

Genetic Modulation of Neural Coherence:

An ODTBT-Based Framework for Understanding MTHFR-Linked EEG Endophenotypes in Autism

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Acknowledgments

The author would like to express deep appreciation to the researchers advancing our understanding of genetic modulation, EEG biomarkers, and recursive systems dynamics in autism. Special thanks to Ezedinma et al. (2024) for their insightful work on MTHFR-linked EEG endophenotypes, which served as the catalyst for this response. Gratitude is also extended Dr. Rupert Sheldrake, whose perspectives have inspired ongoing inquiries into the coherence geometry of mind and metabolism. This work is dedicated to all researchers, clinicians, and families seeking deeper clarity into the structure of neurodivergence and the pathways to healing through phase-based integration.

Abstract

This paper presents a transductive interpretation of a genetically linked EEG endophenotype in autism spectrum disorder (ASD), grounded in the Oscillatory Dynamics Transductive-Bridging Theorem (ODTBT). Building on recent findings identifying a 4.5 Hz parieto-temporal rhythm in children with ASD and MTHFR gene variants, we propose that this signal reflects recursive coherence collapse triggered by molecular entropy saturation. ODTBT models biological systems as nested holons that maintain state through phase-regulated feedback. When entropic load, due to impaired folate metabolism or methylation inefficiency, exceeds coherence capacity, a TWIST transition occurs, resulting in observable low-frequency realignment. This paper situates the EEG signature within a structural coherence framework, linking genetic modulation to systems-level phase dynamics. We discuss implications for early detection, phase-informed diagnostics, and coherence-based intervention strategies. In doing so, this work integrates molecular genetics, neuroenergetics, and recursive systems theory to propose a unified model of genotype-phenotype-phase interaction in neurodevelopment.

Keywords:

ODTBT, TWIST mechanism, recursive coherence, MTHFR, EEG, autism spectrum disorder, entropy, neurodevelopment, phase transitions, metabolic modulation

Author's Note

John Surmont is an independent researcher exploring the intersection of quantum mechanics, classical physics, and recursive field dynamics through the ODTBT framework. His work focuses on modeling the transductive structure of phase coherence and transformation across physical, biological, and cognitive systems.

1. Introduction

Autism spectrum disorder (ASD) is increasingly understood as a neurodevelopmental condition shaped by the interplay between genetic susceptibility, metabolic modulation, and systems-level neuroelectrical dynamics. One of the most widely studied genetic variants in ASD is the methylenetetrahydrofolate reductase (MTHFR) gene, particularly the C677T and A1298C polymorphisms, which influence folate metabolism and homocysteine regulation (Li et al., 2020; Mattson & Shea, 2003). These variants are known to affect methylation cycles, neurotransmitter synthesis, and oxidative stress resilience, processes that are foundational to both neural development and bioelectric stability (Homocysteine Review, 2023).

In a recent short report, Ezedinma et al. (2024) identified a distinct electroencephalogram (EEG) rhythm, centered around 4.5 Hz and localized to parieto-temporal regions, in children with ASD who carry MTHFR polymorphisms. This signature, not observed in typically developing children or ASD children without the variant, may represent a genetically modulated endophenotype. Such findings suggest that low-frequency coherence anomalies may offer a window into genotype-phenotype relationships in autism, providing not only diagnostic insight but also a structural bridge between metabolic genetics and large-scale brain dynamics.

This paper presents a formal response to the Ezedinma et al. (2024) study through the lens of the Oscillatory Dynamics Transductive-Bridging Theorem (ODTBT), a first-principles framework that models emergence as a function of recursive phase coherence across nested biological structures. ODTBT introduces the concept of TWIST (Threshold Waveform Interface for State Transformation), a recursive coherence boundary at which structural reorganization becomes necessary due to saturation or misalignment (Surmont, 2024). The TWIST framework provides a transductive alternative to signal-only or representational models by treating molecular dynamics, electrical phase synchrony, and entropy flow as mutually entangled operators of neurocognitive state.

We propose that the 4.5 Hz rhythm observed in this cohort reflects not noise or dysfunction, but a recursive phase collapse, a coherence anomaly that emerges from entropic buildup at the molecular scale and manifests as low-frequency misalignment at the systems level. From this view, MTHFR-associated EEG patterns may represent observable TWIST signatures, in which metabolic load produces transductive phase instability, ultimately affecting cortical integration and perceptual organization.

By uniting genetic modulation, thermodynamic loading, and oscillatory feedback under a single framework, this paper offers a structural model for understanding how coherence architecture may be both genetically modulated and empirically observed, providing a potential way forward for novel strategies in detection, modeling, and recursive intervention.

2. Recursive Coherence and the TWIST Mechanism

The Oscillatory Dynamics Transductive-Bridging Theorem (ODTBT) offers a structural model for understanding emergence as the result of recursive oscillatory dynamics modulated by thermodynamic and informational constraints (Surmont, 2024). In contrast to linear models of signal transmission or computational cognition, ODTBT frames biological systems as nested holons, self-similar, phase-structured entities that maintain coherence across scales through dynamic entrainment and feedback. Coherence, in this context, is not symbolic or representational, but topological, a function of waveform alignment, recursive feedback, and entropy management.

At the heart of this model lies the TWIST mechanism: the Threshold Waveform Interface for State Transformation. TWIST describes the boundary at which a recursive holon exceeds its phase coherence tolerance and must reconfigure. Rather than viewing transformation as a reaction to external force, ODTBT posits that systems evolve through internal coherence saturation, driven by entropic drift, molecular instability, or recursive misalignment. When this saturation occurs, the system undergoes a TWIST: a reorganization of phase structure and coherence hierarchy.

This recursive saturation model aligns with phenomena observed in nonlinear dynamics, including bifurcation theory and attractor shifts (Strogatz, 2018). It also offers a potential useful lens for interpreting brain state changes: transitions between wakefulness and sleep, integration and dissociation, or order and metastability may all reflect recursive readiness crossing a TWIST threshold. Importantly, this threshold is not fixed, but emergent, influenced by thermodynamic loading, entropy accumulation, and system history.

In the context of MTHFR gene variants and ASD, TWIST provides a structural explanation for how molecular-level changes, such as disrupted methylation or impaired folate metabolism, can propagate upward into systemic phase instability. These molecular disruptions increase entropic load and reduce the system's recursive capacity to maintain coherence, potentially inducing premature or prolonged TWIST events in developing neural architectures. The result: observable coherence anomalies, such as the 4.5 Hz EEG signal identified by Ezedinma et al. (2024), which may mark a recursive saturation point manifesting in neuroelectric space.

The TWIST model therefore offers a transductive bridge: a way to move from genotype to phenotype, from metabolic inefficiency to perceptual difference, through a phase-topological grammar of transformation. Rather than treating neural activity as a product of upstream coding or downstream symptomology, ODTBT treats it as a phase signature of recursive coherence architecture, uniquely sensitive to genetic modulation and metabolic strain.

3. MTHFR, Entropy, and Phase Instability

The methylenetetrahydrofolate reductase (MTHFR) gene plays a pivotal role in the one-carbon metabolic cycle, influencing the conversion of homocysteine to methionine, a process essential for DNA methylation, neurotransmitter synthesis, and redox balance (Mattson & Shea, 2003;

Homocysteine Review, 2023). Variants of the MTHFR gene, particularly C677T and A1298C, reduce enzymatic efficiency and have been associated with altered folate metabolism and increased oxidative stress, both of which are implicated in neurodevelopmental disorders, including autism spectrum disorder (ASD) (Li et al., 2020).

The recent study by Ezedinma et al. (2024) identifies a bilateral parieto-temporal 4.5 Hz EEG rhythm in children with ASD who carry these MTHFR variants. This low-frequency activity is accompanied by reduced alpha power, particularly during wakeful eyes-closed states, and was not observed in neurotypical children or in those with ASD who lacked the variant. This finding raises the possibility of a genetically modulated neuroelectric endophenotype, potentially shaped by recursive disruptions in coherence architecture.

From an ODTBT perspective, this phenotype may reflect recursive entropic saturation, a condition in which molecular inefficiencies accumulate phase strain across holonic levels. MTHFR-related disruptions can increase systemic entropy by impeding methylation-dependent neurotransmitter synthesis (e.g., dopamine, serotonin) and increasing inflammatory or oxidative load. These metabolic stressors may not only impair local cellular function but also alter the recursive readiness of neural structures to maintain synchronized coherence.

Phase instability at the molecular level, especially in transmembrane proteins and ion channels, can, over time, induce misalignment in broader oscillatory structures. The 4.5 Hz rhythm may thus reflect a downshifted coherence attractor, wherein the system has reconfigured into a stable but lower-energy state. This aligns with findings that delta and low-theta band dominance are often associated with reduced functional connectivity and state under-integration in ASD (Wang et al., 2013; Sheikhan et al., 2012).

At the same time, alpha suppression, a hallmark of integrative attention and default-mode regulation, may signal that recursive feedback between cortical and subcortical regions has been weakened. The result is not simply an “EEG abnormality,” but potentially a phase signature of transductive collapse, where the system can no longer sustain the recursive alignment required for higher-order state maintenance.

It may be useful to consider the EEG profile observed by Ezedinma et al. (2024) as more than a correlation; it may represent a biophysical expression of recursive strain accumulation, providing a real-time indicator of where metabolic inefficiencies have crossed a TWIST threshold. While further research is clearly needed to clarify causality and generalizability, this line of reasoning may offer a constructive way to integrate genetic, metabolic, and neuroelectric factors into a single systems-level understanding of ASD subphenotypes.

4. Modeling the EEG Endophenotype Through ODTBT

The 4.5 Hz bilateral parieto-temporal EEG rhythm observed in MTHFR-variant ASD children (Ezedinma et al., 2024) may offer a concrete example of a TWIST-induced state reorganization. Rather than interpreting this signal as a dysfunction in isolation, the Oscillatory Dynamics

Transductive-Bridging Theorem (ODTBT) suggests that such patterns represent a recursive attractor basin, an alternative phase configuration resulting from coherence saturation across holonic levels.

In ODTBT, EEG signals are not merely reflections of localized cortical activity but are emergent products of nested oscillatory interactions, where molecular, cellular, and systemic coherence interact recursively. When entropy accumulates at lower structural levels, due to genetic, metabolic, or thermodynamic stress, recursive strain may propagate upward, destabilizing coherence in meso- and macro-scale neural networks. The result is a shift in the system's dominant waveform, visible in altered power spectra or phase-locking behavior across cortical regions.

The emergence of a stable, low-frequency 4.5 Hz rhythm may reflect a system-wide realignment into a subcoherent mode, in which energy is distributed differently across temporal domains. In other words, this pattern is not random, but a stable state resulting from recursive reconfiguration. In TWIST terms, this EEG signature may represent a post-saturation attractor, a phase-space minimum that the system has adopted following the collapse of a higher-bandwidth coherence regime.

Simultaneously, the observed suppression of alpha power, typically associated with default mode network (DMN) regulation, sensory inhibition, and relaxed wakefulness, suggests a loss of functional top-down coherence. This may indicate a failure of recursive coupling between subcortical and cortical structures, or between network layers such as the thalamus and prefrontal cortex (Helfrich & Knight, 2016). From the ODTBT standpoint, this alpha suppression is not a side effect, but a direct consequence of phase instability that follows recursive misalignment.

Crucially, this pattern may be predictive. If such phase-state configurations are indeed recursive signatures, they could serve as biomarkers of coherence topology, mapping where in the phase hierarchy the system has reorganized. This invites new approaches to classification, early detection, and intervention, particularly in children with known metabolic-genetic vulnerabilities such as MTHFR C677T/A1298C.

In this view, EEG becomes not simply a diagnostic tool, but a structural readout of recursive phase readiness. Interventions, whether nutritional (e.g., folate supplementation), neurofeedback-based, or neuromodulatory (e.g., tACS), could be used to target specific phase domains, potentially guiding the system back toward higher-coherence configurations. While such possibilities remain exploratory, the ODTBT framework offers a coherent structure in which to interpret and test them.

5. Implications for Early Detection and Personalized Intervention

The identification of a 4.5 Hz EEG rhythm uniquely associated with MTHFR gene variants in children with ASD (Ezedinma et al., 2024) presents a valuable opportunity to consider new frontiers in early detection and individualized care. Interpreted through the lens of the Oscillatory

Dynamics Transductive-Bridging Theorem (ODTBT), this neuroelectric signature may serve not merely as a marker of risk, but as a coherence topology diagnostic, reflecting phase misalignment across holonic levels of biological structure.

If EEG patterns are indeed reflective of recursive saturation or TWIST-induced state transitions, then they may also be used to identify where a system is operating within a suboptimal attractor basin. Such attractors, while metabolically stable, may constrain cognitive integration, sensory processing, or adaptive responsiveness. The potential to track or even anticipate these configurations may support earlier identification of subphenotypes that are not always detectable through behavioral screening or static genetic analysis alone.

Moreover, the fact that the 4.5 Hz signal appears only in children with both ASD and MTHFR variants suggests a relationship between genetic predisposition and neural phase behavior. This underscores the value of cross-modal stratification, combining genotyping, EEG, and potentially metabolic biomarkers (e.g., homocysteine, folate levels) to develop a phase-informed diagnostic profile.

Such a profile could inform intervention strategies. For example:

- Folate supplementation or metabolic support may reduce molecular entropy accumulation in children with MTHFR variants, potentially stabilizing coherence at the subcellular or proteomic level (Mattson & Shea, 2003).
- EEG-based neurofeedback may help entrain the system toward higher-frequency coherence attractors, reinforcing recursive alignment and improving functional integration (Wang et al., 2013).
- Non-invasive neuromodulation (e.g., tACS or rTMS) could be calibrated to the TWIST-sensitive bandwidth, potentially reversing or softening phase collapse at specific cortical hubs (Freedman et al., 2024; Helfrich & Knight, 2016).

Importantly, these approaches should not be viewed as deterministic or curative. Rather, they offer potential pathways for restoring phase flexibility, improving recursive resilience, and enabling systems that have reorganized under strain to return to more integrative coherence architectures. Phase-based modeling, such as that provided by ODTBT, may help identify the recursive leverage points where modulation has the highest likelihood of effectiveness.

In this sense, TWIST-informed endophenotyping may help guide not only when and how to intervene, but also why intervention might fail without recursive awareness of coherence topology. A low-frequency EEG signature is not simply a biomarker, it may be a recursive call to reorganize, signaling that phase readiness has fallen below the coherence threshold required for stable perception, learning, or self-regulation.

6. Conclusion

This paper has presented a transductive analysis of a genetically-linked EEG endophenotype in autism spectrum disorder (ASD), using the Oscillatory Dynamics Transductive-Bridging Theorem (ODTBT) to reinterpret a 4.5 Hz signal not as dysfunction, but as a phase-state signature of recursive coherence collapse. Grounded in recent findings by Ezedinma et al. (2024), this signal, observed in ASD children with MTHFR gene variants, may represent a TWIST-mediated attractor basin, one that emerges from metabolic-phase saturation and manifests in neuroelectrical space.

By integrating insights from folate metabolism, thermodynamic stress, EEG dynamics, and recursive field theory, ODTBT offers a framework that links genotype, molecular entropy, and brain-state transitions within a unified coherence architecture. This approach reframes neuroelectric anomalies as dynamic markers of recursive saturation, providing both a theoretical grammar and a set of empirical hypotheses to guide future study.

Importantly, this framework does not presume causality where none has been established. Rather, it seeks to clarify how structural coherence breakdown might propagate upward through holonic scales, influenced by inherited metabolic inefficiencies and resolved through systems-level reorganization. The TWIST mechanism may help explain how and when these transitions occur, and how they might be modulated through targeted intervention.

If validated through further interdisciplinary research, this approach may support the emergence of new diagnostic and therapeutic strategies. EEG coherence mapping, when combined with genotyping and metabolic profiling, may help identify phase-state vulnerabilities early in development. More speculatively, interventions rooted in phase entrainment, whether nutritional, electrical, or behavioral, may assist in stabilizing recursive readiness, enabling more integrated developmental trajectories in children at risk.

Ultimately, the model proposed here invites a broader reconsideration of how structure, function, and transformation interrelate across the brain-body-environment system. As we refine our understanding of coherence architecture, the challenge ahead is not only to detect recursive failure, but to develop interventions that restore phase integrity, at the molecular level, the cognitive level, and the deeply relational level where emergence truly unfolds.

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