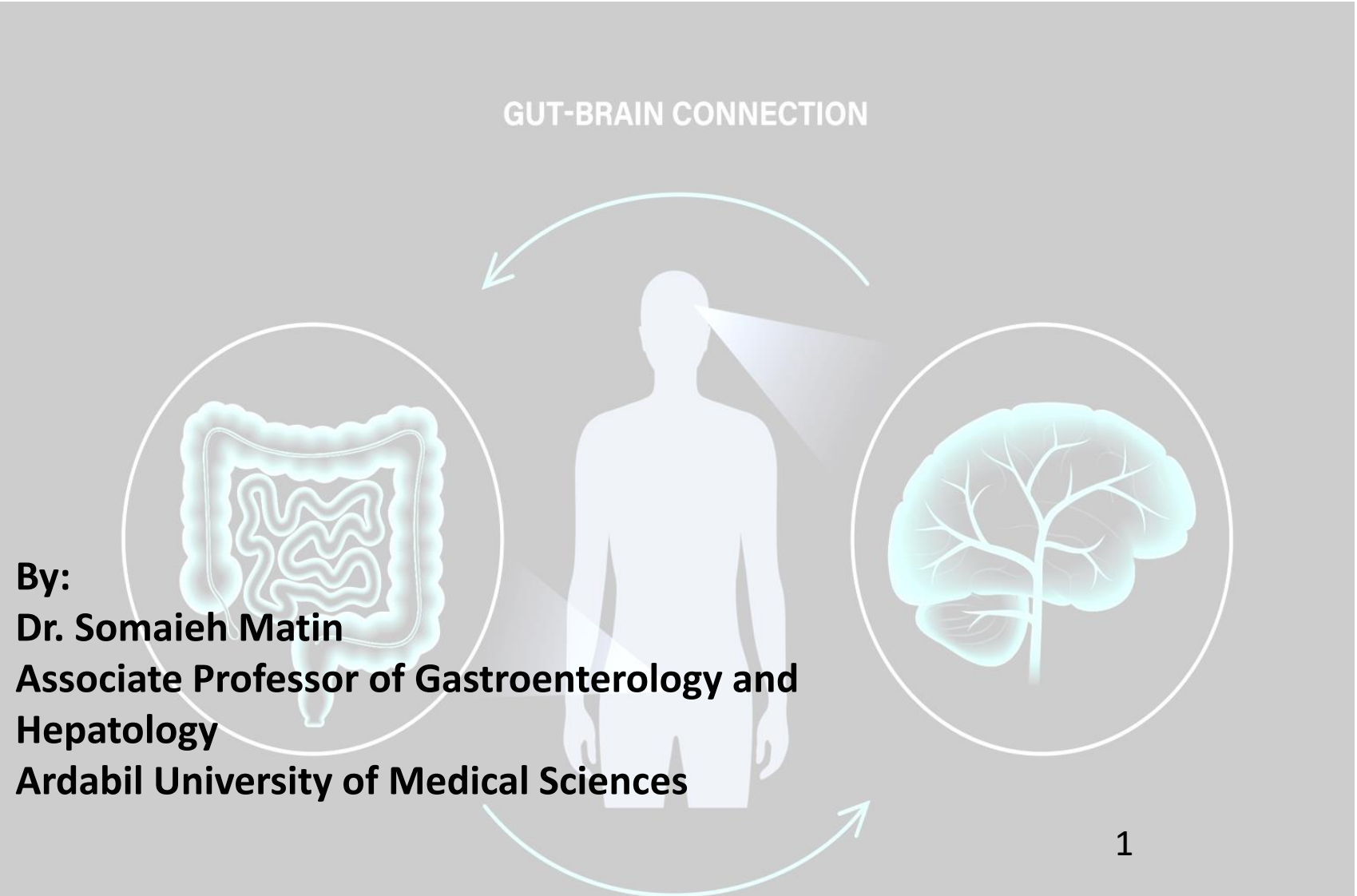
Sleep and Digestive Health



By:
Dr. Somaieh Matin
Associate Professor of Gastroenterology and Hepatology
Ardabil University of Medical Sciences

Factors effect on microbiota-gut-brain axis

- Environmental factors
- Sleep
- Life style
- Diet

Sleep

- ✓Is necessary for mental and physical recovery.
- ✓The gut microbiota (GM) exerts important functions in the regulation of sleep.
- ✓Key question: How does sleep quality impact gastrointestinal (GI) function?

Neuroendocrine, **immune**, and **metabolic pathways** regulate the BGA interactions.

Lozupone et al., 2012

Diagram of sleep cycles (REM, NREM)



Awake Time Is a Natural Break in Sleep

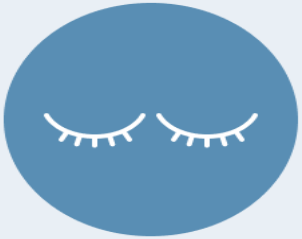


Awake Time

Wake – Stage 0 Sleep

- Awake time is the time spent in bed before and after falling asleep.
- It also includes brief awakenings during sleep.

Light Sleep Guides You Into Deeper Stages



Light Sleep

NREM – Stage 1 + 2 Sleep

- Muscles relax and may jerk.
- Respiration slows.
- Heart rate decreases.
- Body temperature drops.
- Sleep begins or transitions between cycles.
- Waking up is easier.

Deep Sleep Focuses on Restoring Your Body



Deep Sleep

NREM – Stage 3 + 4 Sleep

- Blood pressure drops.
- Body promotes muscle growth and repair:
  1. Blood flow increases to muscles.
  2. Growth hormone is released.
  3. Tissue growth and cell repair occurs.
- Brain flushes waste and shows long, slow brain waves.
- Waking up is more difficult, and you are disoriented or groggy if awoken.

REM Sleep Re-energizes Your Mind



REM Sleep

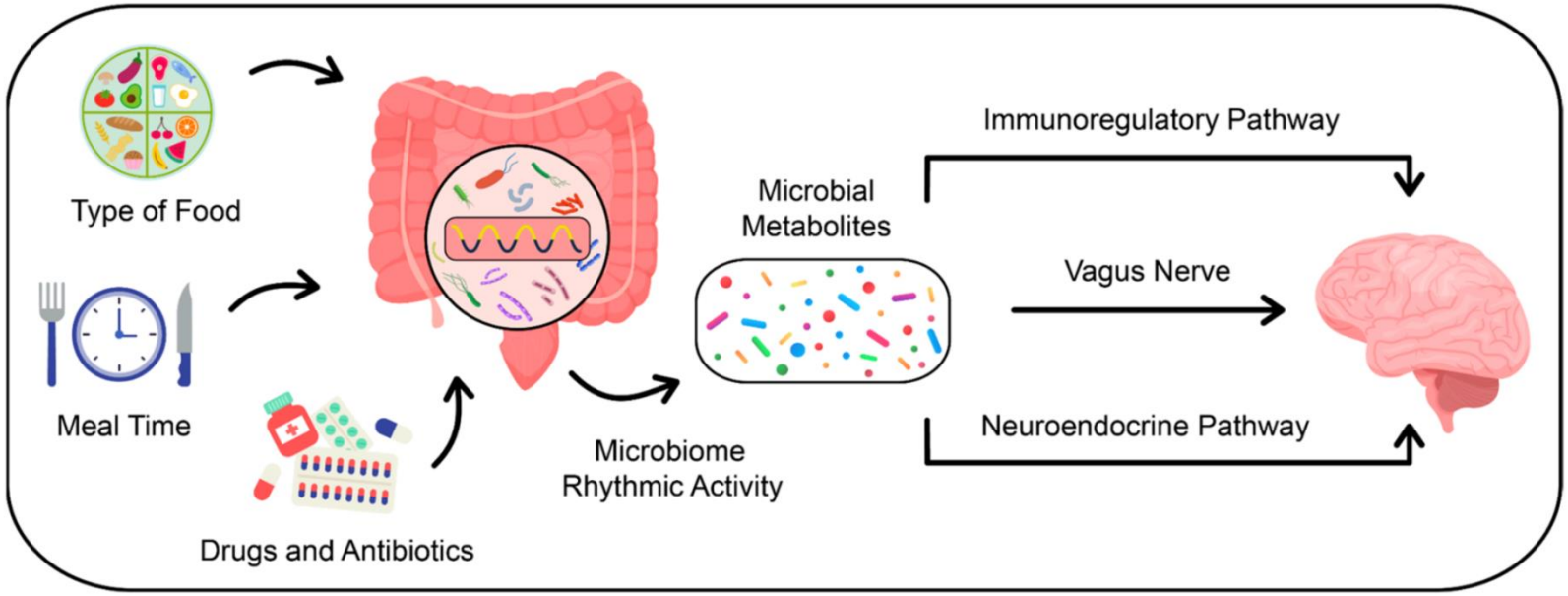
REM – Stage R Sleep

- Respiration increases.
- Heart rate increases.
- Temperature regulation is switched off.
- Vivid dreams may occur.
- Body becomes immobile to stop you from acting out dreams.
- Benefits for memory, learning, and problem solving.

Sleep Stage-Specific Gut Repair

Sleep Stage	Gut Process	Molecular Triggers
NREM3	Tight junction renewal	↑ Growth hormone, ↓ TNF-α
REM	Microbial diversity maintenance	↑ IgA secretion
Wake	Motility activation	↑ Serotonin, ↓ Melatonin

Visual representation of factors influencing the composition and activity of gut microbiota and its pathways of communication with the brain

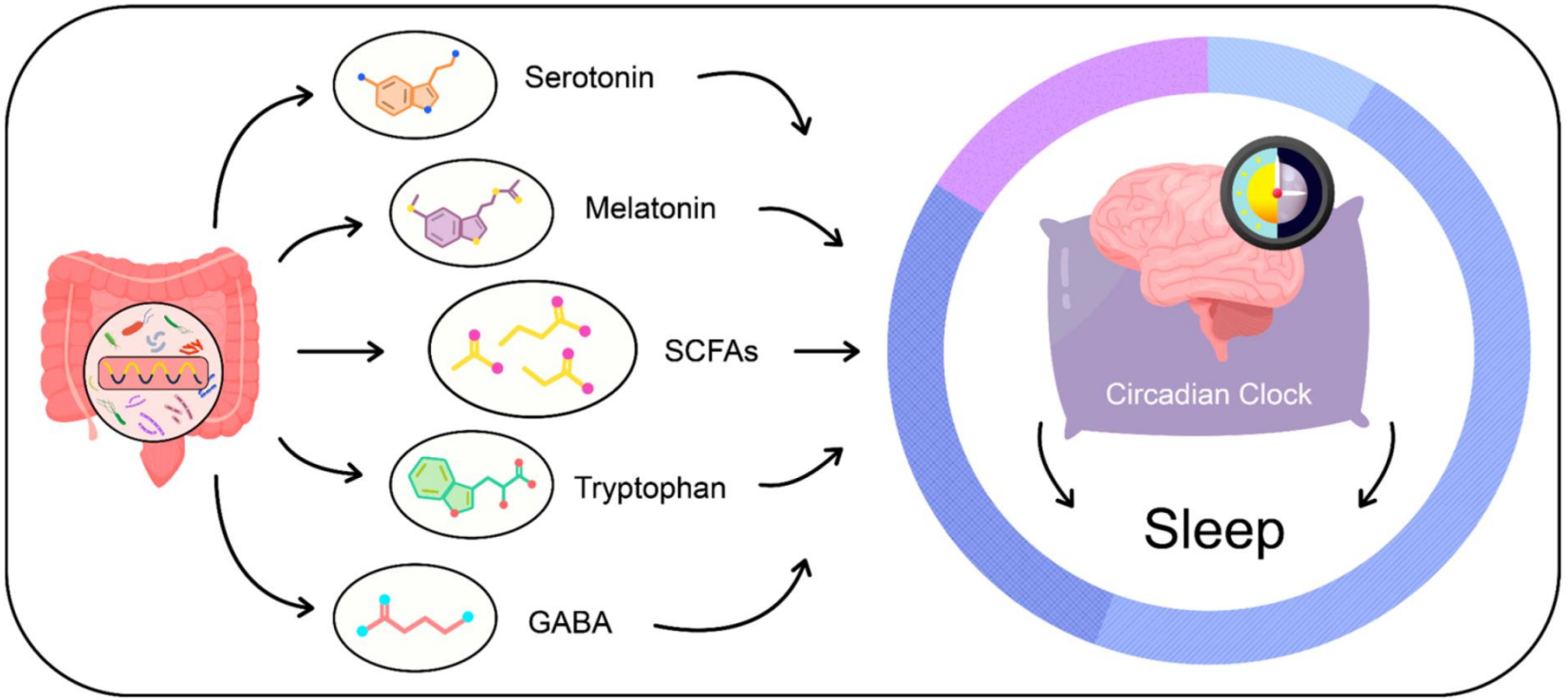


Gut-Brain-Sleep Axis

- **1. Neural Pathway (Vagus Nerve)**
- **80%** of vagal fibers are **afferent** (gut → brain)
- **Clinical impact**:
  - IBS patients show **40% reduced vagal tone** (HRV analysis)
  - VNS improves both **GERD & insomnia**
- **2. Endocrine Pathway (HPA Axis)**
- **Cortisol dysregulation**:
  - ↑ **Nighttime cortisol** in **IBD flares** ($p<0.01$)
  - ↓ **Melatonin** in shift workers with **GERD**
- **3. Immune Pathway (Cytokines)**
- **Key players**:
  - **TNF-α** → Disrupts **REM sleep**
  - **IL-6** → Increases **intestinal permeability**

Metabolites produced by the gut microbiota

Monica et al. Nutrients **2024**, *16*(14), 2259; https://doi.org/10.3390/nu16142259



- Disturbances in the quantitative and qualitative composition of the gut microbiota result in dysbiosis, which can disrupt the bodily functions, and potentially lead to disease and sleep disturbances.

Disturbed Sleep



- ✓Such as sleep deprivation
- ✓ sleep fragmentation
- ✓ obstructive sleep apnea
- ✓insomnia

- Closely linked to cardiovascular diseases, obesity diabetes, mental illness and even mortality.

Bidirectional Relationship Between Sleep and GI Disorders: Clinical Evidence

- **1. Sleep → GI Consequences**
- Increased intestinal permeability:
  - 2.5x higher in poor sleepers ($p<0.01$)
  - Measured by lactulose/mannitol test
- Disease exacerbation:
  - IBS: 68% higher symptom severity (OR 1.68)
  - GERD: 3x more nocturnal reflux episodes

Bidirectional Relationship Between Sleep and GI Disorders: Clinical Evidence

- **2. GI → Sleep Disruption**
- Pain-related awakenings:
  - IBD: 4.2 awakenings/night vs 1.1 controls
  - IBS: 72% report unrefreshing sleep
- Nocturnal symptoms:
- GERD: 83% report sleep disturbance

Bidirectional Relationship Between Sleep and GI Disorders: Clinical Evidence

- **3. Key Mechanisms**
- Circadian disruption → tight junction impairment
- Inflammation → sleep architecture changes
- Melatonin’s dual role in sleep and gut motility.
- Inflammatory markers (e.g., TNF-α, IL-6) elevated in sleep deprivation.

Sleep Disturbances in GI Disorders - Clinical Evidence & Management

- **1. GERD & Sleep Apnea**
- **Key Finding:**
  - 45% of GERD patients have OSA (OR 2.3, *p*<0.01) (*Am J Gastroenterol 2023*)
  - Nocturnal acid breakthrough → 62% more awakenings (PSG-confirmed)
- **Clinical Action:**

▶ Bedtime PPIs (70% symptom reduction)

▶ Sleep study for refractory cases

Sleep Disturbances in GI Disorders - Clinical Evidence & Management

- **2. IBD Flares & Sleep Architecture**
- **Risk Correlation:**
  - Each 1h sleep loss → 27% ↑ flare risk (HR 1.27, 95% CI 1.15-1.40)
  - Crohn's patients with insomnia: 2× hospitalizations (*Gut 2024*)
- **Mechanism:**
  Impaired epithelial repair during deep NREM

Sleep Disturbances in GI Disorders - Clinical Evidence & Management

- **3. IBS & Non-REM Dysregulation**
- **Pathophysiology:**
  - ↓ Deep NREM → ↑ visceral hypersensitivity
  - Butyrate-producing bacteria ↓ 40% in poor sleepers
- **Therapeutics:**
  - Melatonin (40% pain reduction)
  - CBT-I (improves sleep continuity)

disease	Sleep Disorder Prevalence	Main Contributing Factor	Key References
GERD	65-70%	Nocturnal reflux, Sleep apnea	*Am J Gastroenterol, 2024*
IBS	60%	NREM sleep disturbances	*Gut, 2023*
IBD	75-80%	Nighttime pain, Systemic inflammation	*Lancet Gastroenterol Hepatol, 2023*

Gut-Brain-Sleep Axis Molecular Mechanism

Parameter	Finding	Clinical Impact
Neurotransmitter Production	Gut bacteria (e.g., Lactobacillus reuteri) produce 40% of peripheral serotonin	35% improvement in sleep quality with probiotics
Microbial Diversity	25% reduction in IBS patients with sleep disorders	Correlates with melatonin deficiency

Inflammation and Sleep Disorders (2024 Data)

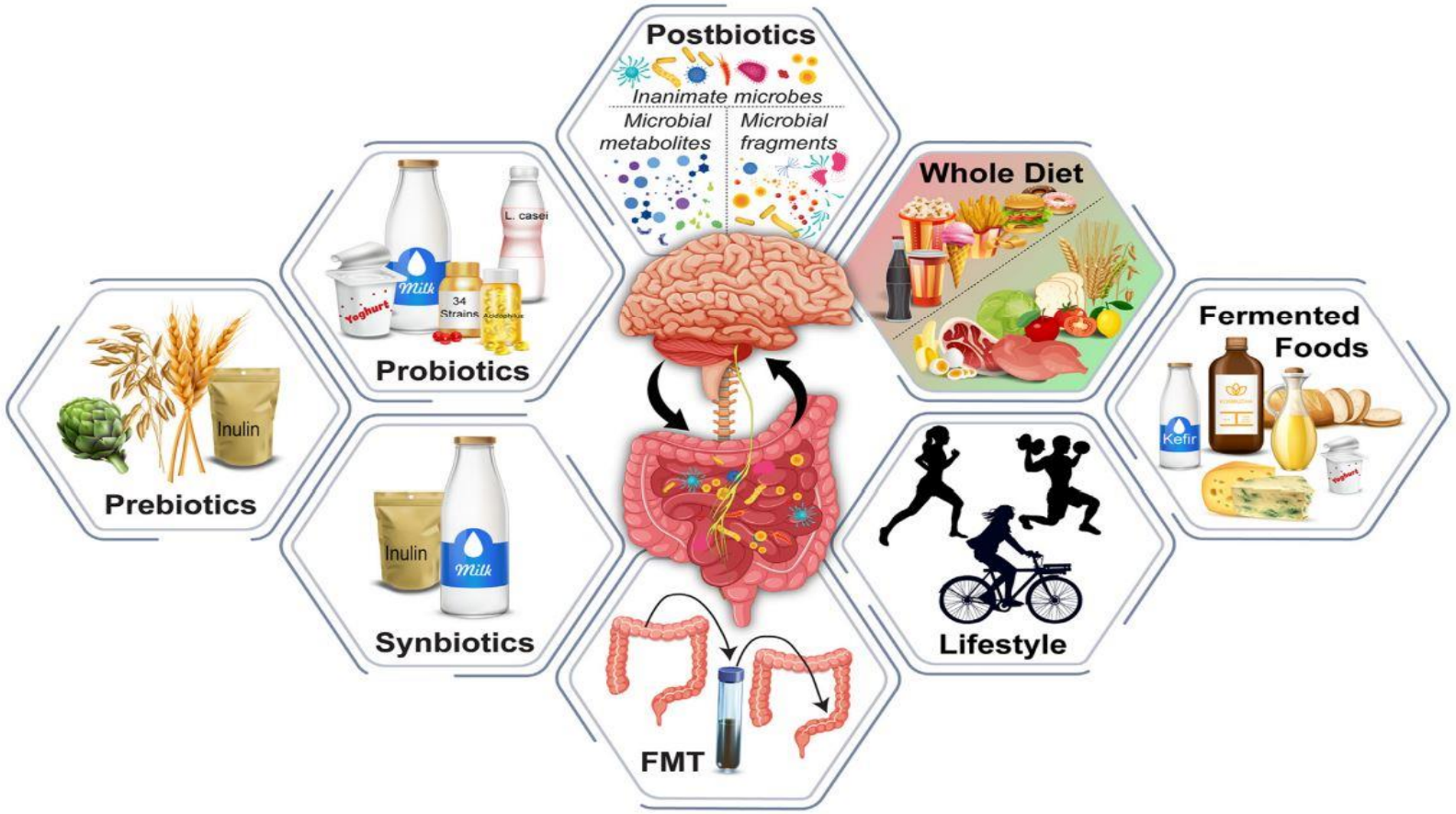
Cytokine	Sleep Impact	Level in IBD Patients	Therapeutic Target
IL-6	Reduces deep (NREM) sleep	3× increase	Anti-IL-6 therapies in trials
TNF-α	Increases nighttime awakenings	2.5× increase	Anti-TNF improves sleep quality
IL-1β	Delays sleep onset	4× increase during flares	IL-1 receptor antagonists

Circadian Rhythm Disorders Clinical Findings:

Disorder	Prevalence	Key Association	Diagnostic Tool
Nocturnal GERD	68%	Abnormal melatonin secretion patterns	Smart pH-monitoring capsules
Shift Work IBS Risk	3.2× higher	Altered gut motility rhythms	Breath tests for microbial dysbiosis

Comprehensive Sleep-GI Diagnostic Framework

- 1. Standardized Sleep Assessment
- All GI Patients:
  - **PSQI** (Pittsburgh Sleep Quality Index)
    - Threshold: Score >5 indicates poor sleep quality
    - IBS patients average PSQI=9.2 vs 3.1 controls (*Gut 2023*)
- High-Risk Screening:
  - **STOP-BANG Questionnaire** (OSA risk)
    - ≥3 points → Urgent polysomnography
    - 72% sensitivity in GERD patients (*Clin Gastroenterol Hepatol 2024*)



Potential therapeutic interventions that can inform future perspectives.

Kenneth J et al., 2025

