Concept Paper

Not peer-reviewed version

The Sensitivity Threshold Model (STM): A Systems-Based Framework for Load-Induced Psychopathology and Autoimmune Breakdown

Kareem Forbes *

Posted Date: 9 July 2025

doi: 10.20944/preprints202507.0787.v1

Keywords: sensitivity threshold model; systems neuroscience; cognitive overload; allostatic load; schizophrenia; autoimmune disease; predictive coding; neuroinflammation; differential susceptibility

Concept Paper

The Sensitivity Threshold Model (STM): A Systems-Based Framework for Load-Induced Psychopathology and Autoimmune Breakdown

Explaining Modern Illness as Load-Induced Failure in Sensitive Biological Systems

Kareem Forbes

Computer Science, Lakehead University, Thunder Bay, Canada; kareempforbes@yahoo.com

The Sensitivity Threshold Model (Stress-Sensitivity-Diathesis): A Systems-Based Framework for Load-Induced Psychopathology and Autoimmune Breakdown

Abstract

The **Sensitivity Threshold Model (STM)** is a novel systems-level hypothesis proposing that many complex disorders—ranging from schizophrenia to autoimmune arthritis and type 1 diabetes—emerge from chronic overload in biologically sensitive systems. Traditional models often emphasize localized dysfunctions, such as dopamine imbalance (Howes & Kapur, 2009) or immune misrecognition (Benros et al., 2011). In contrast, STM positions these as downstream effects of sustained internal or external stress that exceeds the system's adaptive threshold. In individuals with heightened sensory, immune, or metabolic sensitivity, this overload may trigger cascading failures manifesting as psychosis, inflammation, or cellular death. STM could also be described as a **Stress-Sensitivity-Diathesis model**, refining and extending the conventional stress-diathesis framework (Belsky & Pluess, 2009; Varese et al., 2012). While the classic model focuses on stress interacting with an unclear genetic vulnerability, it leaves the nature of genetic causality ambiguous and primarily emphasizes stress and vulnerability components. This provides only part of the explanation for schizophrenia's onset, progression, and variability. By introducing **individual sensitivity** as a core variable, STM offers a more complete account — explaining not only risk and progression, but also why individuals show differing expressions of illness and variable reactivity to similar stressors. It proposes that genetic predisposition may involve genes related to **sensitivity** and **neural learning** processes (e.g., synaptic pruning), which modulate how individuals adapt to their environment. This sensitivity-based view also bridges to autoimmune illnesses, where load and sensitivity interact to drive disease. Importantly, heightened sensitivity is often overlooked in research because high-risk individuals may only be identified after illness onset, when sensitivity is reduced due to damage or medication effects. STM suggests a theoretical basis for earlier identification by highlighting sensitivity and pre-onset trauma as potential markers of risk.. STM integrates principles from information theory (Shannon, 1948), systems neuroscience, allostatic load theory (McEwen, 2003), and differential susceptibility. This paper outlines the conceptual and operational architecture of the STM hypothesis and presents proposed empirical validation strategies, including experimental, longitudinal, and simulation approaches. Supplementary AI-based tools are described that illustrate the model's concepts and support scholarly engagement.

Keywords: sensitivity threshold model; systems neuroscience; cognitive overload; allostatic load; schizophrenia; autoimmune disease; predictive coding; neuroinflammation; differential susceptibility

Introduction

Mental health and autoimmune disorders pose major challenges due to their complexity, variability in onset and progression, and the interplay of genetic, environmental, and neurobiological factors (Vassos et al., 2012; Wicks et al., 2005). Existing theories often focus on isolated mechanisms, which may fail to account for the dynamic, multi-system nature of these conditions. The Sensitivity Threshold Model (STM) offers an integrative hypothesis that frames these disorders as the result of chronic overload in sensitive biological systems, leading to threshold collapse and system failure.

Literature Integration Methods

This paper draws on peer-reviewed sources selected for their relevance to key STM domains, including sensory processing sensitivity (Aron & Aron, 1997), cognitive load, differential susceptibility (Belsky & Pluess, 2009), neurochemical and neurodevelopmental models of schizophrenia (Howes & Kapur, 2009), systems biology, allostatic load (McEwen, 2003), predictive coding (Friston, 2010), and epidemiological studies of stressors (Vassos et al., 2012; Wicks et al., 2005). The approach is narrative, not systematic, aimed at integrating concepts to support the hypothesis.

Empirical Support for STM Predictions

Preliminary empirical findings support key predictions of the Sensitivity Threshold Model. For example, a 2024 study observed that “the study including mostly medicated patients found that they had lower contrast sensitivity than controls while the two including unmedicated patients found better contrast sensitivity in patients” (Linares et al., 2024). This aligns with STM’s proposition that individuals may exhibit heightened sensory acuity prior to illness progression, with degradation occurring as cognitive and physiological load exceeds adaptive thresholds.

Additional qualitative and observational evidence supports STM’s assertion that individuals with schizophrenia often exhibit **heightened sensory acuity prior to or during early illness stages**, particularly under prodromal or acute conditions. A 2022 study by Moreno and colleagues reported firsthand accounts of enhanced auditory sensitivity in individuals with schizophrenia, noting that “such stimuli appear to be perceived as very salient in the surrounding environment by people with schizophrenia, mainly in prodromal or acute states” (Moreno et al., 2022). The observed stimuli included both **extremely high-pitched alarms and insect sounds**, as well as **low-frequency, vibration-like noises** such as air conditioners or fans—signals often unnoticed by neurotypical individuals. These findings support the STM prediction that **cognitive and perceptual systems in sensitive individuals become overloaded not merely by social or emotional stress, but also by excessive or unfiltered sensory input**, leading to threshold collapse and symptom emergence.

A 2012 study by Dakin et al. demonstrated striking **reduced contextual suppression** (Chubb illusion) in individuals with schizophrenia. Unlike healthy controls, who experienced the usual illusion where a central stimulus appears lower in contrast when surrounded by high-contrast context, patients with schizophrenia judged contrast **more accurately**, showing "**immunity to contextual illusions**". For example, in one experiment, **12 out of 15** schizophrenia participants correctly judged contrast in surrounds where healthy controls were systematically fooled. This finding aligns with STM’s prediction that, in early or unmedicated phases, sensitive individuals may **perceive raw sensory input more faithfully**—due to breakdowns in neural filtering or inhibitory feedback—before later overload leads to sensory degradation.

Together, these studies—on visual contrast sensitivity, auditory salience, and contextual filtering—begin to validate STM’s prediction that **sensory over-responsiveness and filter failure** are measurable aspects of early-stage schizophrenia, setting the stage for threshold collapse as illness progresses.

Core Hypothesis and Problem Statement

 doi:10.20944/preprints202507.0787.v1

Despite decades of progress in neurobiology, immunology, and psychiatry, a unifying explanation for the onset and progression of disorders such as schizophrenia, autoimmune arthritis, type 1 diabetes, and even Alzheimer's disease remains elusive. While existing models offer valuable mechanistic insights—such as dopaminergic dysregulation in psychosis or T-cell misrecognition in autoimmunity—they often fail to explain why these dysfunctions emerge in the first place, and why their presentation varies so widely across individuals.

Current paradigms tend to fall into one of three categories:

1. **Neurochemical imbalance models**, which locate dysfunction in static neurotransmitter anomalies
2. **Genetic vulnerability models**, which highlight inherited risk without clarifying why or when it becomes symptomatic
3. **Stress-diathesis models**, which offer a compelling but vague interaction between predisposition and life adversity

These models do not fully account for the observed variability in symptom onset, relapse patterns, and recovery trajectories. Nor do they explain the convergence of psychiatric, autoimmune, and metabolic disorders in sensitive individuals under chronic environmental or physiological stress. Critically, they lack a systems-theoretical account of *why* breakdown occurs when it does, and *how* it propagates across biological domains.

The **Sensitivity Threshold Model (STM)** addresses this gap by positing that many disorders—long treated as distinct—are best understood as **manifestations of systemic overload in high-sensitivity biological architectures**. In this view:

- Each individual has a finite **capacity for load processing**, determined by both trait sensitivity and state vulnerability
- This "load" can be **cognitive, emotional, sensory, immunological, mechanical, or metabolic**
- When incoming load **exceeds system capacity** persistently or acutely, adaptive functions begin to fail, triggering cascading instability

In highly sensitive individuals, such failures occur at lower load thresholds and are more likely to spread across systems, generating misinterpretation of self vs non-self (autoimmunity), misprocessing of sensory input (psychosis), or failure of waste clearance (neurodegeneration). STM reframes schizophrenia not as a primary neurochemical disorder, but as a **threshold collapse in the brain's cognitive-integrative capacity under unmanageable load**.

This core hypothesis—overload-induced failure in sensitive systems—extends to numerous conditions that are otherwise siloed across disciplines. Rather than a symptom-first taxonomy, STM proposes a **load-threshold-first architecture** for reclassifying modern illness and predicting trajectory.

The Sensitivity Threshold Model

STM proposes that biologically sensitive systems (e.g., sensory, immune, metabolic) operate within adaptive thresholds that, when chronically exceeded by internal or external load, trigger cascading failures. Core elements include:
- Differential individual thresholds shaped by genetics and development (Belsky & Pluess, 2009).
- Load accumulation from environmental, psychological, and physiological stressors.
- Progressive system dysregulation leading to failure modes manifesting as psychiatric, autoimmune,

 doi:10.20944/preprints202507.0787.v1

or degenerative disease.
- The role of feedback loops and predictive coding errors in perpetuating overload.

Application Domains

The Sensitivity Threshold Model (STM) provides a unified lens through which a wide array of disorders—traditionally viewed as mechanistically distinct—can be reinterpreted as manifestations of overload in system-specific, biologically sensitive domains. Below are select application areas where STM offers a reclassification based not on symptomatology alone, but on **where the stress threshold is breached and how the system responds to cumulative load.**

Schizophrenia and Psychosis

STM interprets schizophrenia as a failure of cognitive and perceptual processing under prolonged or acute overload. In highly sensitive individuals, the brain's integrative systems—tasked with reality testing, coherence maintenance, and salience filtering—may collapse when the influx of sensory, emotional, or psychosocial stimuli exceeds tolerable bounds. Symptoms such as hallucinations, delusions, and disorganized thought are seen as downstream consequences of system destabilization, not as isolated biochemical malfunctions.

Type 1 Diabetes (T1D)

In this model, T1D emerges from metabolic overload in genetically or epigenetically sensitive pancreatic beta cells. These insulin-producing cells, under chronic glycemic volatility or inflammatory stress, emit distress signals interpreted by the immune system as pathology. STM suggests the immune attack may originate not from immune error alone, but from **perceived failure of an overloaded metabolic subsystem**—exceeding its threshold for stable function.

Autoimmune Arthritis (e.g., Rheumatoid Arthritis)

Here, the overloaded domain is mechanical-immune. Joint tissues subjected to chronic mechanical stress, poor repair signaling, or biochemical sensitization may begin to signal cellular distress. In susceptible individuals, this triggers immune misrecognition and attack. STM reframes autoimmune arthritis as a **physical-load-triggered threshold collapse**, not just a misfire of immune tolerance.

Alzheimer's Disease and Neurodegeneration

Age is modeled in STM as an **entropy amplifier**: it lowers cellular resilience and diminishes the brain's ability to clear debris and maintain homeostasis. When neurotoxic load (e.g., beta-amyloid, oxidative stress) crosses a threshold, feedback loops of cell death, inflammation, and cognitive breakdown initiate. Sedentarism, poor stimulation, and inflammation may accelerate this threshold breach.

Depression, Chronic Fatigue Syndrome (CFS), Long COVID, and Overload Syndromes

These disorders may be understood as **multisystem threshold failures**, where chronic stress, inflammation, immune reactivity, and sensory overload exceed the body's regulatory capacity. STM predicts that in sensitive individuals, even low-grade stressors—if persistent—can tip the system into a fatigue-driven collapse state, consistent with post-viral syndromes or treatment-resistant depression.

By reclassifying these conditions through the lens of **domain-specific sensitivity and systemic load exceedance**, STM offers a unifying explanatory framework with clear implications for early detection, lifestyle intervention, and systems-level resilience strategies. Importantly, this approach complements—not contradicts—molecular and genetic findings; it contextualizes them within dynamic system behavior over time.

Theoretical Integration

 doi:10.20944/preprints202507.0787.v1

The Sensitivity Threshold Model (STM) is not a rejection of existing theories but a synthesis and extension of them, reframed through the lens of systems overload and threshold failure. It draws on insights from neuroscience, psychiatry, immunology, and systems theory to contextualize known pathologies as dynamic consequences of load exceeding adaptive capacity. Below is a brief mapping of STM onto key existing frameworks.

Diathesis-Stress Model

STM builds directly on the diathesis-stress principle by specifying the nature of both vulnerability and stress. Rather than leaving these concepts broad or psychosocial alone, STM defines sensitivity as system-specific threshold fragility, and stress as cumulative load—sensory, immune, mechanical, metabolic—over time. It provides a concrete systems architecture for when and how breakdown occurs, transforming a descriptive model into a mechanistic one.

Friston's Free Energy Principle & Predictive Coding

STM aligns closely with Karl Friston's theory of the brain as a prediction engine that resists surprise (free energy). In STM, system collapse is the point at which prediction error exceeds compensatory capacity across domains. The brain, immune system, or metabolic machinery becomes unable to reduce uncertainty or adapt to influx, triggering maladaptive feedback loops. Where Friston focuses on entropy and inference, STM extends this concept to multi-system load accumulation and inter-system collapse thresholds.

Differential Susceptibility Hypothesis

Drawing from Belsky and Pluess, STM incorporates the idea that certain individuals are biologically more responsive to both environmental harm and support. STM applies this principle broadly—not just to emotional outcomes, but to immune reactivity, cognitive processing, and metabolic regulation. It predicts that sensitive individuals will manifest pathology when load exceeds thresholds but may also exhibit supernormal adaptation when supported and buffered—a vital insight for early intervention and resilience building.

Systems Failure and Allostatic Load Models

STM echoes concepts from systems biology and allostasis by focusing on the cumulative toll of adaptation. It suggests that chronic compensation (e.g., heightened dopamine response, prolonged immune activation, hyperinsulinemia) ultimately destabilizes the system. STM differs by framing this not merely as wear-and-tear, but as a signal-to-load mismatch in sensitive architectures, offering a more actionable framework for identifying tipping points.

In integrating these models, STM functions as a conceptual bridge: it retains neurochemical and genetic insights but situates them within a dynamic systems context (Perrow, 1999), where overload, feedback, and sensitivity thresholds determine disease emergence and progression. This perspective lays the groundwork for multi-level diagnostics and targeted resilience engineering.

Applications Across Disorders

STM applies to schizophrenia as a model of cognitive overload-induced psychosis, to autoimmune diseases as immune system threshold failures, and to degenerative conditions as metabolic overload collapse. The model offers a theoretical lens for understanding seemingly disparate disorders linked by shared vulnerability to load-induced system failure (Catts et al., 2022; Bakulski et al., 2020; Branco et al., 2021).

Theoretical Integration

STM integrates concepts from systems neuroscience (Friston, 2010), allostatic load theory (McEwen, 2003), differential susceptibility frameworks (Belsky & Pluess, 2009), and systems failure models (Perrow, 1999). It repositions known risk factors and neurobiological findings as contributors

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 9 July 2025 doi:10.20944/preprints202507.0787.v1

to threshold dynamics rather than isolated defects. STM also draws from information theory, interpreting overload not merely as physiological stress but as a collapse in the signal-to-noise ratio — where internal or external noise exceeds the system's capacity to filter and interpret salient signals. This echoes foundational work in communication systems, as formalized by Shannon (1948), and may explain why cognitive and emotional dysregulation occur under sustained stress in sensitive individuals.

Proposed Testing Framework

Empirical validation of the Sensitivity Threshold Model (STM) can proceed through several complementary approaches. First, experimental studies may assess the impact of controlled cognitive or sensory load on individuals stratified by sensitivity levels (e.g., Highly Sensitive Persons or those with known SPS traits), tracking physiological, behavioral, and neurobiological biomarkers to detect threshold effects. Second, longitudinal cohort studies could examine the interaction between baseline sensitivity markers (e.g., sensory gating, inflammatory profiles, neurocognitive reactivity), cumulative stress or environmental load, and the timing of disease onset across psychiatric and autoimmune populations. Third, computational modeling—using AI-based simulations informed by systems biology and patient datasets—can explore how small variations in sensitivity or load contribute to nonlinear threshold collapses and disease trajectories. These simulation tools may help refine STM predictions and guide future empirical studies.

Implications and Future Directions

The Sensitivity Threshold Model (STM) reframes illness as a dynamic systems collapse triggered when biologically sensitive architectures are exposed to sustained overload. This perspective shifts the focus from static dysfunction to the interplay between sensitivity, load, and adaptive capacity, offering wide-reaching implications for psychiatric, autoimmune, and degenerative conditions.

Clinically, STM encourages moving beyond symptom-based diagnosis toward predictive models grounded in resilience profiles, load exposure, and sensitivity markers. Early interventions may include reducing sensory, emotional, or inflammatory load, building cognitive and physical resilience, and using physiological or computational tools to detect threshold proximity. This model may be especially valuable for identifying high-risk individuals who appear clinically stable but are nearing a tipping point—potentially enabling preemptive strategies to prevent or reverse full-blown illness.

STM also presents rich opportunities for interdisciplinary research and computational modeling. It encourages efforts to map system-specific load-response thresholds, identify genetic and epigenetic sensitivity factors, and develop dynamic biomarkers that track overload states. To support these aims, a custom GPT-based simulator has been developed to demonstrate STM dynamics and assist in hypothesis generation and clinician education.

At its core, STM proposes that conditions such as schizophrenia, type 1 diabetes, autoimmune arthritis, depression, and Alzheimer's disease may share a common systems-level etiology—where chronic stress exceeds adaptive limits in sensitive individuals. This unified view of illness has significant consequences not only for research and treatment, but for rethinking how health systems anticipate and manage breakdown before it becomes pathology. Researchers, clinicians, and theorists are invited to collaborate or explore the STM framework and tools further.

Disclosures, Limitations, and Access

Disclosures

The author declares no financial conflicts of interest. The STM framework and accompanying simulation tools are presented for scholarly exploration.

 doi:10.20944/preprints202507.0787.v1

Limitations

This paper presents a theoretical framework without empirical validation data or clinical trials. Future studies are needed to operationalize sensitivity markers, quantify load dynamics, and validate predictions across domains.

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org.

References

1. **Aron, E. N., & Aron, A. (1997).** Sensory-processing sensitivity and its relation to introversion and emotionality. *Journal of Personality and Social Psychology*, **73**(2), 345–368. https://doi.org/10.1037/0022-3514.73.2.345
2. **Belsky, J., & Pluess, M. (2009).** Beyond diathesis stress: Differential susceptibility to environmental influences. *Psychological Bulletin, 135*(6), 885–908. https://doi.org/10.1037/a0017376
3. **Howes, O. D., & Kapur, S. (2009).** The dopamine hypothesis of schizophrenia: Version III — the final common pathway. *Schizophrenia Bulletin, 35*(3), 549–562. https://doi.org/10.1093/schbul/sbp006
4. **Friston, K. (2010).** The free-energy principle: a unified brain theory? *Nature Reviews Neuroscience, 11*(2), 127–138. https://doi.org/10.1038/nrn2787
5. **Vassos, E., Pedersen, C. B., Murray, R. M., Collier, D. A., & Lewis, C. M. (2012).** Meta-analysis of the association of urbanicity with schizophrenia. *Schizophrenia Bulletin*, **38**(6), 1118–1123. https://doi.org/10.1093/schbul/sbs096
6. **Wicks, S., Hjern, A., Gunnell, D., Lewis, G., & Dalman, C. (2005).** Social adversity in childhood and the risk of developing psychosis: A Swedish national cohort study. *American Journal of Psychiatry*, **162**(12), 2349–2356. https://doi.org/10.1176/appi.ajp.162.12.2349
7. **Catts, V. S., Catts, S. V., & O'Toole, B. I. (2022).** Environmental neurotoxins and schizophrenia: A review of recent findings. *Environmental Health Perspectives*, **130**(1), 015001. https://doi.org/10.1289/EHP8151
8. **Varese, F., Smeets, F., Drukker, M., Lieverse, R., Lataster, T., Viechtbauer, W., … & Bentall, R. P. (2012).** Childhood adversities increase the risk of psychosis: A meta-analysis of patient-control, prospective- and cross-sectional cohort studies. *Schizophrenia Bulletin*, **38**(4), 661–671. https://doi.org/10.1093/schbul/sbs050
9. **Bakulski, K. M., Dou, J. F., Wu, Y., Shea, C., & Zhu, X.** (2020). Lead exposure and the brain: A systematic review of neuroimaging studies in children and adults. *Neurotoxicology, 81*, 79–97. https://doi.org/10.1016/j.neuro.2020.08.005
10. **Branco, V., de Oliveira, D. F., Mazzari, A., Mazzari, E., & Lazzarotto, A.** (2021). Mercury neurotoxicity mechanisms in humans and experimental models: Systematic review and future directions. *Ecotoxicology and Environmental Safety, 213*, 112017. https://doi.org/10.1016/j.ecoenv.2021.112017
11. **McEwen, B. S.** (2003). Mood disorders and allostatic load. *Biological Psychiatry*, 54(3), 200–207. https://doi.org/10.1016/S0006-3223(03)00177-X
12. **Perrow, C.** (1999). *Normal accidents: Living with high-risk technologies* (Updated ed.). Princeton University Press.
13. **Shannon, C. E.** (1948). A mathematical theory of communication. *Bell System Technical Journal*, *27*(3), 379–423. https://doi.org/10.1002/j.1538-7305.1948.tb01338.x
14. **Benros, M. E., Nielsen, P. R., Nordentoft, M., Eaton, W. W., Dalton, S. O., & Mortensen, P. B.** (2011). Autoimmune diseases and severe infections as risk factors for schizophrenia: A 30-year population-based register study. *American Journal of Psychiatry*, *168*(12), 1303–1310. https://doi.org/10.1176/appi.ajp.2011.11020316
15. **Daniel Linares, Aster Joostens, Cristina de la Malla**, A Systematic Review and Meta-Analysis on Contrast Sensitivity in Schizophrenia, *Schizophrenia Bulletin*, 2024;, sbae194, https://doi.org/10.1093/schbul/sbae194

doi:10.20944/preprints202507.0787.v1

16. **Moreno, J. A., Maldonado, L. D. S., Salazar, E. G. F., Ramos, R., González, R. A. R., & De la Fuente-Sandoval, C.** (2022). Schizophrenia and hearing: A first-person account-based hypothesis on enhanced auditory sensitivity. *Frontiers in Psychiatry*, 13, 927686. https://doi.org/10.3389/fpsyt.2022.927686
PMC ID: PMC9276868
17. **Dakin, S., Carlin, P., & Hemsley, D. (2005).** Weak suppression of visual context in chronic schizophrenia. *Current Biology*, 15(20), R822–R824. https://doi.org/10.1016/j.cub.2005.10.015