

Fibromyalgia in Women: A Brain–Behavior–Immune Perspective on Global Prevalence, Neurobiological Plasticity, and Recovery Trajectories

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Abstract

Fibromyalgia (FM) is a chronic oncoplastic pain marked by widespread pain, persistent fatigue, sleep disruption, and cognitive difficulties. Current evidence suggests that its pathophysiology is largely driven by central nervous system dysfunction, with altered pain processing and impaired communication across brain–behavior–immune networks. FM affects women disproportionately. Worldwide prevalence estimates vary, ranging from 0.2% to 6.6% in the general population and from 2.4% to 6.8% among women. Longitudinal studies highlight considerable variability in clinical course, with 20–47% of patients no longer meeting diagnostic criteria within one to two years.

Keywords

Fibromyalgia; Nociceptive pain; Neuroimmune interaction; Central sensitization; Women's health; Neuroplasticity

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1. Introduction

Fibromyalgia has historically been viewed as a rheumatologic or functional disorder; however, advances in neuroscience and psychoneuroimmunology have shifted this paradigm [1,4]. Neuroimaging and psychophysical studies demonstrate amplified pain signaling, impaired descending inhibition, and altered connectivity within pain-modulatory networks [2,5]. These findings underpin the classification of FM as a nociceptive pain condition [3,6]. Notably, FM disproportionately affects women, a phenomenon not fully explained by psychosocial factors alone [7,8].

2. Global Epidemiology with Emphasis on Women

Global prevalence estimates of fibromyalgia vary due to differences in diagnostic criteria and study design [9,13]. A comprehensive review reported prevalence ranging from 0.2% to 6.6% in the general population and from

2.4% to 6.8% among women [9]. Clinical cohorts frequently report female-to-male ratios between 7:1 and 9:1 [7,14]. Population-based studies suggest a narrower sex gap, indicating potential diagnostic and ascertainment bias [13,15].

3. Neurobiological and Immune Mechanisms

Sex differences in pain processing are well documented. Women exhibit enhanced temporal summation and reduced conditioned pain modulation, features resembling the neurophysiological profile of fibromyalgia [16,17]. Neuroendocrine dysregulation, immune activation, and altered neurotransmitter signaling further contribute to central sensitization [4,18,19]. Importantly, these mechanisms remain plastic and responsive to behavioral and physiological interventions [20].

Fibromyalgia as a Brain–Behavior–Immune Disorder Recovery Through Neuroplasticity

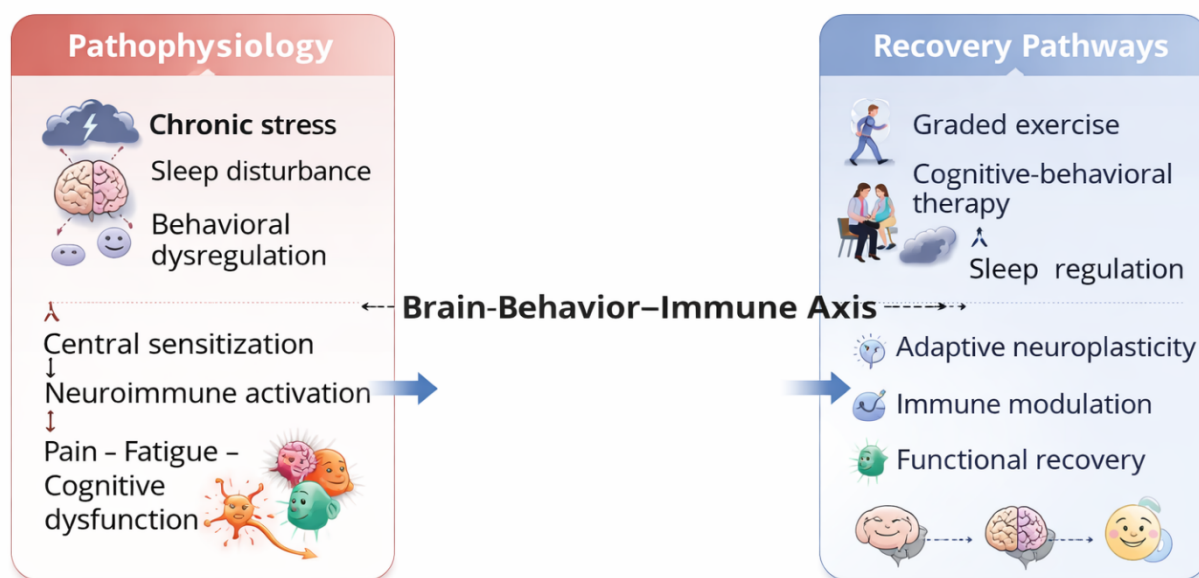


Figure 1. Conceptual Brain–Behavior–Immune Model of Fibromyalgia Pathophysiology and Recovery

This conceptual framework illustrates fibromyalgia as a disorder of maladaptive neuroplasticity within the brain–behavior–immune axis. Chronic stress, sleep disturbance, and behavioral dysregulation contribute to central sensitization and neuroimmune activation, resulting in persistent pain, fatigue, and cognitive dysfunction. Targeted recovery pathways—including graded exercise, cognitive-behavioral therapy, and sleep regulation—promote adaptive neuroplasticity and immune modulation, facilitating functional recovery in a subset of patients.

4. Results

Synthesis of epidemiological data demonstrates a consistently higher prevalence of fibromyalgia among women across geographical regions and study designs [7–9,13]. Clinical cohorts show pronounced female predominance, whereas population-based studies applying symptom-severity criteria report reduced sex disparity, suggesting partial diagnostic bias [13–15]. Longitudinal analyses reveal that fibromyalgia does not follow a uniform chronic trajectory. Across prospective cohorts, 20–47% of patients transition to a criteria-negative state within one to two years, and objective remission is observed in approximately 24% of selected samples [10–12]. Neurobiological findings from imaging and experimental pain studies consistently demonstrate central sensitization, impaired inhibitory control, and altered brain connectivity patterns associated with symptom severity [2,5,17].

5. Discussion

The present synthesis highlights fibromyalgia as a dynamic disorder of the brain–behavior–immune axis with a disproportionate impact on women. Epidemiological findings confirm global female predominance, while longitudinal data challenge deterministic views of chronicity by demonstrating remission-like trajectories in a substantial subset of patients [10–12]. These outcomes are biologically plausible within a neuroplastic framework, wherein central sensitization and neuroimmune activation can be modulated over time [4,6,20]. Sex-specific differences in pain modulation, stress responsivity, and immune signaling likely contribute to both disease vulnerability and recovery potential [16–19]. However, many studies lack adequate power for sex-stratified analyses, limiting mechanistic interpretation. Standardization of recovery definitions and integration of longitudinal neurobiological markers remain critical priorities for future research.

6. Brain–Behavior–Immune–Oriented Recovery Programs

Evidence-based recovery programs emphasize non-pharmacological interventions targeting maladaptive neuroplasticity [20–22]. Graded physical activity improves pain modulation and reduces immune activation, while cognitive-behavioral therapy attenuates stress-related neural amplification [21,22]. Sleep regulation is essential for synaptic and immune homeostasis and supports sustained symptom improvement [18,23].

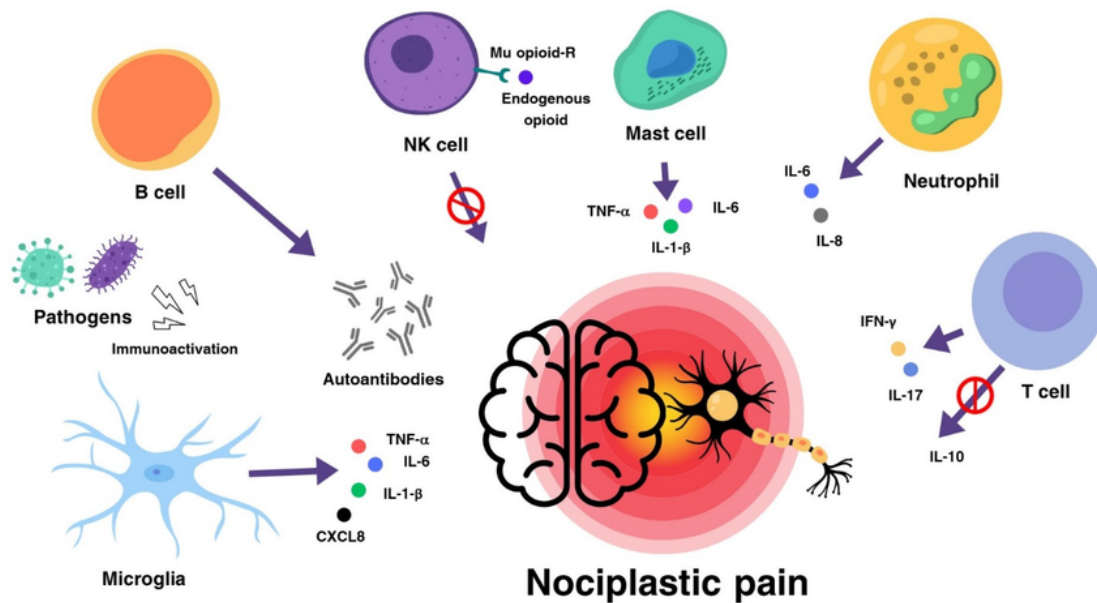


Figure 2. Neuroimmune Crosstalk Underlying Nociceptive Pain in Fibromyalgia

This figure illustrates the interaction between immune cells (B cells, T cells, NK cells, mast cells, neutrophils, and microglia) and the central nervous system in fibromyalgia. Dysregulated cytokine signaling (e.g.,

TNF- α , IL-6, IL-1 β) and impaired opioid-mediated immune modulation contribute to central nociceptive pain through sustained neuroinflammation and altered pain processing.

Peripheral and Central Sensitization in Fibromyalgia

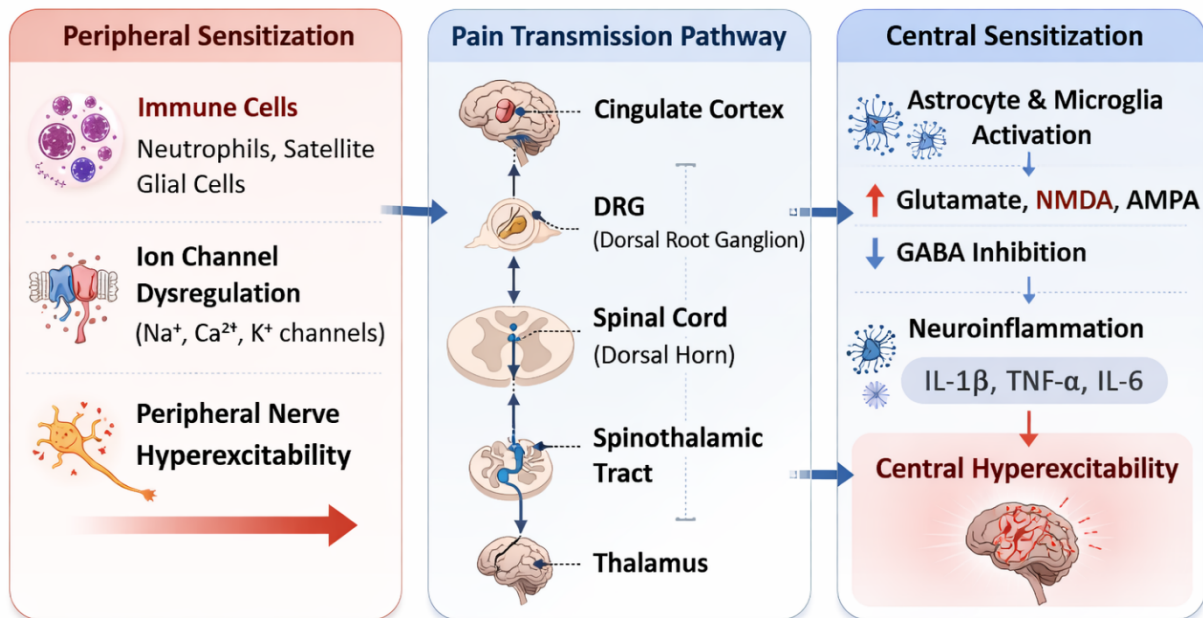


Figure 3. Central Sensitization and Neuroinflammatory Mechanisms Across the Pain Axis

Schematic representation of peripheral and central sensitization mechanisms in fibromyalgia. Peripheral immune activation and satellite glial cell dysfunction promote hyperexcitability, while supraspinal and spinal

neuroinflammatory processes—including astrocyte and microglial activation, excitatory neurotransmission, and impaired inhibitory control—drive central sensitization and persistent pain.

Neurogenic Inflammation and Neuroimmune Interactions in Fibromyalgia

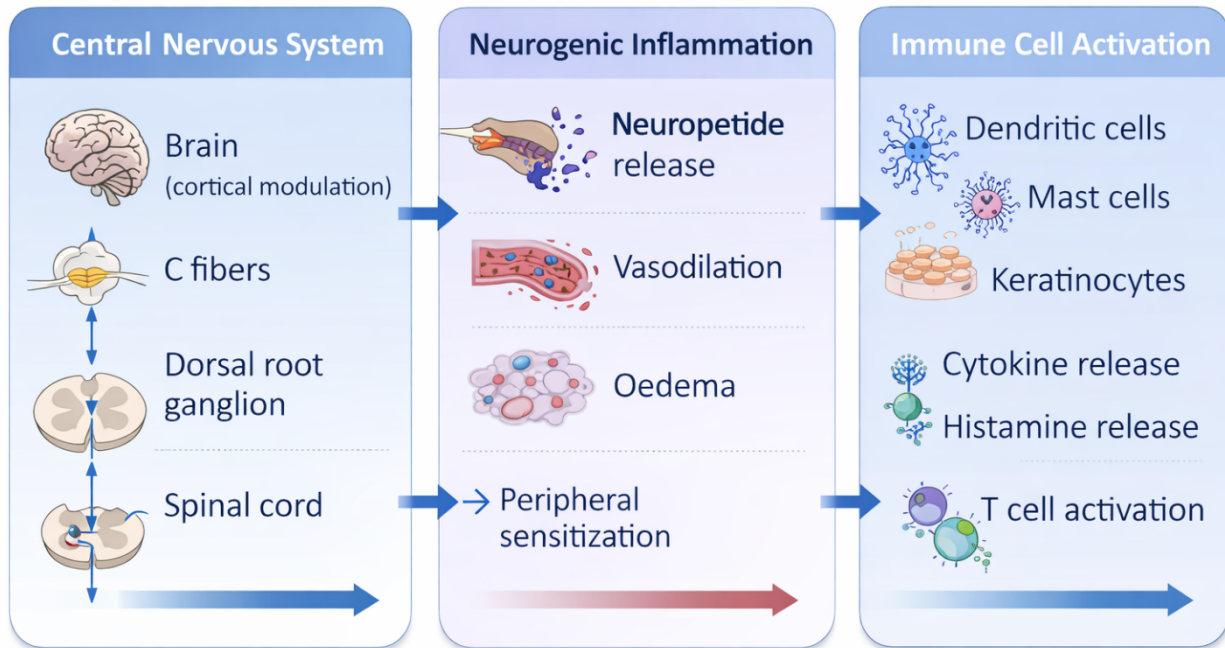


Figure 4. Peripheral Neurogenic Inflammation Linking Immune Activation to Central Pain Processing

Illustration of neurogenic inflammation in fibromyalgia, highlighting the role of peripheral C-fibers, dorsal root ganglion signaling, neuropeptide release, immune cell activation, and vascular changes. Peripheral immune responses amplify nociceptive input to the spinal cord and brain, contributing to sustained pain sensitization.

7. Conclusion

Fibromyalgia disproportionately affects women worldwide, with prevalence estimates among women reaching 2.4–6.8%. Despite its chronic classification, fibromyalgia demonstrates heterogeneous trajectories, including remission-like states in a subset of patients. A brain–behavior–immune framework underscores the modifiability of central sensitization and supports multimodal, neuroplasticity-oriented interventions.

Parameter	Reported Range	Population	References
Global prevalence	0.2–6.6%	General population	[9,13]
Prevalence in women	2.4–6.8%	Women	[9]
Female-to-male ratio	7:1–9:1	Clinical cohorts	[7,14]
Criteria-negative status	20–47%	1–2 year follow-up	[10]
Objective remission	~24%	Selected cohorts	[11,12]
Global prevalence	0.2–6.6%	General population	[9,13]

Table 1. Global Prevalence and Outcome Statistics of Fibromyalgia in Women

Highlights

- Fibromyalgia is conceptualized as a nociplastic disorder of the brain–behavior–immune axis.
- Women exhibit higher global prevalence reflecting sex-specific pain and immune modulation.
- Central sensitization is dynamic and potentially reversible.

- Neuroplasticity-oriented interventions support recovery trajectories.

Declaration of Competing Interest

All authors declared no conflict of interest.

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