

**Ninety second nation: sleep fragmentation as a public health hypothesis in prolonged conflict**

Noam Shomron PhD<sup>1</sup> and Dmytro Martsenkovskiy MD PhD<sup>2</sup>

<sup>1</sup>Gray Faculty of Medical and Health Sciences, Tel Aviv University, Tel Aviv, Israel

<sup>2</sup>Department of Psychiatry and Narcology, Institute of Mental Health, Bogomolets National Medical University, Kyiv, Ukraine

**TO THE EDITOR:**

*In the morning you will say, 'If only it were evening!' and in the evening, you will say, 'If only it were morning!', because of the fear in your heart and the sights you will behold (Deuteronomy 28:67).*

It begins with a siren, a deep, pulsating wail tearing through the night over Tel Aviv. It is 3:42 in the morning. A university student jolts awake and rushes to a reinforced room. A young couple gathers their infant and runs for the stairwell. An elderly man descends slowly toward a neighborhood shelter. They each have 90 seconds or less to get to safety. Since 7 October 2023, Israel's Home Front Command has issued over 60,000 rocket alerts and more than 7000 UAV alerts nationwide. For much of the population, this interval, often shorter near border regions, marks the boundary between safety and danger. Beyond acute threat, these alerts impose a repeated physiological stressor that intrudes into one of the most vulnerable human states: sleep.

**PURPOSE AND SCOPE**

This letter to the editor does not present original epidemiological or laboratory data. Rather, it synthesizes existing neuroscientific and clinical

evidence on sleep fragmentation and contextualizes its relevance to public health in prolonged conflict settings. Using Israel and Ukraine as illustrative cases, we outlined plausible neurobiological mechanisms, clarified evidentiary limits, and identified research and policy questions requiring urgent attention.

**SLEEP FRAGMENTATION: DEFINITION AND DISTINCTION**

Nocturnal sirens induce sleep fragmentation, repeated brief arousals that disrupt sleep continuity and architecture, without necessarily reducing total sleep duration. This situation differs from sleep deprivation, which reflects reduced sleep time. Fragmentation specifically disrupts slow-wave and rapid eye movement (REM) sleep, phases that are essential for synaptic consolidation, glymphatic clearance, metabolic regulation, and neuroendocrine balance. Chronic interruption of these cycles has been linked to impaired cognition, circadian dysregulation, and increased vulnerability to neurodegenerative and cardiometabolic disease.

**NEUROBIOLOGICAL MECHANISMS: EVIDENCE AND INFERENCE**

Most mechanistic evidence linking sleep fragmentation to neurocognitive and emotional dysfunction derives from animal models and controlled human experiments, with real-world civilian data largely observational. Experimental studies demonstrate that repeated sleep disruption reduces brain-derived neurotrophic factor, increases oxidative stress, and alters hippocampal gene expression and synaptic plasticity, impairing long-term potentiation and memory. Human studies using experimental fragmentation protocols reveal deficits in attention, executive function, and

emotional regulation, in addition to reduced prefrontal connectivity and attenuated P300 responses.

Over longer durations, animal models show that chronic sleep fragmentation accelerates  $\beta$ -amyloid accumulation, tau phosphorylation, systemic inflammation, and hypothalamic-pituitary-adrenal axis dysregulation, implicating disrupted slow-wave sleep and impaired glymphatic clearance. While causality is clear in experimental systems, extrapolation to civilian conflict exposure must be approached with caution. Siren-induced arousals plausibly act as a causal stressor, yet pre-existing anxiety and hypervigilance can further degrade sleep continuity, producing bidirectional effects. Nonetheless, converging evidence supports a central conclusion: sustained fragmentation of sleep undermines neural plasticity and emotional stability.

**CONFLICT SETTINGS AS CHRONIC STRESS MODELS**

Israel has experienced missile threats for decades, but the current conflict is unprecedented in its geographic reach and duration. For over 2 years, no region has been exempt from nocturnal alerts, transforming short-term vigilance into a sustained environmental stressor affecting an entire civilian population. Parallel findings emerge from Ukraine, where cross-sectional studies report high rates of trauma exposure, insomnia, nightmares, depression, and post-traumatic stress disorder (PTSD) among adults and students, with evidence of intergenerational transmission of psychological distress. These studies have established strong associations between war exposure, disturbed sleep, and mental health, although they cannot isolate causal neurobiological pathways.

**REAL-WORLD IMPLICATIONS**

In ongoing conflicts, the biological pathways we described are not theoretical. They are activated almost nightly. Even when total sleep time is preserved, repeated arousals are consistent with the cognitive and emotional impairments observed in experimental sleep disruption. Unpredictable alerts amplify sympathetic activation, elevate cortisol, suppress melatonin, and destabilize cortico-limbic regulation, rendering the amygdala hyper-reactive while weakening prefrontal control. Neuroimaging studies corroborate increased limbic reactivity and reduced prefrontal engagement under fragmented sleep, mechanisms that are linked to anxiety, mood disorders, and PTSD.

Although written from an Israeli perspective, these effects are not unique to one population. Sleep fragmentation respects no borders, and its neuropsychological toll is shared by civilians navigating chronic threat across conflict zones. This commentary is based on literature synthesis rather than direct causal

data, as it lacks sleep recordings, biomarkers, or longitudinal neurocognitive assessments in conflict-exposed populations, underscoring the need for prospective studies using wearable sleep monitoring, neuroendocrine markers, and long-term mental-health outcomes.

**IMPLICATIONS FOR RESEARCH AND PUBLIC HEALTH**

Urban life under sustained threat now unfolds in cycles of hyperarousal and incomplete sleep, 90 seconds at a time. Sleep hygiene must be redefined to consider chronic environmental stress. Public health responses should integrate neuroscience, epidemiology, and civil defense, addressing alert fatigue as a quantifiable health risk. Practical measures may include optimizing alert duration and volume, improving residential sound attenuation, expanding sleep-health screening, and embedding sleep resilience into national preparedness plans. Protecting civilians requires not only safeguarding buildings but preserving minds. Sleep health reflects societal

well-being, and in prolonged conflict, it becomes both a clinical and moral imperative.

**ACKNOWLEDGMENTS**

The authors thank Prof. Talma Hender and Prof. Yuval Nir for commenting on the manuscript.

**Correspondence**

**Dr. N. Shomron**

Gray Faculty of Medical and Health Sciences, Tel Aviv University, Tel Aviv 69978, Israel

**Email:** nshomron@tauex.tau.ac.il

**References**

1. Shvartsur R, Savitsky B. Civilians under missile attack: post-traumatic stress disorder among the Jewish and Bedouin population of Southern Israel. *Isr J Health Policy Res* 2024; 13 (1): 38.
2. Musiek ES, Holtzman DM. Mechanisms linking circadian clocks, sleep, and neurodegeneration. *Science* 2016; 354 (6315): 1004-8.
3. Shomron N. The best-worst job in the world: when reality meets the brain. *J Mol Neurosci* 2024; 74 (4): 96.
4. Pavlova I, Rogowska AM. Exposure to war, war nightmares, insomnia, and war-related posttraumatic stress disorder: a network analysis among university students during the war in Ukraine. *J Affect Disord* 2023; 342: 148-56.

**Capsule****Innate antiviral and immune functions associated with the HIV reservoir decay after anti-PD-1 therapy**

**Talla** et al. performed a prespecified exploratory, longitudinal multiomic profiling of 30 PLWH (29 males and one female) with cancer in the phase 1 CITN-12 clinical trial, in which pembrolizumab was evaluated for safety and preliminary antitumor activity. The therapy was generally well tolerated, with most adverse events graded 1–2 and objective antitumor response observed in five participants (one complete response and four partial responses). Within 24 hours of treatment, we observed an expansion of proliferating HIV-specific effector CD8<sup>+</sup> T cells and a decline in plasma TGFβ. Furthermore, among the 14 participants tracked to the end of treatment (ranging

from 44 to 315 days after therapy initiation), nine display early induction and sustained expression of interferon-stimulated genes (ISGs), antiviral restriction factors and Toll-like receptor (TLR) signaling and a reduction in the HIV reservoir. Mapping these transcriptomic signatures across more than 1000 public single-cell RNA sequencing datasets reveals that anti-PD-1-induced programs are present in subsets of across subsets of disease states, indicating that some people already display a heightened antiviral state.

*Nat Med* 2026; 32 (2): 505

Eitan Israeli