OPEN ACCESS Freely available online

Theme: Child and Adolescent Mental Health: Current Challenges and Innovations

Theoretical Article (Hypothesis & Theory) Vol. 2, Special Iss. 1, July-December 2026 | ISSN: 3107-9024

Journal of Psychiatry and Psychological Sciences

Observer-Agent Divergence: A Developmental Systems Hypothesis Integrating Attachment, Neuroimmune Regulation, and Caregiver Co-Regulation in Autism Spectrum Disorder

Adam David Kain[1*], **Marcia Maia**[2]

[1]*Independent Research, Melbourne, Kulin Nation, Australia*
[2]*Independent Researcher, Neuroimmunology and Psychiatry, Manaus, Brazil*

[*]**Correspondence to:** Adam David Kain, Independent Research, Melbourne, Kulin Nation, Australia, E-mail: adam.d.kain@gmail.com

Received: July 06, 2026; **Manuscript No:** JPPC-26-4819; **Editor Assigned:** July 09, 2026; **PreQc No:** JPPC-26-4819 (PQ); **Reviewed:** July 27, 2026; **Revised:** August 18, 2026; **Manuscript No:** JPPC-26-4819 (R); **Published:** August 27, 2026

Citation: Kain AD, Maia M (2026). Observer-Agent Divergence: A Developmental Systems Hypothesis Integrating Attachment, Neuroimmune Regulation, and Caregiver Co-Regulation in Autism Spectrum Disorder. J. Psychiatr. Psychol. Sci. Vol.2 Special Iss. 1 August (2026), pp:1-9

ABSTRACT

Background

Autism Spectrum Disorder (ASD) presents with significant heterogeneity in outcomes, particularly regarding emotional and behavioural dysregulation. Despite advances in early intervention, a substantial subset of autistic children continues to experience persistent emotional-behavioural problems (EBPs) that peak in middle childhood and contribute to caregiver burnout and reduced quality of life.

Aims

This paper addresses a specific question: Why do some autistic children develop persistent emotional dysregulation while others, with comparable cognitive and diagnostic profiles, do not? We propose a developmental systems hypothesis that integrates attachment theory, neuroimmune regulation, and caregiver-child dynamics to offer a candidate explanation.

Hypothesis

We introduce the construct of Observer-Agent Divergence (OAD) the systematic misalignment between the behavioural meaning inferred by external observers (caregivers, clinicians) and the internal, predictive modelling priorities governing the child's neurocognitive state. We distinguish acute OAD (normative, often repaired) from persistent or unrepaired OAD, and hypothesise that the latter functions as a relational stressor. Via established pathways linking early relational adversity to pro-inflammatory programming (elevated IL-6, CRP), persistent OAD may contribute to a self-reinforcing cycle of dysregulation, threat-hyperreactivity, and impaired social cognition in vulnerable autistic children.

Innovation

We propose a clinically modest, complementary intervention architecture: The Relational Entropy Audit and Consistency in Safety Protocol. This approach trains caregivers to identify their own subtle affective signals, replace anxiety-driven interventions with disciplined, low-arousal environmental stability, and implement explicit acceptance signaling. The protocol is designed to complement existing developmental and behavioural interventions by targeting the relational environment as a modifiable determinant of inflammatory and neural regulation.

Methodological Approach

This paper presents a conceptual synthesis rather than an empirical study; no primary participant sample was recruited. The hypothesis was developed through a targeted narrative synthesis of literature across attachment theory, predictive processing, and neuroimmunology, selected for direct relevance to caregiver-child affective signaling and inflammatory pathways in ASD (see Methods: Conceptual Synthesis Approach).

Research Agenda

We outline specific, testable predictions including biomarker validation, neuroimaging studies, longitudinal mediation models, and pilot randomised controlled trials that would substantiate or falsify the hypothesis.

Recommendations

We recommend that biomarker validation (Prediction 1) and open-label feasibility piloting of the Consistency in Safety Protocol precede any randomised controlled trial, and we identify longitudinal mediation and neuroimaging studies as priority areas for future research (See Recommendations and Priorities for Future Research).

Conclusion

If validated, this framework would reframe a subset of ASD-related dysregulation not as an intrinsic deficit, but as an environmentally-modulated signal of relational entropy, demanding not suppression of the child's alarm signals, but disciplined recalibration of the relational field.

Keywords:

INTRODUCTION

Child and adolescent mental health face a persistent challenge: despite increasing diagnostic precision and a proliferation of early interventions, a substantial proportion of autistic children continue to experience significant emotional and behavioral dysregulation that peaks in middle childhood (ages 8–10) and remains resistant to treatment [1,2]. Current models, predominantly behavioral and cognitive in orientation, have demonstrated efficacy for some outcomes, yet they do not adequately explain the marked heterogeneity in trajectories observed across individuals with comparable diagnostic profiles.

This paper addresses a focused, clinically relevant question: Why do some autistic children develop persistent emotional dysregulation while others, with similar cognitive and diagnostic characteristics, do not?

We propose a candidate explanatory framework situated within developmental systems psychiatry an approach that treats mental health outcomes as emergent properties of dynamic interactions between biological predispositions, relational environments, and socioecological contexts [3]. Rather than proposing a novel aetiology for ASD itself, we hypothesise that specific patterns of caregiver-child interaction particularly those characterised by subtle affective discordance and failures of repair may influence the developmental trajectory of dysregulation in genetically and neurocognitively vulnerable children.

Our central construct, Observer-Agent Divergence (OAD), provides a formal language for describing a phenomenon widely observed in clinical practice but rarely operationalised in research: the gap between how a child's behaviours is perceived and managed externally, and the internal predictive processes driving that behaviours. We then integrate OAD with established evidence linking early relational stress to neuroimmune programming, proposing a testable biological pathway for the observed stability and treatment resistance of dysregulation in a subset of autistic youth [4-5].

We conclude by outlining a clinically modest but empirically rigorous intervention protocol designed to reduce persistent OAD by training caregivers in somatic regulation and disciplined non-intervention not as a standalone treatment, but as a complement to existing developmental and behavioral supports.

Scope of the Study

This paper is a theoretical and hypothesis-generating work; it does not report primary empirical data. Its scope is deliberately bounded in four respects. First, it addresses a specific subset of autistic children those exhibiting persistent, treatment-resistant emotional and behavioural dysregulation despite comparable cognitive and diagnostic profiles to peers without such trajectories and does not claim generalisability to all autistic individuals. Second, it does not propose an aetiological account of Autism Spectrum Disorder itself; ASD is treated as a pre-existing neurocognitive profile that may confer differential vulnerability to relational stress, not as an outcome of caregiving. Third, the paper is confined to a single candidate mechanism persistent, unrepaired Observer-Agent Divergence and its proposed neuroinflammatory sequelae among the many biological and environmental factors known or hypothesised to contribute to EBP trajectories in ASD (sensory processing differences, structural connectivity, genetic loading, socioeconomic stress). Fourth, the Relational Entropy Audit and Consistency in Safety Protocol are presented as a complementary, adjunctive intervention architecture requiring independent feasibility and efficacy testing (Section: Implementation Science Considerations, Predictions 1–5, Section: A Research Agenda: Specific, Testable Predictions); they are explicitly not proposed as a replacement for established behavioral, developmental, or pharmacological interventions, nor as a clinical recommendation at this stage.

Significance of the Study

Persistent emotional and behavioral dysregulation in ASD carries substantial costs: it is associated with caregiver burnout,

school placement instability, and elevated risk of psychiatric comorbidity [6], yet current behavioral and cognitive intervention models do not adequately explain why children with comparable diagnostic and cognitive profiles follow markedly different trajectories. This study is significant for three groups. For clinicians and allied health practitioners, it offers a mechanistic, testable account of caregiver-child interaction Observer-Agent Divergence that could refine existing behavioral and developmental interventions rather than replace them. For caregivers, the framework offers a non-blaming, destigmatising reframe: dysregulation is proposed as an environmentally-modulated stress response amenable to relational recalibration, not as evidence of caregiver failure or an immutable characterological deficit in the child. For the research community, the paper proposes a specific, falsifiable biological bridge linking subtle caregiver affective signaling to pro-inflammatory programming and neural connectivity changes that has not, to our knowledge, been formally articulated or tested in ASD cohorts, and it generates five a priori predictions (Section: A Research Agenda: Specific, Testable Predictions) intended to guide biomarker, neuroimaging, longitudinal, and trial-based research.

Methods: Conceptual Synthesis Approach

This paper does not involve primary data collection, human participants, or a defined clinical sample; accordingly, "methods" here refers to the literature synthesis procedure used to construct the Observer-Agent Divergence framework, consistent with conventions for Hypothesis and Theory articles.

Literature Selection Strategy

Relevant literature was identified through targeted, iterative searches across three converging domains: (a) attachment theory and caregiver-child interaction research, (b) predictive processing and mentalization accounts of autism, and (c) neuroimmunology and psychoneuroimmunological research linking early relational stress to inflammatory programming. Searches were conducted using standard academic databases (PubMed, PsycINFO, and Google Scholar) supplemented by reference-tracing from key theoretical sources (e.g., Winnicott, Fonagy, Feldman, Sameroff) and recent (2020–2026) empirical and meta-analytic literature on cytokine profiles, neuroinflammation, and emotion dysregulation in ASD.

Inclusion Logic

Sources were selected for direct conceptual or empirical relevance to one of three functions within the argument: (i) establishing the clinical problem (persistence and heterogeneity of EBPs in ASD), (ii) supporting the biological plausibility of a relational-stress-to-inflammation pathway, or (iii) situating OAD relative to existing theoretical constructs (mentalization, biobehavioral synchrony, transactional models) to establish its distinct contribution rather than duplication of prior work (Section: OAD in Relation to Established Constructs).

Construct Derivation ("Sampling" of Theoretical Domains)

The Observer-Agent Divergence construct was derived through cross-domain synthesis rather than induction from a dataset. Three literatures were deliberately drawn together: developmental object relations and attachment repair theory (providing the acute/persistent distinction, Section: Acute versus Persistent OAD: The Role of Repair), predictive processing accounts of autistic cognition (providing the internal-agent model, Section: The Internal Agent (The Predictive Modelling Lens)), and psychoneuroimmunology (providing the proposed biological pathway, Section: A Developmental Systems Hypothesis: Integrating Attachment and Neuroimmune Regulation). This cross-domain method is standard for theory-building papers in developmental systems psychiatry and is presented here explicitly so that the construct's evidentiary basis and its limits are transparent to the reader [6].

Analytic Approach

No statistical analysis was performed. The analysis undertaken was conceptual and integrative: identifying convergence and gaps across the three literatures above, and translating that convergence into (a) a formal construct definition (Section: The Observer-Agent Divergence (OAD) Construct), (b) a testable biological hypothesis (Section: A Developmental Systems Hypothesis: Integrating Attachment and Neuroimmune Regulation), and (c) a set of falsifiable, quantifiable predictions (Section: A Research Agenda: Specific, Testable Predictions) suitable for future empirical evaluation. This approach follows established conventions for hypothesis-generating and theory-building manuscripts, which are evaluated on internal coherence, consistency with existing evidence, and generativity of testable predictions rather than on statistical inference from a sample [7].

The Observer-Agent Divergence (OAD) Construct

A primary limitation of current diagnostic and therapeutic frameworks is their reliance on externally observable behaviours as proxies for internal states. This is particularly problematic in ASD, where the child's internal processing architecture characterised by heightened perceptual sensitivity, systemising tendencies, and a preference for predictability may systematically diverge from neurotypical communicative and affective norms.

We formally define the central construct as follows:

Observer-Agent Divergence (OAD): The systematic discrepancy between (a) the behavioural meaning, affective valence, or motivational state inferred by an external observer (caregiver, clinician, teacher) based on observable phenomena, and (b) the actual predictive modelling demands, sensory processing requirements, or adaptive resource allocation governing the child's internal neurocognitive state at that moment.

The External Observer (The Behavioral Lens)

External observers particularly caregivers under chronic stress operate under time constraints and conditioned neurotypical expectations. They map the child's rapid shifts, avoidant gaze, or repetitive movements onto familiar behavioral categories: dysregulation, non-compliance, social deficit. The observer does not have direct access to the child's internal predictive load. As a result, interventions are often deployed to suppress the observable behaviours (e.g., redirecting stimming, demanding eye-contact) without addressing the internal variable (e.g., sensory overload, predictive processing demands).

The Internal Agent (The Predictive Modelling Lens)

Internally, the autistic child is frequently engaged in demanding ongoing predictive inference attempting to generate accurate predictions about sensory input, environmental predictability, and social contingencies. Behaviours that appears "erratic" or "fragmented" to the observer may reflect the child's adaptive allocation of cognitive resources to resolve a specific predictive challenge, rather than a failure of regulation. A behavioral "switch" (e.g., sudden withdrawal) is not a change in who the child is, but a shift in where computational resources are allocated.

OAD in Relation to Established Constructs

Observer-Agent Divergence shares conceptual territory with several established frameworks, yet differs in important respects:

- Predictive processing accounts emphasise the child's internal prediction errors. OAD extends this by focusing on the external observer's misattribution of those prediction errors a relational, rather than purely cognitive, phenomenon [8].
- Mentalization concerns the capacity to interpret one's own and others' mental states. OAD describes a systemic failure in this interpretation between agents, not a deficit within either agent individually [9].
- Caregiver attunement and interpersonal synchrony refer to the temporal coordination of behaviour and physiology. OAD captures semantic misalignment the observer's incorrect inference about the meaning of the child's state which can persist even when behavioural synchrony is intact [10].
- Emotion misattunement describes affective mismatches. OAD is broader: it encompasses cognitive, sensory, and predictive misalignments, not only emotional ones.
- Transactional developmental models describe bidirectional influences. OAD specifies one mechanism within that transaction the translation failure and proposes a measurable pathway (neuroimmune) through which it may exert effects [11].

In essence, OAD is not a replacement for these constructs but a mechanistic specification of how misalignment between internal and external interpretations may contribute to the dysregulation observed in a subset of autistic children.

Acute versus Persistent OAD: The Role of Repair

A critical distinction is required: not all OAD is harmful. Developmental psychology has long emphasised that caregiver-child mismatches are normative and expected. Healthy development depends on the repair of these mismatches, not their absence [12].

We therefore distinguish:

Acute OAD: A time-limited misalignment, typically followed by caregiver re-attunement, repair, and resolution. This is common, developmentally normal, and unlikely to contribute to sustained dysregulation.

Persistent or unrepaired OAD: Chronic misalignment characterised by repeated failures of repair, caregiver unavailability for re-attunement, or caregiver signals that consistently misattribute the child's internal state. We hypothesise that persistent OAD, rather than OAD per se, contributes to the pro-inflammatory cascade and downstream dysregulation.

This distinction aligns OAD with established attachment research and avoids the implication that any mismatch is harmful. It also generates a specific, testable prediction: the association between OAD and inflammatory markers will be moderated by repair frequency dyads with high OAD but high repair will show weaker or no association (see Prediction 5, Section: A Research Agenda: Specific, Testable Predictions).

The Current Challenge: Persistent Dysregulation in ASD

Longitudinal research consistently demonstrates that emotional and behavioural problems (EBPs) in ASD are not static; they fluctuate over development, with a notable peak during middle childhood (ages 8–10) [4,13]. This peak is associated with increased caregiver distress, school placement instability, and heightened risk of psychiatric comorbidity [1].

Critically, studies examining the bidirectional relationship between caregiver mental health and child EBPs suggest that this feedback loop is partially decoupled in ASD cohorts. Unlike typical developmental samples, where maternal depression and child behaviour exhibit a strong bidirectional coupling, the link in ASD is asymmetrical: maternal distress predicts child outcomes more consistently than child distress predicts maternal outcomes, though the relationship is attenuated compared to neurotypical samples [14]. This decoupling is consistent with though not direct evidence for the OAD construct. If the child's behaviour is governed by internal predictive processes that are systematically illegible to the caregiver, then the caregiver's emotional state while influenced by the child's observable output may not accurately track the child's internal regulatory needs. Interventions designed to reduce maternal anxiety, in this framework, may not automatically improve the child's regulation if they do not also address the translation gap between the two systems.

A Developmental Systems Hypothesis: Integrating Attachment and Neuroimmune Regulation

We propose that persistent, unrepaired OAD functions as a relational stressor that, in vulnerable children, may contribute to the inflammatory and neural dysregulation observed in persistent EBP trajectories.

The Role of Subtle Caregiver Affective Signals

Drawing on developmental object relations theory, we hypothesise that subtle, often pre-conscious affective signals including facial micro-expressions, vocal prosodic shifts, and autonomic state changes (e.g., heart rate variability, skin conductance) may contribute to OAD [8,15]. These signals are not necessarily "unconscious" in a psychoanalytic sense, but rather operate below the threshold of the caregiver's explicit awareness or intentional control. Evidence from studies of parent-child biobehavioural synchrony suggests that such signals are detectable and may influence child outcomes [16].

For the autistic child, who may exhibit heightened perceptual sensitivity to environmental discordance, these subtle signals are not trivial. When the caregiver's gaze or vocal tone consistently broadcasts "your way of being is concerning or insufficient," the child may register an implicit threat to the relational anchor, destabilising identity formation and increasing allostatic load.

Over-Protection as a Functional Equivalent to Relational Unavailability

We further hypothesise that over-protective caregiving characterised by anticipatory intervention, pre-emptive problem-solving, and low tolerance for the child's distress can function as a variant of relational unavailability [8]. The over-protective caregiver is physically present but psychically preoccupied with their own anxiety. They intervene not in response to the child's actual signal, but to reduce their own distress at witnessing the child's struggle.

This pattern may deny the child the opportunity for autonomous predictive modelling and frustrative tolerance, potentially reducing the child's capacity for identity formation through environmental negotiation. We emphasise that this is proposed as a hypothetical mechanism for a subset of dyads, not a generalised characterisation of parenting in ASD.

Proposed Biological Pathway: Relational Stress to Neuroinflammation

Substantial evidence links early relational adversity and chronic caregiver-child discordance to the programming of a pro-inflammatory set-point via epigenetic mechanisms [4,17]. Elevated inflammatory markers (IL-6, TNF-α, CRP) have been consistently documented in children exposed to high relational stress; meta-analytic evidence indicates elevated IL-6 (Hedges' g = 0.365) and other cytokines in ASD cohorts [2,18].

We hypothesise that persistent OAD may contribute to:

- Microglial priming, sustaining low-grade neuroinflammation (2).
- Altered connectivity in the default mode network (DMN) and salience network (particularly anterior insula and anterior cingulate cortex), regions critical for self-referential processing and threat detection [10,19].
- Amygdala hyper-reactivity to social threat cues, manifesting clinically as irritability, withdrawal, or "meltdown" responses to seemingly minor social stressors [12].

We explicitly emphasise that we are not proposing that caregiving causes ASD. Rather, we hypothesise that for autistic children with already heightened sensory and perceptual sensitivity, persistent OAD-related relational stress may amplify dysregulation, influencing the trajectory of EBPs independent of the child's core autistic features.

Proposed Innovation: The Relational Entropy Audit and Consistency in Safety Protocol

If the OAD-neuroinflammation hypothesis is valid, then an intervention architecture that reduces persistent OAD frequency and stabilises the relational field should complement existing developmental and behavioural therapies.

The Relational Entropy Audit (Translational Assessment)

Building on accountability frameworks, we propose a family-administered or clinician-guided audit of the parent-child interaction, focusing on three metrics:

- Metric A (Interpretive Accuracy): Does the caregiver accurately identify the internal trigger of the child's behaviour before intervening? (Measured via prompted video review.)
- Metric B (Repair Latency): What is the time interval between the child's behavioural shift and the caregiver's re-attunement? Shorter latency is not inherently better; a pause that allows the child to self-regulate may be preferable.
- Metric C (Somatic Congruence): Is the caregiver's physiological state (heart rate variability, respiratory rate) aligned with a low-arousal, witnessing mode, or are they broadcasting sympathetic activation?

This audit is designed as a formative tool, not a judgmental one, enabling caregivers to identify patterns of persistent OAD in their dyad.

Consistency in Safety Protocol

We propose a structured, skills-based training module for caregivers, positioned as an adjunct to existing interventions:

Somatic Mirror Training

Caregivers receive biofeedback (via wearable devices or guided video-microanalysis) to detect their own subtle affective signals of anxiety or disappointment. They practice replacing high-arousal interventions with a neutral, low-arousal anchor signal a steady hand placement, a slow blink, or a rhythmic low-frequency vocalisation delivered without demanding eye-contact.

The Consent Check

Before helping, caregivers are trained to pause and explicitly query: "Do you need help, or do you want to try alone?" This restores the child's agency and reduces caregiver assumption of incompetence.

Disciplined Non-Intervention

Caregivers practice scheduled periods of non-directed observation, during which they refrain from commentary, correction, or redirection. The goal is to improve the caregiver's capacity to tolerate the child's self-directed behaviour without imposing external expectations.

Unconditional Identity Affirmation

Caregivers learn to broadcast a signal of unconditional identity affirmation a phrase or gesture conveying "Your processing style is accepted here" without conditioning it on eye-contact, verbal response, or other neurotypical reciprocity markers. This signal is operationalised as a specific, observable behaviour (e.g., a neutral verbal acknowledgment following a child's self-directed action, or a steady, warm gaze without demand) that can be reliably coded and tested for association with child outcomes.

Implementation Science Considerations

Prior to efficacy trials, we emphasise that the proposed protocol requires systematic evaluation of:

- Feasibility: Can caregivers complete the training within existing service delivery constraints?
- Fidelity: Can the protocol be delivered consistently across different clinicians and settings?
- Caregiver acceptability: Do caregivers perceive the protocol as helpful, culturally appropriate, and worth the time investment?
- Adverse effects: Does the protocol inadvertently increase caregiver self-criticism, anxiety, or family conflict?

These implementation outcomes should be evaluated in open-label pilot studies before proceeding to randomised controlled trials. We emphasise that this protocol is hypothetical and requires empirical validation; it is not proposed as a replacement for behavioural therapy, medication, or educational supports.

A Research Agenda: Specific, Testable Predictions

To substantiate or falsify this framework, we propose a staged empirical programme with a priori predictions.

Prediction 1 (Biomarker Cross-Sectional):

In a well-characterised ASD cohort (n ≥ 120), salivary CRP and IL-6 levels will show a moderate positive association ($r > 0.30$) with the frequency of persistent OAD episodes as measured by blinded video-coding of caregiver-child interaction, independent of chronological age, IQ, and DSM severity scores. This prediction tests the most basic claim of the model that persistent OAD is measurably associated with peripheral inflammatory markers before any causal or longitudinal claim is tested. A null result here ($r < 0.10$, or an association fully explained by autism severity) would substantially undermine the model at its foundation, since it is the precondition for Predictions 2–4. This effect size is consistent with meta-analytic findings for cytokine elevations in ASD [20].

Prediction 2 (Longitudinal Mediation)

In a prospective cohort from ages 3 to 12, early caregiver emotional availability (measured via the Emotional Availability Scales) at age 3 will predict IL-6 levels at age 10, which will in turn mediate a clinically meaningful proportion of the association between early caregiver anxiety and adolescent EBPs (CBCL scores) at age 12. This prediction moves from cross-sectional association (Prediction 1) to a developmental, mediating pathway, directly testing whether inflammation functions as the proposed mechanistic bridge between relational quality and behavioural outcome, rather than being incidental to both. We predict this pathway will be significant specifically in the ASD cohort, with a weaker or absent effect in neurotypical controls, since the model proposes that heightened sensory and perceptual sensitivity in ASD confers differential vulnerability to this pathway [21].

Prediction 3 (Neuroimaging)

Autistic adolescents with high IL-6 and high persistent OAD frequency will demonstrate (a) reduced functional connectivity within the default mode network and (b) increased amygdala reactivity to neutral faces on fMRI, compared to low-OAD autistic adolescents, with IL-6 mediating this relationship [22]. This prediction tests the proposed neural substrate directly, rather than inferring it from behaviour or peripheral markers alone. Confirmation would support microglial priming and salience-network alteration as the proximate neural mechanism linking OAD to dysregulation (Section: Proposed Biological Pathway: Relational Stress to Neuroinflammation); disconfirmation would suggest the peripheral inflammatory association (Predictions 1–2), if present, operates through a different or non-neural pathway.

Prediction 4 (Pilot RCT)

A 12-week pilot randomised controlled trial comparing the "Consistency in Safety" caregiver training (with biofeedback) plus treatment-as-usual (TAU), versus TAU alone. Primary outcome: reduction in child EBPs on the CBCL at 6-month follow-up. Secondary outcomes: reduction in caregiver salivary cortisol and self-reported burnout. This prediction tests clinical utility directly, independent of whether the full biological pathway (Predictions 1–3) is confirmed a positive trial result with unchanged inflammatory markers would still support the protocol's behavioural value, while indicating the mechanism of action differs from that proposed. We hypothesise a clinically meaningful improvement (e.g., ≥ 0.5 SD reduction on the CBCL) in the intervention group, with corresponding decreases in IL-6.

Prediction 5 (Moderation by Repair)

The association between OAD frequency and inflammatory markers will be moderated by repair frequency dyads with high OAD but high repair will show weaker or no association. This prediction directly operationalises the acute-versus-persistent OAD distinction introduced in Section: Acute versus Persistent OAD: The Role of Repair, it tests whether it is truly the failure of repair, rather than mismatch frequency alone, that drives the proposed inflammatory pathway. Support for this prediction would validate the theoretical distinction as clinically meaningful rather than semantic; its absence would suggest OAD frequency alone, independent of repair, is the operative variable a materially different clinical implication, since it would deprioritise repair-focused intervention components. This would directly test the acute vs. persistent OAD distinction.

We explicitly state that the absence of these predicted effects, or evidence that interventions reduce EBPs without altering inflammatory markers, would substantially weaken or falsify the model.

DISCUSSION

Clinical and Ethical Implications

If supported, this framework has significant implications for child and adolescent mental health. It would:

Provide a testable biological bridge between relational dynamics and neurodevelopmental outcomes (directly evaluated by Predictions 1–3, Section: A Research Agenda: Specific, Testable Predictions).

Offer a destigmatising reframe: dysregulation in a subset of autistic children may be understood as an environmentally-modulated stress response, not an intrinsic characterological deficit (consistent with the Significance of the Study, Section: Significance of the Study).

Shift the focus of intervention from suppressing the child's alarm signals to stabilising the relational field, potentially reducing the need for pharmacological adjuncts in some cases (operationalised in the Relational Entropy Audit and Consistency in Safety Protocol, Section: Proposed Innovation: The Relational Entropy Audit and Consistency in Safety Protocol, and tested directly in Prediction 4).

Afford caregivers a compassionate, non-blaming pathway to enhance their capacity for regulated presence.

However, we caution strongly against reductionist interpretations. This model does not propose a single "cause" of dysregulation, nor does it relieve the clinician or system of responsibility for addressing broader structural determinants of family stress, including socioeconomic instability and inadequate mental health infrastructure. The caregiver-child dyad exists within a wider ecological context; interventions targeting the dyad must be supported by systemic reforms that restore time, community, and resources to families.

Limitations and Falsifiability

We emphasise the following limitations:

Indirect evidence: The neuroimmune pathway proposed is supported by evidence from other populations and meta-analyses in ASD; direct prospective evidence linking OAD to inflammatory markers in ASD cohorts is lacking.

Alternative explanations: The stability of EBPs in ASD could equally be explained by sensory processing differences, cognitive rigidity, structural connectivity anomalies, or genetic factors that have no relationship to caregiver dynamics.

Causal direction: Even if associations between OAD and inflammation are found, causality is not established; bidirectional or third-variable explanations remain plausible.

We propose that the hypothesis would be substantially weakened by:

Consistent failure to find elevated inflammatory markers in high-persistent-OAD ASD cohorts (i.e., disconfirmation of Prediction 1).

Absence of a correlation between persistent OAD frequency and inflammatory marker levels after controlling for established predictors (e.g., autism severity, sensory processing differences, baseline caregiver stress, child language ability) a null result on Prediction 1's covariate-adjusted model. This would indicate that OAD does not provide incremental explanatory value beyond existing models.

Evidence that interventions improving EBPs do so without any change in inflammatory markers the specific outcome pattern described under Prediction 4 suggesting inflammation is epiphenomenal.

Evidence that OAD is fully accounted for by child-based factors (e.g., autism severity) with no independent contribution of caregiver affective signals, which Prediction 5's moderation test is designed to detect.

A Complementary Role for the Framework

We wish to emphasise that this model is intended to offer a complementary perspective rather than a replacement for existing developmental and behavioural frameworks. The neuroimmune and relational factors we propose are hypotheses, not established facts. We present this as an extension of developmental systems theory, not as a revolutionary departure.

RECOMMENDATIONS AND PRIORITIES FOR FUTURE RESEARCH

We recommend a staged empirical programme rather than parallel pursuit of all five predictions. Priority should be given first to Prediction 1 (cross-sectional biomarker association), as it is the least resource-intensive test and functions as a gating condition for the rest of the model: a null result here would substantially weaken the rationale for the longitudinal, neuroimaging, and trial-based work that follows. Contingent on a positive Prediction 1 result, we recommend open-label feasibility and fidelity piloting of the Consistency in Safety Protocol (Section: Implementation Science Considerations) before any randomised controlled trial is attempted, given that caregiver acceptability and potential adverse effects (e.g., increased caregiver self-criticism) have not yet been characterised.

Longitudinal mediation (Prediction 2) and neuroimaging (Prediction 3) studies represent the most resource-intensive tier and are recommended as medium-term priorities, ideally conducted within existing longitudinal ASD cohorts rather than as standalone studies, to reduce cost and improve statistical power. We further recommend that future work explicitly test the moderation-by-repair hypothesis (Prediction 5) early, as it has direct and immediate implications for whether intervention should target mismatch frequency, repair capacity, or both.

Finally, we recommend that any future empirical work adopt pre-registration of hypotheses and analysis plans, consistent with the falsifiability criteria outlined in Section: Limitations and Falsifiability, to guard against confirmation bias given the authors' stated positionality as parents of children impacted by ASD.

CONCLUSION

We have proposed that Observer-Agent Divergence the systematic misalignment between external behavioural inference and the child's internal predictive modelling processes may function as an under-recognised relational stressor that contributes to persistent emotional dysregulation in a subset of autistic children. By distinguishing acute, repaired mismatches from persistent, unrepaired OAD, and by integrating evidence from attachment theory and neuroimmunology, we offer a testable pathway linking caregiver

subtle affective signals to pro-inflammatory programming and altered neural connectivity.

The proposed Relational Entropy Audit and Consistency in Safety Protocol represent a clinically modest, complementary intervention architecture designed to reduce persistent OAD, stabilise the relational field, and support the child's capacity for self-regulation not as a replacement for existing therapies, but as an adjunct targeting an overlooked determinant of outcome.

We emphasise that autistic cognition may possess adaptive strengths in systems modelling, pattern detection, and predictive inference that warrant greater empirical investigation and respect (9). Our obligation is not to normalise autistic processing into neurotypical conformity, but to ensure that the relational environments in which autistic children develop are sufficiently stable, predictable, and affirming to allow their unique cognitive architectures to flourish.

If validated, this framework would reframe a subset of ASD-related dysregulation not as an intrinsic deficit, but as an environmentally-modulated signal of relational entropy demanding not chemical suppression of the child's alarms, but a disciplined, compassionate recalibration of the relational field.

DECLARATIONS

Positionality Statement

The authors, Adam David Kain and Marcia Maia, are both parents of children impacted by Autism Spectrum Disorder. This lived experience has informed the development of the Observer-Agent Divergence construct and the proposed intervention framework, grounding the theoretical model in direct, sustained observation of caregiver-child dynamics in the context of neurodivergence. The authors declare that this positionality has shaped, rather than biased, the research question, with the aim of contributing to more compassionate, empirically-grounded, and clinically actionable developmental systems psychiatry. The hypothesis presented is offered as a complement to, not a replacement for, existing evidence-based interventions, and is explicitly intended to generate testable empirical predictions rather than to prescribe clinical practice.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

ETHICS STATEMENT

This is a theoretical hypothesis and review paper. No human participants, animals, or primary data were involved. Any future empirical studies deriving from this hypothesis would require appropriate ethical approval.

AUTHOR CONTRIBUTIONS

Kain conceptualised the Observer-Agent Divergence construct and drafted the manuscript. Maia contributed the neuroimmunological framework, clinical synthesis, and reviewed the manuscript for intellectual content. Both authors are parents of children impacted by ASD, and this lived experience informed the development of the hypothesis and the proposed intervention architecture. Both authors approved the final version.

REFERENCES

1. McDonald RG, Cargill MI, Khawar S, Kang E. Emotion dysregulation in autism: A meta-analysis. Autism. 2024;28(12): 2986-3001.
2. Al Rasbi Z, Orsud H, Zoughbor SH, Hajar M, Mahboob A, Sadek B. The role of interleukin-37 and interleukin-38 in the development and remission of autism spectrum disorder: a comprehensive review of neuroinflammatory mechanisms and potential therapeutic implications. Frontiers in Immunology. 2025;16:1716197.
3. Belous M, Jelaga D, Caraman N, Nastas I. Neuroinflammation in autism spectrum disorder: what do current studies show? A narrative review. In: Satellite Conference "New horizons in mental health", 20-23 2025, Chisinau, Republic of Moldova. Chișinău: Universitatea de Stat de Medicină și Farmacie "Nicolae Testemițanu"; 2025:55a.
4. Danese A, McEwen BS. Adverse childhood experiences, allostasis, allostatic load, and age-related disease. Physiol Behav. 2012;106(1): 29-39.
5. Kulasinghe K, Whittingham K, Mitchell AE. Emotional availability in the mother-child relationship for families of young children with autism spectrum disorder in Australia: A cross-sectional survey. Research in developmental disabilities. 2022;131:104365.
6. Feldman R. Parent-infant synchrony: A biobehavioral model of mutual influences in the formation of affiliative bonds. Monogr Soc Res Child Dev. 2012;77(2):42-51.
7. Fonagy P, Gergely G, Jurist EL, Target M. Affect Regulation, Mentalization, and the Development of the Self. New York: Other Press; 2002.
8. Green A. On Private Madness. London: Hogarth Press; 1986.
9. Insel T, Cuthbert B, Garvey M, et al. Research domain criteria (RDoC): toward a new classification framework for research on mental disorders. Am J Psychiatry. 2010;167(7):748-751.
10. Keysers C, Silani G, Gazzola V. Predictive coding for the actions and emotions of others and its deficits in autism spectrum disorders. Neurosci Biobehav Rev. 2024;167:105877.
11. Lord C, Elsabbagh M, Baird G, Veenstra-Vanderweele J. Autism spectrum disorder. Nat Rev Dis Primers. 2018;4:18024.
12. Mahony C, O'Ryan C. A molecular framework for autistic experiences: Mitochondrial allostatic load as a mediator between autism and psychopathology. Frontiers in Psychiatry. 2022;13:985713.
13. Mok SW, et al. Natural products-based polypharmacological modulation of the peripheral immune system for neuropsychiatric disorders. Pharmacol Ther. 2020;208:107480.
14. Moser C, Yang CH, Hogan AL, Fairchild A, Roberts J, Klusek J. Mother–Child Biobehavioral Synchrony and Its Association With Social Functioning in Autistic School-Aged Children. Autism Research. 2026;19(2):e70168.
15. Northrup JB, Nuske HJ, Hipwell AE, Mazefsky CA. Review and developmental model: Early childhood emotion regulation and co-regulation in autism. Journal of the American Academy of Child & Adolescent Psychiatry. 2025.

16. Sameroff AJ. The Transactional Model of Development: How Children and Contexts Shape Each Other. Washington, DC: American Psychological Association; 2009.
17. Volk T, Lukito S, Radua J, Luksch H, Roessner V, Beyer N. Atypical cytokine profiles in people on the autism spectrum: a comprehensive systematic review and meta-analysis including 54 cytokines. Molecular Psychiatry. 2026:1-2.
18. Taurino A, Musso P, Risoli T, Coppola G, Stifano C, Cassibba R. Attachment Security and Autism Spectrum Disorder: A Scoping Review. Review Journal of Autism and Developmental Disorders. 2025:1-5.
19. Al-Salihy AA. Toward an immunological classification of autism spectrum disorder: A PRISMA-ScR–compliant scoping review. Journal of Neuroimmunology. 2026:578962.
20. Tronick E, Beeghly M. Infants' meaning-making and the development of mental health problems. Am Psychol. 2011;66(2): 107-119.
21. Winnicott DW. Playing and Reality. London: Tavistock Publications; 1971.
22. Winnicott DW (1971). Playing and Reality. Tavistock Publications.