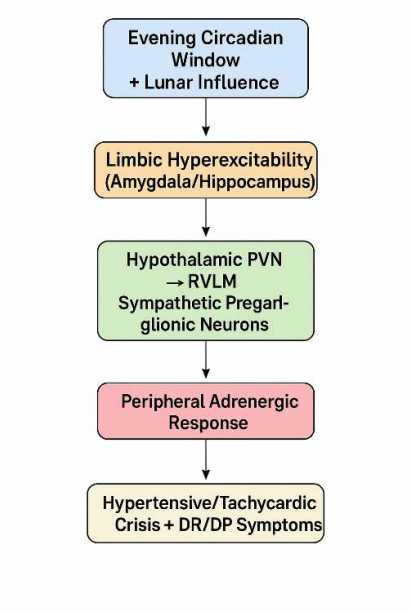
**Paroxysmal Nocturnal Hypertensive Episodes in a Patient with Limbic Kindling and Circadian Dysregulation: A Case-Based Physiological Model**




**Abstract**

We present a case of a normotensive individual with a history of panic attacks who developed sudden nocturnal hypertensive crises with marked sympathetic hyperactivity. Episodes were temporally associated with circadian nighttime windows and phases of the full moon. Standard anxiolytic and beta-blocker therapy provided incomplete control. Introduction of a neural excitability modulator targeting limbic circuits resulted in resolution of hypertensive episodes. This case supports a model of **Limbic-Autonomic Hyperexcitability with Circadian Dysregulation**, integrating limbic sensitization (*kindling*), autonomic instability, and environmental synchronizers. We propose a physiological framework for understanding paroxysmal autonomic syndromes with temporal and environmental triggers.

**Introduction**

Paroxysmal hypertensive crises in previously normotensive individuals represents a clinical challenge. While traditionally attributed to adrenal, renal, or vascular causes, emerging evidence suggests a subset of cases may arise from **central nervous system hyperexcitability**, particularly in limbic structures. *Kindling* phenomena—progressive sensitization of neural circuits by repeated subthreshold stimulation—have been described in the amygdala and associated limbic areas, leading to exaggerated autonomic responses. Circadian and environmental modulators, including nocturnal hormonal fluctuations and lunar-related stimuli, may further influence the timing and severity of such episodes. This report presents a case illustrating these interactions and proposes an integrated physiological model.

**Case Presentation**

A previously normotensive female adult with a history of panic attacks well-controlled on a combination of monoamine oxidase inhibitors (MAOIs), benzodiazepines, and occasional propranolol developed sudden nocturnal hypertensive episodes. Key features included:

- **Blood pressure:** peaks up to 190/110 mmHg
- **Heart rate:** approximately 100 bpm
- **Timing:** primarily between 21:00–22:00
- **Associated symptoms:** palpitations, anxiety, derealization, depersonalization
- **Pattern:** retrospective analysis indicated clustering during full moon phases

Prior interventions with clonidine, beta-blockers, amlodipine, and rescue nifedipine partially controlled the episodes but did not prevent recurrence. Introduction of a neural excitability modulator (levetiracetam, 125 mg TID) was associated with stabilization:

- **Blood pressure:** 90/60 mmHg
- **Heart rate:** 65 bpm
- **Resolution:** nocturnal hypertensive crises ceased
- **Edema from amlodipine** necessitated its discontinuation
- **Occasional atenolol** was used symptomatically for transient palpitations

The clinical evolution suggests a **central, limbic-autonomic etiology** rather than primary vascular pathology.

**Pathophysiological Considerations**

**1. Limbic Hyperexcitability (Kindling)**

- Amygdala and hippocampus circuits were likely sensitized from prior panic attacks.
- Subthreshold activation of limbic neurons can facilitate **paroxysmal autonomic discharges**, producing sudden sympathetic hyperactivity.

**2. Autonomic Circuitry**

- Limbic output converges on hypothalamic nuclei (paraventricular nucleus) → rostral ventrolateral medulla → sympathetic preganglionic neurons → peripheral adrenergic release.
- Clinically, this manifests as **paroxysmal hypertension, tachycardia, and hyperadrenergic symptoms**.

**3. Circadian Modulation**

- Episodes coincided with **evening windows (21:00–22:00)**, when:
    - cortisol levels decrease
    - melatonin secretion increases
    - cortical prefrontal inhibition is diminished
- These changes reduce the threshold for limbic-triggered sympathetic discharges.

**4. Environmental Synchronizers**

- Retrospective clustering during full moon phases suggests **lunar-related modulatory effects**:
    - nocturnal illumination influencing melatonin
    - minimal gravitational and geomagnetic influences affecting fluid dynamics and autonomic tone
- These act as **secondary triggers**, amplifying limbic-autonomic excitability in predisposed individuals.

**Syndromic Model**

We propose the **Limbic-Autonomic Hyperexcitability with Circadian Dysregulation (LAHCD)** framework:

1. **Predisposing factors:** previous panic disorder, limbic sensitization.
2. **Primary mechanism:** micro discharges in limbic circuits (*kindling*).
3. **Autonomic expression:** sympathetic bursts mediated via hypothalamic and medullary pathways.
4. **Temporal patterning:** evening circadian window of vulnerability.
5. **Environmental modulation:** lunar phase, light exposure, geomagnetic fluctuations.
6. **Pharmacological modulation:** agents stabilizing limbic excitability reduce crisis frequency and severity.

**Figure 1 (hypothetical schematic, textual representation)**:

Evening Circadian Window + Lunar Influence

↓

Limbic Hyperexcitability (Amygdala/Hippocampus)

↓

Hypothalamic PVN → RVLM → Sympathetic Preganglionic Neurons

↓

Peripheral Adrenergic Response

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Hypertensive/Tachycardic Crisis + DR/DP Symptoms

**Discussion**

This case illustrates the intersection of **neural sensitization, autonomic instability, circadian rhythms, and environmental modulation**. Traditional panic disorder frameworks inadequately explain nocturnal paroxysmal hypertensive episodes in previously normotensive individuals. The LAHCD model emphasizes:

- **Kindling-induced limbic hyperexcitability** as the central driver
- **Autonomic circuits** as the effectors of crisis
- **Circadian and lunar modulators** as amplifiers of susceptibility

The observed therapeutic response to a **limbic excitability modulator** supports the central role of limbic circuits. This integrative perspective may have broader implications for understanding:

- paroxysmal hypertension without adrenal pathology
- nocturnal panic and autonomic crises
- chronobiological triggers in neuropsychiatric disorders

Further studies could evaluate:

- real-time monitoring of limbic-autonomic activity
- chronobiological interventions
- environmental modulatory effects (lunar, geomagnetic, light exposure)

This case highlights the value of integrating **neurophysiology, chronobiology, and environmental factors** in explaining complex paroxysmal syndromes.

**Conclusion**

Paroxysmal nocturnal hypertensive crises may emerge from **limbic-autonomic dysregulation** with **circadian and environmental modulators**. Recognition of **kindling phenomena** and temporal susceptibility windows provides a physiological framework for understanding these events. Interventions stabilizing limbic excitability can normalize autonomic output and prevent nocturnal crises, supporting the concept of **multisystemic, neurophysiologically grounded paroxysmal syndromes**.