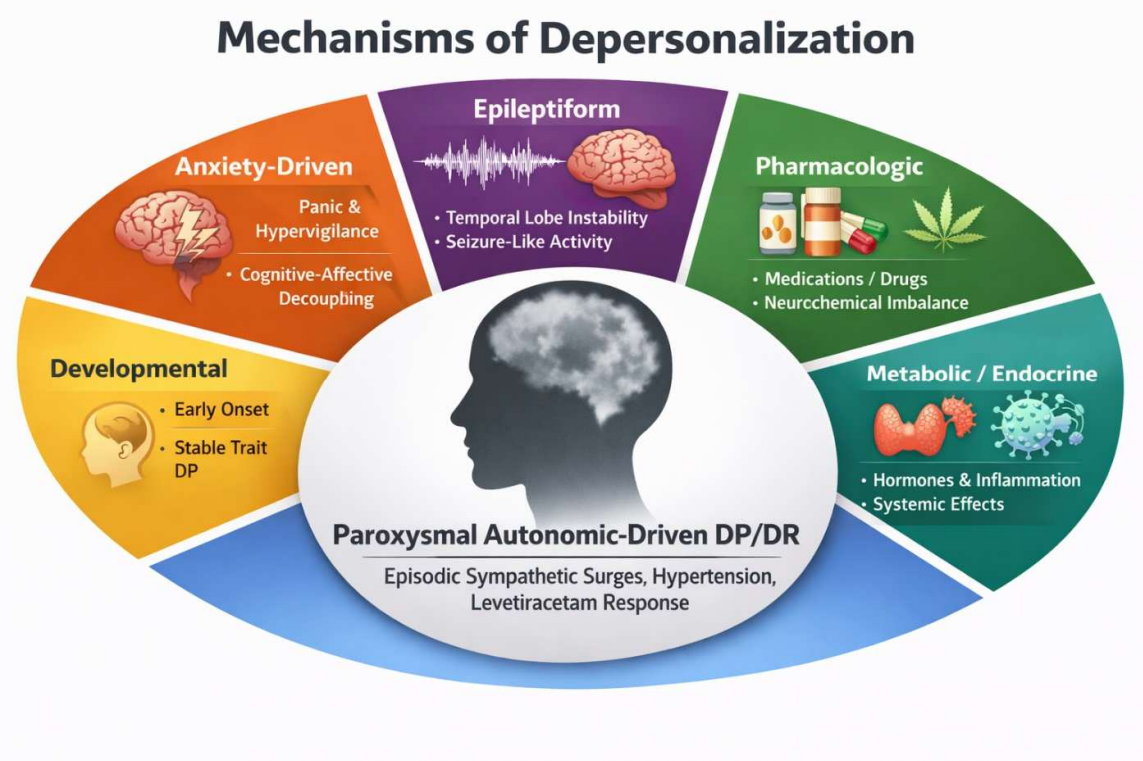
Depersonalization as a Neurophenomenological Signal:

A Case-Based Reassessment of Anxiety Nosology Beyond DSM Categories



Abstract

Depersonalization and derealization are traditionally classified within dissociative or anxiety-related disorders in the DSM framework. This categorization presumes a primarily psychological or affective etiology and often obscures underlying neurophysiological mechanisms. We present a teaching-level case of a patient with a long-standing history of severe panic disorder, previously stable under monoamine oxidase inhibitor therapy, beta-blockade, and benzodiazepines, who later developed episodic depersonalization accompanied by severe paroxysmal autonomic instability. These episodes demonstrated rhythmic periodicity, poor responsiveness to conventional anxiolytic strategies, and robust resolution following antiepileptic modulation with levetiracetam. This case challenges the adequacy of current anxiety-based diagnostic constructs and supports a reconceptualization of depersonalization as a neurophenomenological endpoint arising from diverse mechanisms. We propose a mechanism-based framework for classifying depersonalization and argue for a reassessment of anxiety as an explanatory category in psychiatry.

Introduction

Anxiety has become one of the most expansive and heterogeneous categories in modern psychiatric nosology. Since the dissolution of the neurosis construct and the progressive refinement of DSM classifications, anxiety-related diagnoses have absorbed a wide range of phenomenological states, including panic, depersonalization, derealization, somatic distress, and autonomic symptoms. While this symptom-based taxonomy has improved diagnostic reliability, it has done so at the cost of mechanistic specificity.

Depersonalization, in particular, occupies an ambiguous position. It is classified as a dissociative disorder, frequently conceptualized as anxiety-driven, and often explained through psychodynamic, cognitive, or stress-response narratives. However, accumulating clinical observations suggest that depersonalization is not a unitary disorder but rather a mode of conscious experience that emerges from failures of integration across multiple physiological systems.

This paper presents a case that exposes the limitations of anxiety-centered interpretations and illustrates the need for a mechanism-based reconceptualization of depersonalization.

Case Presentation

Psychiatric and Medical Background

The patient is an adult with a long-standing history of severe panic disorder characterized by recurrent panic attacks, anticipatory anxiety, and autonomic symptoms. For several years, the patient remained clinically stable under a regimen consisting of phenelzine (Nardil), propranolol, and clonazepam. During this period, panic attacks were well controlled, functional capacity was preserved, and depersonalization symptoms were absent or minimal.

Emergence of New Symptomatology

After years of stability, the patient developed new episodes marked by sudden and severe tachycardia and hypertension. These episodes were not temporally associated with medication changes, dietary factors, or known MAOI-related adverse effects. Importantly, the phenomenology differed from prior panic attacks: fear and catastrophic cognitions were not primary, and autonomic instability was more intense and sustained.

Initial management with clonidine (Catapres) and additional beta-blockade (atenolol) partially stabilized blood pressure and heart rate, suggesting significant sympathetic overactivation. However, episodic recurrences persisted.

Evolution of Periodicity and Phenomenology

Over time, these episodes developed an irregular but reproducible rhythmic pattern, with **clustering around full lunar cycles**. During autonomic crises, the patient experienced pronounced depersonalization—described as a loss of embodied self-experience with preserved insight and intact cognition. The depersonalization occurred concurrently with autonomic symptoms rather than preceding them.

Intervention and Outcome

The addition of levetiracetam resulted in a marked reduction in both autonomic instability and depersonalization episodes. Following stabilization, clonazepam was progressively tapered without recurrence of panic symptoms or worsening of depersonalization. This pharmacological response proved decisive in reframing the underlying mechanism.

Diagnostic Limitations of DSM Anxiety Categories

This case does not conform to DSM-based anxiety diagnoses for several reasons:

1. **Panic disorder** does not typically produce sustained hypertensive crises or rhythmic periodicity independent of situational triggers.
2. **Depersonalization/Derealization Disorder**, as defined in DSM, presumes a primary dissociative process and fails to account for severe autonomic dysregulation.
3. **Anxiety relapse** does not adequately explain the selective response to antiepileptic therapy or the improvement observed with benzodiazepine tapering.

The DSM framework, by privileging symptom clusters over mechanisms, encourages misclassification and may lead to ineffective or inappropriate treatment strategies.

Mechanistic Considerations

Cortical–Autonomic Integration

Autonomic regulation is mediated by distributed networks involving the insular cortex, anterior cingulate cortex, hypothalamus, and brainstem nuclei. These regions integrate interoceptive signals with affective and cognitive representations to produce a coherent sense of embodied selfhood.

Paroxysmal dysregulation within this network can generate severe sympathetic activation while preserving consciousness and insight.

Depersonalization as a State-Dependent Phenomenon

In this patient, depersonalization emerged during periods of intense autonomic instability, suggesting it was a **consequence** rather than a cause of the underlying disturbance. The phenomenology is best understood as a failure of affective–interoceptive binding, resulting in a subjective sense of detachment without psychotic disorganization.

Levetiracetam as a Mechanistic Probe

Levetiracetam's modulation of synaptic vesicle protein SV2A reduces neuronal hyperexcitability and abnormal synchronization. Its efficacy in this case supports the hypothesis of a paroxysmal network instability rather than a primary anxiety disorder. Importantly, levetiracetam has no intrinsic anxiolytic properties, reinforcing the non-psychological nature of the intervention.

Chronobiological Modulation

The association with lunar cycles should not be interpreted mystically. Circadian and circalunar rhythms influence sleep architecture, melatonin secretion, and neuronal excitability. In individuals with vulnerable regulatory systems—particularly those adapted to long-term monoaminergic modulation—minor rhythmic perturbations may lower thresholds for paroxysmal autonomic events.

Here, the lunar cycle likely functioned as a weak synchronizer rather than a causal agent.

Toward a Mechanism-Based Classification of Depersonalization

This case supports a broader conceptual shift: depersonalization should be understood as a **neurophenomenological endpoint** rather than a diagnosis. Different mechanisms may converge on similar subjective experiences.

Proposed classes include:

- Anxiety-driven cognitive–affective decoupling
- Autonomic–paroxysmal depersonalization
- Epileptiform or network-instability depersonalization
- Pharmacologically induced depersonalization
- Metabolic, inflammatory, or endocrine-related depersonalization
- Structural or neurodegenerative causes

Such a framework prioritizes mechanism over symptom appearance and guides treatment more effectively than DSM categories.

Reassessing the Anxiety Construct

Anxiety, as currently defined, functions more as a descriptive modifier than a mechanistic explanation. While anxiety may coexist with or modulate many conditions, it should not be reflexively assigned etiological primacy. This case demonstrates that a history of anxiety does not preclude the later emergence of fundamentally different physiological syndromes.

Psychiatric training must therefore distinguish between **anxiety as experience** and **anxiety as cause**.

Clinical and Educational Implications

- Depersonalization should prompt evaluation of autonomic and neurophysiological function.
- Persistent or paroxysmal autonomic symptoms warrant reconsideration of anxiety-based diagnoses.
- Case-based reasoning remains essential in complex presentations.
- Mechanism-oriented thinking can prevent chronic misdiagnosis and polypharmacy.

Conclusion

Depersonalization is not a disorder in itself but a signal indicating disrupted integration within the nervous system. This case illustrates how reliance on DSM anxiety categories can obscure underlying mechanisms and delay effective treatment. A shift toward mechanism-based classification is necessary to advance both clinical practice and psychiatric education.

Acknowledgment

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