and arsenic have been associated with oxidative stress, impaired mitochondrial enzyme activity, and altered neurodevelopmental functioning [2, 7, 21, 22, 23]. Similarly, mycotoxins may disrupt mitochondrial respiration, glutamatergic signaling, and neuroimmune regulation while contributing to excitotoxicity and synaptic dysfunction [23, 36, 37, 38, 39].

2.5 Clinical Correlates and Biological Heterogeneity

Although the relative contribution of these biological mechanisms varies across individuals, growing evidence suggests that many converge on common pathways involving impaired cellular energy metabolism, neuroinflammation, synaptic dysfunction, and altered neural connectivity [6, 7, 8, 24, 25, 26, 27, 28, 29, 71, 72, 73]. This biological convergence may contribute to abnormalities in neurodevelopment, cortical regulation, neural synchronization, and large-scale network organization observed in ASD [24, 25, 26, 27, 28, 29], supporting the need for biologically informed and individualized approaches to assessment and intervention.

2.6 Emerging Biomarkers and Multimodal Frameworks for Precision ASD

The marked biological heterogeneity of Autism Spectrum Disorder (ASD) has generated increasing interest in objective biomarkers capable of characterizing underlying physiological dysfunction and informing precision-based approaches to assessment and intervention. Although no single biomarker currently demonstrates sufficient sensitivity or specificity for clinical diagnosis [74], accumulating evidence indicates that disturbances across multiple biological systems contribute to distinct ASD phenotypes and may improve biological stratification when integrated with complementary neurophysiological and clinical measures [74].

Research has implicated multiple interconnected biological pathways in ASD, including mitochondrial dysfunction, oxidative stress, immune dysregulation, folate-dependent methylation abnormalities, gut–brain signaling, and neuron-derived extracellular vesicles (EVs). Collectively, these biomarkers provide complementary information regarding cellular bioenergetics, redox homeostasis, immune activation, and neurodevelopment rather than representing isolated pathological mechanisms. Neuron-derived EVs have emerged as particularly promising research biomarkers because they contain proteins, lipids, messenger RNA, microRNA, and other molecular cargo originating from neurons and glial cells, potentially providing a non-invasive window into central nervous system (CNS) molecular processes and partially bridging the longstanding gap between conventional peripheral biomarkers and brain-specific pathophysiology. Importantly, most biochemical biomarkers currently investigated in ASD are measured in peripheral biological samples and therefore may not directly reflect CNS physiology [75]. Although alterations in peripheral glutathione metabolism have been consistently reported [76], recent **in vivo** proton magnetic resonance spectroscopy (^1H -MRS) studies have not uniformly demonstrated corresponding alterations in cortical glutathione



concentrations, highlighting ongoing uncertainty regarding the relationship between peripheral redox biomarkers and central neurobiology [76, 77, 78].

Similarly, resting-state EEG and QEEG measures exhibit substantial heterogeneity across ASD populations. Although recent meta-analyses have identified group-level alterations involving alpha-, theta-, and gamma-band oscillatory activity [79], large-scale investigations demonstrate that individual electrophysiological features generally lack sufficient reproducibility to function as reliable standalone biomarkers [80]. Emerging analyses of the **aperiodic (1/f) component** of the EEG power spectrum may provide complementary information regarding cortical excitation–inhibition dynamics and neuronal population activity; however, these approaches also remain investigational [81, 82, 83].

2.7 Representative Biological Mechanisms Linking Biomarkers and QEEG

Although definitive one-to-one relationships between biochemical biomarkers and QEEG measures have not been established, converging evidence suggests that several biological pathways may influence cortical network organization through shared mechanisms affecting neuronal metabolism, synaptic function, and excitation–inhibition balance.

Mitochondrial dysfunction is among the most consistently reported biological abnormalities in ASD and may provide a mechanistic link between systemic metabolic abnormalities and altered cortical network function. Biomarkers including lactate, pyruvate, carnitine, acylcarnitines, ATP-related metabolites, and mitochondrial DNA (mtDNA) abnormalities reflect impaired oxidative phosphorylation and reduced cellular energy availability [84, 7]. Because fast-spiking parvalbumin-positive interneurons possess exceptionally high metabolic demands, impaired ATP production may preferentially disrupt inhibitory neurotransmission, alter gamma oscillatory synchronization, and contribute to cortical network dysregulation [85]. Consequently, abnormalities in gamma-band activity, functional connectivity, coherence, excitation–inhibition indices, and emerging aperiodic (1/f) measures have been proposed as potential electrophysiological correlates of altered cortical network dynamics, although direct validation in ASD remains limited [86, 83].

Oxidative stress and redox dysregulation represent complementary mechanisms through which systemic metabolic abnormalities may influence cortical physiology [87]. Reduced glutathione (GSH), altered GSH/GSSG ratios, increased reactive oxygen species, and oxidative DNA damage indicate impaired antioxidant defenses. These abnormalities can disrupt mitochondrial function and GABAergic neurotransmission [76, 88]. Experimental studies demonstrate that glutathione depletion preferentially affects parvalbumin interneurons and gamma synchronization [89]. Immune dysregulation and neuroinflammation provide another biologically plausible mechanism linking systemic physiology with cortical network function. Elevated concentrations of IL-6, TNF- α , and IL-1 β have been associated with altered glutamatergic signaling, impaired inhibitory neurotransmission, microglial activation, and changes in synaptic plasticity [90]. Experimental evidence further indicates that inflammatory mediators influence neuronal excitability and cortical oscillatory dynamics, suggesting that chronic



neuroinflammation may contribute to altered electrophysiological activity observed in ASD.

Methylation pathways, micronutrient metabolism, and gut–brain signaling represent additional biological systems capable of influencing cortical development and neuronal function. Altered one-carbon metabolism may affect neurotransmitter synthesis and myelination, whereas gut-derived metabolites may influence neurotransmission through bidirectional gut–brain communication [91]. Preliminary intervention studies suggest that nutritional and microbiome-directed therapies may influence electrophysiological measures, supporting continued investigation of these pathways within multimodal biomarker frameworks; however, electrophysiological correlates remain preliminary and require replication in larger studies.



Biological Pathway	Representative Biomarkers	Proposed Mechanistic Link	Potential QEEG Relevance	Interpretive Status
Mitochondrial dysfunction	Lactate, pyruvate, carnitine, acylcarnitines, ATP-related metabolites, mtDNA abnormalities	Impaired oxidative phosphorylation may reduce ATP availability and preferentially affect metabolically demanding inhibitory interneurons.	Gamma-band synchronization, coherence, functional connectivity, excitation-inhibition indices, and emerging aperiodic 1/f measures	Biologically plausible; direct biomarker-QEEG validation in ASD remains limited
Oxidative stress and redox dysregulation	Reduced GSH, altered GSH/GSSG ratio, increased ROS, oxidative DNA damage	Impaired antioxidant defenses may worsen mitochondrial function and disrupt GABAergic neurotransmission.	Gamma synchronization, cortical excitability, spectral stability, and network timing measures	Supported by experimental models; ASD-specific electrophysiological correlates require replication
Immune dysregulation and neuroinflammation	IL-6, TNF-alpha, IL-1 beta, hs-CRP, inflammatory cytokine profiles	Inflammatory signaling may alter glutamatergic transmission, inhibitory tone, microglial activation, and synaptic plasticity.	Altered oscillatory activity, coherence, phase-lag dynamics, and large-scale network organization	Mechanistically plausible; peripheral markers should not be treated as direct CNS measures
Methylation and micronutrient metabolism	One-carbon metabolism markers, folate and B-vitamin status, methylation-related metabolites	Altered methylation capacity may influence neurotransmitter synthesis, myelination, and neurodevelopmental signaling.	Developmental network organization, connectivity maturation, and spectral regulation	Preliminary; electrophysiological correlates are not yet established clinical biomarkers
Gut-brain signaling and microbiome-related metabolism	Gut-derived metabolites, microbiome profiles, organic acids, inflammatory and metabolic signatures	Bidirectional gut-brain signaling may influence neurotransmission, immune tone, and neuroactive metabolite availability.	Functional connectivity, cortical regulation, and treatment-related electrophysiological change	Emerging area; requires larger multimodal studies and replication
Multimodal biomarker integration	Biochemical markers, QEEG, neuroimaging, HRV, clinical outcomes, and investigational EV or RNA markers	Combined measures may better capture ASD heterogeneity than any single diagnostic biomarker.	Biological stratification, treatment monitoring, and precision assessment frameworks	Promising research framework; clinical utility depends on prospective validation

Table 1. Representative Biological Mechanisms Linking Biomarkers and QEEG Findings in ASD Note.

Peripheral biochemical biomarkers should be interpreted as indirect indicators of systemic physiology rather than direct measures of central nervous system function. Abbreviations: ATP, adenosine triphosphate; ASD, autism spectrum disorder; EV, extracellular vesicle; GSH, reduced glutathione; GSSG, oxidized glutathione; HRV, heart rate variability; hs-CRP, high-sensitivity C-reactive protein; IL, interleukin; mtDNA, mitochondrial DNA; QEEG, quantitative electroencephalography; ROS, reactive oxygen species; TNF- α , tumor necrosis factor- α . * Neuron-derived extracellular vesicles are emerging research biomarkers that may provide a non-invasive "liquid biopsy" of CNS molecular processes but remain investigational[92, 93] ** BDNF is primarily a research biomarker and is not currently established as a diagnostic biomarker for ASD[94, 95] *** Aperiodic (1/f) spectral measures are emerging QEEG metrics that may provide insight into cortical excitation–inhibition dynamics and neuronal population activity but are not currently established clinical biomarkers[86]

Note: Unless otherwise specified, the biochemical biomarkers listed are measured in peripheral biological samples (e.g., blood or urine) and should not be interpreted as direct measures of central nervous system physiology[75]. Current evidence indicates that relationships between peripheral biomarkers and cortical neurophysiology remain incompletely understood, underscoring the importance of integrating biochemical, neurophysiological, and clinical measures when investigating ASD heterogeneity[75].

As summarized in Table 1, ASD is associated with abnormalities across multiple interacting biological systems rather than a single pathological pathway[7]. Mitochondrial dysfunction, oxidative stress, immune dysregulation, altered metabolism, and neurophysiological abnormalities likely interact to influence neuronal energy metabolism, synaptic function, cortical network organization, and behavioral outcomes[96]. Rather than identifying a single diagnostic biomarker, current evidence supports integrating complementary biochemical, neurophysiological, and clinical measures to identify biologically meaningful ASD subgroups and monitor treatment-related neurobiological change. Advances in multivariate analytical approaches integrating biochemical biomarkers, QEEG, neuroimaging, and clinical outcomes may ultimately provide a more comprehensive framework for biological stratification and precision-based assessment in ASD.

3. Neurophysiological Abnormalities in Autism Spectrum Disorder

Neuroimaging and electrophysiological studies consistently demonstrate disrupted oscillatory activity, excitation–inhibition balance, and large-scale connectivity affecting social, executive, sensory, and behavioral networks [24, 25, 26, 27, 28, 29, 30, 31, 49, 50, 51, 52, 53, 54].

3.1 Cortical Dysregulation and Functional Connectivity

ASD is increasingly conceptualized as a disorder of atypical large-scale neural connectivity characterized by reduced long-range integration, excessive local connectivity, and abnormalities involving the Default Mode Network



(DMN), Salience Network (SN), and Frontoparietal Network (FPN) [24, 25, 26, 57, 58]. Electrophysiological studies demonstrate abnormalities in EEG coherence, oscillatory synchronization, and cortical timing that may contribute to impairments in sensory integration, attention, cognitive flexibility, and adaptive information processing [29, 30, 31, 32, 33, 34, 35]. One of the most widely supported neurophysiological models of ASD proposes disruption of excitation–inhibition (E/I) balance, whereby altered glutamatergic and GABAergic regulation impairs cortical synchronization and large-scale network coordination [9, 20, 21, 22, 23, 24, 25, 26]. Dysfunction of parvalbumin-positive interneurons has further been implicated in abnormalities of neural synchronization, sensory processing, and higher-order cognitive functioning [23, 24, 25].

3.2 Functional Brain Networks Implicated in ASD

Network-level abnormalities in ASD involve disturbances within and between major intrinsic brain systems responsible for social cognition, executive control, emotional regulation, and sensory processing [25, 26]. Altered connectivity within the Default Mode Network (DMN), Salience Network (SN), and Frontoparietal Network (FPN) has been associated with impairments in self-referential processing, attentional regulation, cognitive flexibility, and behavioral adaptation [26, 57, 58, 59, 60, 61]. Additional abnormalities involving temporal-limbic circuits, attentional systems, sensorimotor networks, and the mirror neuron system may further contribute to deficits in emotional processing, social communication, sensory integration, and imitation learning [62, 63, 64, 65, 55, 56, 66].

3.3 Electrophysiological Biomarkers in ASD

QEEG studies have consistently identified atypical spectral power distributions and abnormalities in cortical synchronization in ASD [29, 49, 50]. Increased slow-wave activity, particularly within Delta and Theta bands, may reflect delayed cortical maturation and impaired network regulation, whereas abnormalities in Alpha, Beta, and Gamma oscillations suggest disturbances in cortical inhibition, sensory gating, and excitation–inhibition balance [29, 49, 50].

EEG coherence and phase synchronization studies further demonstrate abnormalities in interregional neural communication involving frontal, temporal, and parietal regions [29, 30, 31, 52]. Reduced long-range coherence combined with excessive local synchronization supports developmental disconnection models of ASD characterized by impaired large-scale neural integration [24, 25, 26]. Disturbances in phase synchronization and cross-frequency coupling may impair temporal coordination, multisensory integration, attentional regulation, and cognitive flexibility [29, 30, 31, 52].

Importantly, electrophysiological abnormalities in ASD appear highly heterogeneous and dynamic across developmental stages and behavioral states [24, 25, 26, 29, 30, 31]. Collectively, these findings support the role of QEEG-derived biomarkers in characterizing abnormalities in cortical regulation, neural synchronization, and functional connectivity relevant to ASD pathophysiology and precision-guided neuromodulation approaches.

4. Photobiomodulation in ASD



4.1 Mechanisms of Photobiomodulation

Transcranial photobiomodulation (tPBM) is a non-invasive neuromodulation technique that utilizes red and near-infrared (NIR) light to influence cellular metabolism, mitochondrial bioenergetics, cerebral hemodynamics, and neural activity through multiple photobiological mechanisms [97, 98, 99]. The best-established mechanism involves photon absorption by mitochondrial cytochrome c oxidase (CCO), the terminal enzyme of the electron transport chain and the principal photoacceptor implicated in photobiomodulation [97]. Activation of CCO enhances mitochondrial respiration, oxidative phosphorylation, oxygen utilization, and ATP production, resulting in increased cellular bioenergetic capacity and metabolic efficiency [97, 98, 99]. These effects are accompanied by modulation of reactive oxygen species signaling, nitric oxide release, and downstream transcriptional pathways that support neuronal survival, synaptic function, and activity-dependent neuroplasticity [97, 98, 99].

Emerging evidence indicates that photobiomodulation is not reducible to a single molecular target, and recent mechanistic work specifically demonstrates that 1064 nm light engages cytochrome c oxidase and vascular/hemoglobin-mediated pathways concurrently rather than as mutually exclusive routes. Wang et al. showed that near-infrared laser exposure produces an interplay between up-regulation of cytochrome-c-oxidase and hemoglobin oxygenation, providing foundational evidence that bioenergetic activation and vascular oxygen delivery are coupled phenomena at this wavelength rather than separable mechanisms. Contemporary models extend this framework beyond mitochondrial photostimulation to incorporate membrane-associated receptors and ion channels—including transient receptor potential channels, voltage-gated ion channels, and opsin-family photoreceptors—as well as extracellular redox-sensitive signaling pathways, all of which may contribute to calcium signaling, neurovascular regulation, immune modulation, and large-scale network effects observed following tPBM [97]. Kitchen et al. provided a rationale for 1068 nm photobiomodulation therapy grounded in the engagement of water-gated ion channels and the modulation of heat shock proteins, suggesting that water-mediated photophysics and chaperone-based cellular survival pathways differentiate the longer wavelength from the bioenergetic/vascular axis that dominates at 1064 nm. Although cytochrome c oxidase-mediated bioenergetic enhancement remains the most extensively validated mechanism across the NIR range, growing evidence indicates that the therapeutic effects of tPBM likely arise from coordinated interactions among mitochondrial, vascular, neuroimmune, membrane-mediated, and chaperone-based signaling pathways that vary in their relative weighting by wavelength rather than acting as independent alternatives to a single molecular target.

Wavelength selection is an important consideration in transcranial photobiomodulation because photon transmission through the scalp, skull, cerebrospinal fluid, and cortical tissue varies according to wavelength, irradiance, fluence, beam geometry, tissue optical properties, and individual anatomy [43, 98, 99, 100, 101]. Near-infrared wavelengths between approximately 800 and 1100 nm fall within the biological optical window, allowing relatively deep tissue penetration while maintaining biologically relevant interactions with mitochondrial and non-mitochondrial photoacceptors [102].

Current clinical evidence in ASD is concentrated within the 810–850 nm range, where multiple pediatric and adult studies have reported



improvements in behavioral, cognitive, social, and electrophysiological outcomes—notably the sham-controlled randomized clinical trial by Fradkin et al., the current gold standard for 850 nm tPBM in pediatric ASD, which provides the highest-tier formal sham-controlled RCT evidence for both behavioral and EEG-based brain electrophysiology outcomes in children aged 2–6 years and anchors the 810–850 nm clinical-evidence base above the existing retrospective pediatric home-based protocol [103] and the adult open-label ASD/ADHD study [104]. [104, 105, 103] Computational dosimetry studies further suggest that 810 nm may provide favorable cortical energy deposition under many transcranial conditions. However, recent modeling also demonstrates that intracranial light delivery is strongly influenced by patient-specific variables, including skin pigmentation, melanin content, scalp thickness, skull composition, and tissue optical properties, which may substantially alter wavelength-dependent effects [105] Consequently, wavelength selection cannot be reduced to a simple comparison of penetration depth or cortical energy deposition alone.

Interest in the 1064–1070 nm range derives from its distinct optical and biological properties rather than claims of superiority. Although these wavelengths exhibit greater water absorption than shorter NIR wavelengths, they also demonstrate reduced tissue scattering and may engage additional biological mechanisms beyond classical cytochrome c oxidase activation. Experimental studies have shown that 1064–1070 nm stimulation can increase cerebral blood flow, improve tissue oxygenation, enhance mitochondrial redox metabolism, modulate cortical oscillatory activity, and alter functional connectivity within large-scale brain networks [106, 107] These findings suggest that longer wavelengths may influence brain function through a combination of bioenergetic, vascular, electrophysiological, and network-level mechanisms.

Emerging evidence further indicates that wavelengths within the 1064–1070 nm range may interact with interfacial water, transient receptor potential channels, non-visual opsin pathways, and calcium-dependent signaling cascades, providing potential mechanisms independent of or complementary to cytochrome c oxidase-mediated photobiomodulation [108]. In addition, studies conducted in non-ASD neurological models have reported effects on microglial activation, endoplasmic reticulum stress, dendritic spine preservation, and neuroimmune signaling following 1070 nm stimulation [109]. Although these findings remain preliminary and require direct validation in ASD populations, they suggest that longer wavelengths may engage biological pathways that are not fully captured by conventional mitochondrial models alone.

Accordingly, the rationale for investigating 1064–1070 nm photobiomodulation in ASD is not based on presumed superiority over 810–850 nm protocols but on the possibility that different wavelengths may preferentially influence overlapping yet distinct physiological targets. Determining the relative therapeutic significance of these wavelength-dependent mechanisms will require direct comparative studies incorporating standardized dosimetry, physiological biomarkers, neuroimaging, and electrophysiological outcome measures.

4.2 tPBM Effects on Neurophysiology, Connectivity, and Neuroinflammation



tPBM may influence neural synchronization, functional connectivity, and cortical regulation through its combined effects on mitochondrial bioenergetics, cerebral perfusion, neuroplasticity, and immune modulation [29, 39, 41, 42, 43, 44]. Electrophysiological and neuroimaging studies have demonstrated changes in cortical activity, hemispheric organization, and systems-level coordination following tPBM administration [21, 22, 23, 40, 42, 43, 44]. These mechanisms may be particularly relevant to ASD, where atypical connectivity, impaired network integration, excitation–inhibition dysregulation, and abnormalities in neural synchronization are frequently observed [6, 20, 21, 22, 23, 24, 25, 26].

Experimental and clinical studies further suggest that tPBM may reduce excessive reactive oxygen species (ROS) production, support endogenous antioxidant defenses, attenuate microglial activation, and decrease pro-inflammatory mediators, including interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF- α), and interleukin-1 beta (IL-1 β) [2, 7, 8, 29, 39]. By supporting mitochondrial respiration while reducing oxidative and inflammatory burden, tPBM may promote greater stability of oscillatory activity, improved temporal coordination, improved coordination across distributed neural systems [8, 11, 23, 24, 25, 26, 29, 39].

Enhanced synchronization and network integration may contribute to improvements in sensory gating, attentional regulation, cognitive flexibility, emotional regulation, and adaptive behavior [21, 22, 23, 41, 42, 43, 44]. Collectively, current evidence suggests that tPBM may support improved neural communication and functional network organization in ASD through interconnected effects on cellular metabolism, cortical regulation, and large-scale neural network function [24, 25, 26, 41, 42, 43, 44].

4.3 Safety and Clinical Advantages of PBM

Current evidence suggests that tPBM is a safe, well-tolerated, and non-invasive intervention when administered within established therapeutic parameters [21, 22, 23, 39, 40, 45, 46, 47]. Studies in ASD have reported good treatment compliance and minimal adverse effects, which are typically mild and transient [21, 22, 23, 45, 46, 47]. Its low sensory burden may be particularly advantageous for individuals with ASD who experience sensory sensitivities [21, 22, 23]. However, additional controlled studies are needed to establish long-term safety, optimize stimulation parameters, and characterize response variability across heterogeneous ASD populations [21, 22, 23, 41, 45, 46, 47].

5. QEEG-Guided Precision Neuromodulation

5.1 Neurophysiological Biomarkers and Precision Intervention in ASD

ASD exhibits substantial biological and neurophysiological heterogeneity, with individuals demonstrating diverse patterns of cortical dysregulation and functional connectivity abnormalities [24, 29, 30, 42, 43, 44, 49, 50]. QEEG provides an objective framework for identifying individualized electrophysiological signatures associated with altered cortical regulation and network function [29, 30, 42, 43, 49, 50]. By characterizing these individualized patterns of neural dysregulation, QEEG may support biomarker-informed



assessment, treatment planning, and outcome monitoring within precision neuromodulation frameworks [42, 43, 51].

5.2 QEEG-Guided tPBM Protocol Development

QEEG-guided targeting is based on the identification of individualized patterns of cortical dysregulation and functional connectivity abnormalities. Findings such as excessive theta activity, abnormal beta or high-beta power, hemispheric asymmetries, dysregulated coherence patterns, altered phase-lag dynamics, and abnormalities within large-scale functional networks may help identify cortical regions and networks most likely to benefit from intervention. Source-localization methods such as swLORETA can further assist in identifying dysregulated network hubs and regions demonstrating atypical activation or connectivity. For example, individuals presenting with frontal-executive dysregulation, abnormal default mode network connectivity, or disrupted frontotemporal coherence may receive protocols tailored to address abnormalities within these specific networks while monitoring electrophysiological changes through repeated QEEG assessments [29, 30, 40, 42, 43, 47, 48, 67].

5.3 Clinical Utility of QEEG-Guided PBM

Integration of QEEG biomarkers into tPBM protocols may support individualized treatment planning and objective monitoring of neurophysiological change [42, 43, 51]. Longitudinal QEEG assessments can evaluate changes in spectral power, coherence, phase-lag dynamics, hemispheric asymmetry, functional connectivity, and large-scale network organization, providing objective indicators of treatment response and supporting refinement of stimulation parameters over time [29, 30, 42, 43, 49, 50]. Importantly, QEEG may also facilitate identification of differential response patterns among individuals with ASD, reflecting the substantial heterogeneity of the condition. While some individuals may demonstrate improvements in oscillatory regulation and network integration, others may exhibit more limited or region-specific changes. Repeated neurophysiological assessment may therefore assist in determining whether treatment protocols require modification, continuation, or further optimization. By providing objective measures of cortical function that can be tracked longitudinally, QEEG may contribute to a more adaptive and data-informed approach to neuromodulation and outcome evaluation in ASD [29, 30, 42, 43, 49, 50, 51].

5.4 Illustrative Cases and Electrophysiological Findings

To illustrate the potential clinical applicability of QEEG-guided tPBM, adolescent and adult single case studies are presented. These cases were derived from a pilot exploratory investigation designed to evaluate the neurophysiological effects of 1070 nm tPBM and explore pulsing frequency optimization in ASD. The participants included a 16-year-old adolescent and a 45-year-old adult with ASD Level 1. Both received 10 sessions of whole-head tPBM delivered at 1070 nm and 30 Hz using a programmable Neuronic helmet device for 30 minutes per session, three times per week. The 30 Hz pulsing parameter was selected based on preliminary frequency optimization testing conducted during the pilot phase, which explored the neurophysiological effects of multiple pulsing frequencies.



Preliminary optimization testing evaluated multiple pulsing frequencies, and 30 Hz was selected because it demonstrated favorable electrophysiological responses and good tolerability within the pilot protocol.

Most published transcranial photobiomodulation studies in neurodegenerative and neurodevelopmental disorders have preferentially employed 40 Hz pulsing[105, 110]—the most commonly utilized gamma-frequency protocol in tPBM research[111, 103]—because of its proposed effects on gamma oscillations[112], neural synchronization[113, 114], and microglial function[115]. However, no optimal stimulation frequency for ASD has been established, and whether these findings translate directly to the disorder remains uncertain[116, 105]. During the present pilot investigation, several pulsing frequencies were evaluated using serial QEEG assessments[117], and 30 Hz demonstrated the most favorable combination of electrophysiological response and participant tolerability[31, 118]. Consequently, 30 Hz was adopted for subsequent treatment sessions, shifting from a predetermined standard to an individualized, QEEG-guided parameter[119, 110]. Because 30 Hz remains within the gamma frequency range associated with neural synchronization and network modulation[120], it may offer some of the theoretical benefits attributed to gamma-band stimulation while, in pediatric ASD populations—a clinical context in which sensory hypersensitivity and altered cortical excitability are common clinical features[121, 68, 122]—potentially reducing the likelihood of excessive sensory activation in susceptible individuals[123]. These electrophysiological and tolerability[102] observations, together with the absence of a universally validated optimal frequency and our pilot investigation identifying 30 Hz as yielding the most favorable electrophysiological response and tolerability profile[31, 118], support 30 Hz as a clinically relevant alternative and validate this exploratory, patient-specific methodology over a monolithic treatment approach. Further controlled studies are needed to determine whether specific pulsing frequencies differentially influence clinical outcomes, network connectivity, and treatment tolerability in ASD.

QEEG recordings were obtained before and after intervention using NeuroGuide normative analyses, with outcomes including spectral power, coherence, asymmetry, phase, phase-lag, and functional connectivity measures. Although exploratory in nature, both cases demonstrated convergent electrophysiological changes suggestive of improved cortical organization, neural synchronization, and functional network integration following the 1070 nm, 30 Hz tPBM protocol. These observations are not intended to establish efficacy but rather to illustrate how electrophysiological biomarkers may inform individualized neuromodulation strategies and facilitate monitoring of neurophysiological change over time. Consequently, the present cases should be viewed primarily as proof-of-concept demonstrations illustrating how QEEG-guided parameter selection may inform future optimization of wavelength and pulsing frequency in precision neuromodulation protocols for

Case 1: Adolescent with ASD – Sequential QEEG Absolute Power and



Domain	Baseline	Post-5 Sessions	Post-10 Sessions	14-Day Follow-Up
Delta Activity	Mild diffuse dysregulation	Reduced abnormalities	Further normalization	Maintained
Theta Power	Diffusely elevated, especially frontal-central regions	Reduced elevation	Marked reduction toward normative range	Maintained
Alpha Organization	Reduced and poorly organized	Improved organization	Further normalization and stabilization	Maintained
Beta Power	Elevated across multiple cortical regions	Reduced excess activity	Further reduction toward normative levels	Maintained
High-Beta Activity	Excessive fast-wave activity	Reduced	Markedly reduced	Maintained
Spectral Distribution	Diffuse abnormalities across bands	More organized pattern	Improved frequency differentiation	Maintained
Hemispheric Symmetry	Impaired	Improved	Further improved	Maintained
Overall Cortical Regulation	Dysregulated	Partial normalization	Significant improvement	Maintained

Table 2. Sequential QEEG Absolute Power Findings Following 1070 nm tPBM (30 Hz) in an Adolescent with ASD Interpretation.

The table is based on QEEG maps generated using NeuroGuide Deluxe (Applied Neuroscience, Inc.) and the NeuroGuide normative database. Data are presented as age-normed z-score deviations. Progressive normalization of cortical oscillatory activity was observed across slow- and fast-frequency bands, accompanied by improved alpha organization and hemispheric symmetry. Many changes remained evident at the 14-day follow-up assessment.

Analysis of the sequential QEEG absolute power maps demonstrated progressive reductions in diffuse cortical power abnormalities across delta, theta, alpha, beta, and high-beta frequency bands. Baseline recordings revealed diffuse theta dysregulation, excessive beta and high-beta activity, impaired alpha-band organization, and widespread elevations in spectral power, particularly within frontal and central regions. Following intervention, normative activity patterns expanded across multiple frequency bands, accompanied by improved hemispheric symmetry and more organized spectral distribution. The most notable changes were observed within theta-, alpha-, and beta-band activity, with reductions in excessive fast-wave activity and improved alpha organization. Many of these improvements remained evident at the 14-day follow-up assessment, suggesting greater oscillatory stability and more organized cortical activity following intervention.



Domain	Baseline	Post-5 Sessions	Post-10 Sessions	14-Day Follow-Up
Amplitude Asymmetry	Elevated	Reduced	Further reduction	Maintained
Frontal-Temporal Coherence	Dysregulated	Partial normalization	Improved	Maintained
Alpha-Band Synchronization	Reduced	Improved	Further improved	Maintained
Theta Phase-Lag	Excessive variability	Reduced variability	Further normalization	Maintained
Alpha Phase-Lag	Abnormal timing relationships	Improved	Further improved	Maintained
Functional Connectivity	Diffuse dysregulation	Partial improvement	Improved network organization	Maintained
Neural Synchronization	Impaired	Improved	Further improved	Maintained
Network Integration	Reduced	Improved	Further improved	Maintained

Table 3. Sequential QEEG Connectivity Findings Following 1070 nm tPBM (30 Hz) in an Adolescent with ASD Interpretation.

The table is based on QEEG NeuroGuide-derived z-score maps and illustrates changes in amplitude asymmetry, coherence, and phase-lag dynamics. Connectivity analyses demonstrated progressive improvements in coherence, phase-lag dynamics, hemispheric symmetry, and large-scale network organization, suggesting enhanced cortical timing and functional integration.

Analysis of the connectivity maps demonstrated progressive reductions in amplitude asymmetry, coherence abnormalities, and disrupted phase-lag relationships over time. Baseline recordings revealed frontal-temporal coherence dysregulation, excessive theta- and alpha-band phase-lag variability, impaired large-scale neural synchronization, and hemispheric asymmetry. Subsequent assessments showed fewer abnormal connections, improved hemispheric symmetry, and more organized functional connectivity and coherence patterns. The most prominent changes involved normalization of frontal-temporal coherence, improved alpha-band synchronization, and reduced phase-lag variability. Collectively, these findings suggest improvements in cortical timing, neural synchronization, and large-scale network integration, domains frequently reported as disrupted in ASD. Several of these changes remained evident at the 14-day follow-up assessment, indicating that the observed effects were not limited to the immediate post-stimulation period and may reflect early neurophysiological adaptation.



Objective neurocognitive assessment using CNS Vital Signs demonstrated improvements across multiple cognitive domains following intervention. The most notable gains were observed in complex attention, cognitive flexibility, executive functioning, reaction time, and overall neurocognitive performance, with additional improvements in processing speed and reasoning. Furthermore, both self-report and parent observations indicated improvements in sleep quality, emotional regulation, social responsiveness, and interpersonal communication. The convergence of electrophysiological, cognitive, and behavioral changes suggests potential functional correlates of the observed improvements in cortical organization and network regulation, although these observations should be interpreted cautiously given the exploratory nature of the case.

Table 4. Changes in CNS Vital Signs Neurocognitive Scores Following 1070 nm Transcranial Photobiomodulation

Domain	Pre	Post	Change
Neurocognition Index (NCI)	97	104	+7
Complex Attention	89	117	+28
Cognitive Flexibility	80	101	+21
Executive Function	79	99	+20
Reaction Time	100	112	+12
Reasoning	113	121	+8
Processing Speed	89	95	+6

Note: Positive values indicate improvement relative to baseline performance.

The largest score increases were observed in complex attention, cognitive flexibility, executive functioning, and reaction time, **suggesting possible improvements in attentional control, cognitive adaptability, and executive regulation following intervention.**

Case 2: Adult with ASD – Sequential QEEG Absolute Power and Connectivity Findings

Domain	Initial Baseline	Post-5 Sessions	Post-10 Sessions	14-Day Follow-Up
Delta Activity	Diffuse slow-wave dysregulation	Reduced abnormalities	Further movement toward normative levels	Largely maintained
Theta Power	Elevated across multiple cortical regions	Reduced elevation	Further normalization	Maintained



Alpha Organization	Impaired and poorly organized	Improved organization	More stable and differentiated	Maintained
Beta Power	Diffusely elevated, particularly in frontal and central regions	Reduced excessive activity	Further reduction toward normative range	Largely maintained
High-Beta Activity	Elevated and diffusely distributed	Reduced	Further reduced	Maintained
Frontal-Central Power	Markedly elevated	Partial reduction	Clearer normalization	Maintained
Spectral Distribution	Diffuse abnormalities across frequency bands	More organized frequency distribution	Improved differentiation across bands	Maintained
Hemispheric Symmetry	Reduced	Improved	Further improved	Maintained
Overall Cortical Regulation	Diffusely dysregulated	Partial normalization	Improved oscillatory regulation	Persistent improvement

Table 5. Sequential QEEG Absolute Power Findings Following 1070 nm tPBM at 30 Hz in an Adult with ASD Interpretation.

The table is based on QEEG maps generated using NeuroGuide Deluxe (Applied Neuroscience, Inc.) and the NeuroGuide normative database. Data are presented as age-normed z-score deviations.

Pre- and post-intervention QEEG absolute power findings following 10 sessions of 1070 nm transcranial photobiomodulation (30 Hz pulse frequency) in an adult with Autism Spectrum Disorder (ASD). NeuroGuide-derived z-score maps illustrated changes in spectral power across delta, theta, alpha, beta, and high-beta frequency bands. Data are presented as age-normed z-score deviations. Analysis of the sequential QEEG absolute power maps demonstrated a progressive reduction in diffuse cortical power abnormalities across frequency bands. Baseline recordings revealed widespread elevations in spectral power, particularly within frontal and central regions, accompanied by abnormalities involving slower-frequency activity, impaired alpha organization, and diffuse cortical dysregulation. Following intervention, reductions in excessive power and expansion of normative activity patterns were observed across multiple frequencies, with the greatest changes occurring within slower-frequency and alpha-band activity. Improvements in oscillatory regulation remained evident at the 14-day follow-up assessment, suggesting greater stability of cortical activity and more organized spectral organization following intervention.



Domain	Initial Baseline	Post-5 Sessions	Post-10 Sessions	14-Day Follow-Up
Amplitude Asymmetry	Widespread abnormalities	Reduced asymmetry	Further improvement	Largely maintained
Frontal Connectivity	Dysregulated	Partial improvement	More organized	Maintained
Temporal Connectivity	Dysregulated	Reduced abnormalities	Improved organization	Maintained
Interhemispheric Connectivity	Impaired and unstable	Improved symmetry	Further improved	Maintained
Coherence	Diffusely dysregulated	Reduced abnormal connections	More organized coherence patterns	Persistent improvement
Phase-Lag Dynamics	Abnormal timing relationships	Reduced disturbance	Improved temporal organization	Largely maintained
Default Mode Network	Dysregulated	Partial improvement	Improved organization	Maintained
Mirror Neuron Network	Dysregulated	Partial improvement	Improved functional organization	Maintained
Pain-Related Network Organization	Abnormal	Reduced dysregulation	Improved organization	Maintained
Diffuse Network Instability	Marked	Reduced	Further reduced	Persistent improvement
Large-Scale Network Integration	Impaired	Partial improvement	Improved integration	Maintained

Table 6. Sequential QEEG Connectivity Findings Following 1070 nm tPBM at 30 Hz in an Adult with ASD

The table is based on QEEG NeuroGuide-derived z-score maps and illustrates changes in amplitude asymmetry, coherence, and phase-lag dynamics. Pre- and post-intervention QEEG connectivity findings following 10 sessions of 1070 nm transcranial photobiomodulation (30 Hz pulse frequency) in an adult with Autism Spectrum Disorder (ASD). NeuroGuide-derived z-score maps illustrate changes in amplitude asymmetry, coherence, and phase-lag dynamics. Data are presented as age-normed z-score deviations.

Analysis of the connectivity maps demonstrated progressive reductions in amplitude asymmetry abnormalities, coherence dysregulation, and phase-lag disturbances over time. Baseline recordings showed widespread abnormalities involving frontal, temporal, and interhemispheric connections, accompanied by



diffuse network instability and impaired large-scale communication patterns. Following intervention, a reduction in the density and extent of abnormal connections was observed, accompanied by improved hemispheric symmetry and more organized coherence and functional connectivity patterns. Improvements appeared particularly evident within default mode, mirror neuron, and network organization associated with pain processing, accompanied by reduced diffuse network instability. Many of these changes remained evident at the 14-day follow-up assessment, suggesting persistent improvements in network regulation beyond the immediate treatment period.

Case Synthesis and Summary

Despite differences in age, developmental stage, and baseline electrophysiological presentation, both participants demonstrated convergent improvements in spectral power organization, coherence regulation, phase-lag dynamics, hemispheric asymmetry, and functional connectivity following the 1070 nm, 30 Hz tPBM protocol. Although the specific patterns of dysregulation differed between cases, both demonstrated movement toward more organized cortical activity, improved neural synchronization, and greater large-scale network integration over the course of treatment. Improvements in oscillatory regulation, cortical timing, hemispheric balance, and connectivity patterns were observed across multiple QEEG domains, suggesting greater network stability and improved coordination of large-scale neural communication.

Notably, several electrophysiological improvements remained evident at the 14-day post-treatment assessment in both participants, suggesting that the observed changes were not limited to immediate post-stimulation effects and may reflect early neurophysiological adaptation. The observation of similar neurophysiological trends across adolescent and adult participants suggests that PBM-related changes in cortical network organization may be observable across different stages of development and adulthood.

In addition to the observed electrophysiological changes, preliminary functional improvements were reported across both cases. The adult participant reported improved sleep quality, reduced anxiety, enhanced mood, decreased pain intensity, and reduced tinnitus severity following treatment. In the adolescent case, both self-report and parent observations indicated improvements in sleep quality, emotional regulation, social responsiveness, and interpersonal communication. Objective neurocognitive assessment using CNS Vital Signs demonstrated improvements across attention, executive functioning, cognitive flexibility, reaction time, and overall neurocognitive performance. While these observations should be interpreted cautiously given the exploratory nature of the cases and absence of a control condition, the convergence of electrophysiological, cognitive, and behavioral changes suggests potential functional correlates of the observed improvements in cortical organization and network regulation.

These observations are broadly consistent with proposed neurophysiological mechanisms through which photobiomodulation may influence mitochondrial function, cortical regulation, and neural synchronization [29, 30, 31, 39, 40, 41, 42, 43, 44].



However, the findings should be interpreted cautiously, as the cases are exploratory in nature and cannot establish treatment efficacy or causality. Rather, they illustrate the potential utility of QEEG biomarkers for identifying neurophysiological abnormalities, guiding individualized neuromodulation strategies, and monitoring changes in cortical network function over time. Collectively, these preliminary findings support further investigation of QEEG-guided tPBM in larger controlled studies to determine its clinical relevance, optimal implementation parameters, and long-term effects in individuals with ASD [21, 22, 23, 29, 30, 31, 41, 42, 43, 44, 45, 46, 47, 48].

Across both cases, the most salient electrophysiological changes were observed in coherence regulation, spectral power organization, hemispheric asymmetry, and phase-lag dynamics, collectively suggesting early stabilization of cortical timing and improved large-scale network integration following 1070 nm, 30 Hz tPBM.

Domain	Convergent Findings Across Cases
Spectral Power	Reduction of diffuse power abnormalities across slow frequencies delta and theta, improved alpha organization, decreased high-beta activity, and greater oscillatory stability
Coherence	Improved frontal-temporal coherence regulation and reduced dysregulated connectivity
Phase Lag	Reduced phase-lag variability and improved cortical timing dynamics
Asymmetry	Improved hemispheric symmetry and interhemispheric coordination
Functional Connectivity	Reduced diffuse network instability and evidence of early network reorganization
Follow-Up Findings	Many electrophysiological improvements remained evident 14 days post-treatment, suggesting early stabilization of cortical network function

Table 7. Convergent Electrophysiological Findings Observed Across Adolescent and Adult ASD Cases Following 1070 nm Transcranial Photobiomodulation

Limitations, Future Directions, and Conclusion

The findings presented in this chapter suggest that QEEG-guided tPBM may provide a useful framework for investigating neurophysiological dysregulation and monitoring cortical network changes in ASD. The single case adolescent and adult studies demonstrated convergent improvements in spectral power organization, coherence regulation, phase-lag dynamics, hemispheric asymmetry, and functional connectivity following a 1070 nm, 30 Hz tPBM protocol. The observation of similar electrophysiological trends across an adolescent and an adult participant highlights the potential applicability of this approach across different stages of development.



However, these findings should be interpreted cautiously. The presented cases are exploratory, involve a small sample, lack a sham-control condition, and rely primarily on QEEG-derived biomarkers rather than comprehensive clinical outcome measures. Consequently, the findings cannot establish treatment efficacy, causality, or underlying mechanisms of action. Furthermore, the substantial heterogeneity of ASD, variability in stimulation parameters and study methodologies, and relatively short follow-up period limit generalizability and conclusions regarding long-term clinical significance.

Nevertheless, the convergence of evidence from mitochondrial biology, neurophysiology, and neuromodulation research supports continued investigation of biomarker-informed approaches to ASD. Future research should focus on optimizing stimulation parameters, clarifying biological mechanisms, identifying predictors of treatment response, and evaluating long-term neurophysiological and clinical outcomes. Larger randomized controlled trials employing standardized protocols, multimodal outcome measures, and extended follow-up periods will be necessary to determine the clinical utility, optimal implementation parameters, and long-term effects of QEEG-guided tPBM in heterogeneous ASD populations.

While definitive conclusions await larger controlled investigations, the convergence of findings across mitochondrial biology, cortical network neuroscience, and electrophysiological monitoring suggests that QEEG-guided tPBM may represent a promising precision-neuromodulation framework for investigating individualized interventions in ASD.

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