The mechanics beneath chronic complex illness

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The mechanics beneath chronic complex illness

How autonomic gain, sleep failure, central sensitisation, connective-tissue load, immune priming and energy restriction may converge in ME/CFS, Long COVID, fibromyalgia and dysautonomia.

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MAY 25

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This is the second piece in the Somatica pair.

The first article introduced the map: **Martial Law of the Soma**, the idea that some chronic complex illnesses behave less like one broken part and more like a whole system reorganising around protection.

This piece goes underneath that map.

It is more technical, but the aim is still translation. I am not trying to replace medical research, diagnose anyone, or claim a final theory of ME/CFS, Long COVID, fibromyalgia, dysautonomia, hypermobility, trauma physiology or neurodivergent burnout.

The question here is narrower:

How does a body move from flexible regulation into a state where

energy, sleep, pain, cognition, circulation and recovery all become unstable together?

The answer is unlikely to be one cause.

It is more likely to be a coupled system: alarm regulation, autonomic control, sleep maintenance, immune signalling, connective-tissue load, pain processing, metabolism and cognitive modelling all beginning to feed each other.

That is the territory of Somatica Mechanistica.

The claim, stated carefully

The claim is not that ME/CFS, Long COVID, fibromyalgia, POTS, hEDS, trauma physiology and neurodivergent burnout are all the same disease.

They are not.

The better claim is this:

chronic complex illness can sometimes be understood as layered regulatory collapse, where different triggers push the body into overlapping defensive states.

In one person, the dominant face may be pain and sensory amplification. In another, it may be orthostatic intolerance and heart-rate instability. In another, it may be post-exertional malaise and low-power collapse. In another, it may be cognitive fog, sleep failure, nausea, migraine, shutdown or functional neurological symptoms.

The labels differ because the dominant surface differs.

The shared pattern is that the system no longer returns cleanly to baseline.

This is why ME/CFS and Long COVID matter together. Komaroff and Lipkin's review argues that ME/CFS and Long COVID share symptoms and biological abnormalities, while still requiring careful work to separate subtypes and mechanisms [1]. NICE guidance also makes clear that ME/CFS is not simply "fatigue", but involves post-exertional malaise, unrefreshing sleep, cognitive difficulty and activity intolerance [2].

So the Somatica claim is not:

virus → fatigue.

It is closer to:

trigger → instability → poor recovery → sensitisation → tighter restriction → deeper instability.

That is a different model.

Evidence posture

Before going further, the evidence has to be separated.

Some parts are well supported. Some are plausible integrations. Some are speculative and need testing.

High confidence means the mechanism is established generally, even if its exact role in every patient differs.

Moderate confidence means there is converging evidence, but it may apply to subgroups or require better longitudinal proof.

Speculative means the idea is mechanistically useful, but should be treated as a hypothesis rather than an established fact.

This matters because chronic illness discourse often collapses in both directions. Either everything becomes vague and psychosomatic, or every interesting mechanism becomes treated as proven.

Both are bad.

The useful middle is:

strong enough to investigate, careful enough to refine.

1. The control layer: autonomic gain

The body does not only have organs. It has control systems deciding how strongly signals are amplified, how much energy is released, how quickly threat is detected, how sleep is entered, how blood pressure is maintained, and when output should be restricted.

A useful centre point here is the **Central Autonomic Network**, or CAN. This is not one switch in the brain. It is a distributed regulatory system involving brainstem, hypothalamic, limbic and cortical regions that coordinates autonomic and bodily state [3].

The simplest version is this:

the alarm system stops pulsing and starts idling high.

That does not always mean panic. It means baseline regulation becomes biased toward vigilance.

The **locus coeruleus**, a brainstem nucleus involved in noradrenaline signalling, matters because noradrenaline helps regulate arousal, attention, wakefulness, pain modulation and response readiness. Reviews of the locus coeruleus-norepinephrine system describe it as important across sleep-wake organisation and arousal regulation [4].

In a healthy state, this system can shift flexibly between alertness and rest. Under chronic load, it may become tonically biased: too much background arousal, not enough clean signal-to-noise.

This gives the classic pattern:

wired, but not resourced.

alert, but not restored.

reactive, but not strong.

From a control perspective, this is high gain with poor recovery.

This should not be overclaimed. The locus coeruleus does not "explain everything." A better statement is that locus coeruleus/noradrenaline dysregulation is a plausible upstream amplifier in a wider coupled system involving autonomic instability, sleep disruption and sensory gain.

2. The autonomic layer: when the body becomes noisy

Once the alarm system runs hot for long enough, the autonomic nervous system can stop being background regulation and become a symptom generator.

Heart rate becomes unstable.

Standing becomes expensive.

Blood pressure regulation becomes inconsistent.

Digestion becomes unreliable.

Temperature control gets strange.

Adrenaline-shaped symptoms appear even when the person is not psychologically panicking.

This is where dysautonomia and POTS-like patterns fit.

The important point is feedback. The brain becomes vigilant, so the body becomes more reactive. The body becomes reactive, so it sends more alarming signals back to the brain. The person can be mentally calm while the body is producing threat-shaped data.

That is not "just anxiety."

It is a loop.

In this model, dysautonomia is not always the first cause. Sometimes it is the point where central alarm spills into body regulation and then becomes self-reinforcing.

A useful transfer rule:

CNS high-gain can spill into ANS instability; ANS instability then becomes evidence that reinforces CNS high-gain.

3. Sleep as maintenance failure

Sleep is where this model becomes much stronger.

A lot of chronic illness advice treats sleep as lifestyle.

Somatica treats sleep as maintenance infrastructure.

Deep sleep is not just the absence of waking. It is one of the main states where the brain and body can lower arousal, regulate immune tone, consolidate memory, reset thresholds and perform clearance processes.

The glymphatic system is often described as a brain waste-clearance pathway. Xie et al. reported that sleep was associated with increased interstitial space and increased convective exchange between cerebrospinal fluid and interstitial fluid in mice, supporting the idea that sleep has a major role in metabolic clearance [5]. That does not mean glymphatic dysfunction is proven as the master cause of ME/CFS or Long COVID. It means sleep architecture gives us a plausible bridge between non-restorative sleep, cognitive fog, neuroimmune persistence and poor recovery.

ME/CFS sleep research also supports sleep as more than a side issue. Jackson and Bruck's review described sleep abnormalities in ME/CFS,

while NICE guidance places unrefreshing sleep and sleep disturbance among core diagnostic features [2,6].

The loop is simple:

High arousal fragments sleep.

Fragmented sleep blocks maintenance.

Poor maintenance increases noise.

Noise increases arousal.

A person can be asleep for hours and still fail to enter the kind of state that repairs the system. That explains why “sleep more” can be true but insufficient. The relevant question is not just duration.

It is yield.

Did sleep restore autonomic flexibility?

Did pain sensitivity reduce?

Did cognition reset?

Did heart rate normalise?

Did the system wake from maintenance, or from suspended emergency mode?

In Somatica terms:

sleep quantity is not the same as maintenance access.

4. Central sensitisation: when the volume knob stays high

Central sensitisation is one of the most important established mechanisms in fibromyalgia and related chronic pain states.

The simple version:

the nervous system becomes more responsive to input, so normal signals feel louder, sharper, more painful or more threatening than they should.

Woolf describes central sensitisation as increased responsiveness of central nociceptive neurons to normal or subthreshold input, producing

pain hypersensitivity such as allodynia and hyperalgesia [7].

This matters because central sensitisation is bigger than pain.

It can help explain why light, sound, touch, movement, temperature, posture, emotion and cognitive demand start interacting. The system is no longer just detecting pain. It is amplifying signal.

Fibromyalgia research has also moved beyond purely descriptive pain models. Albrecht et al. used PET imaging and reported widespread glial activation signal in fibromyalgia, supporting a role for neuroimmune activity in at least some pain-processing circuits [8].

This is not proof of one universal fibromyalgia mechanism. But it does support the broader claim that these symptoms can have biological grounding even when routine tests are normal.

At this layer, the body may begin to generalise danger. A local issue becomes a global sensitivity. A small input becomes a whole-system response. Pain and fatigue start behaving less like simple outputs and more like network states.

The body can learn amplification.

And once it learns it, the system needs more than reassurance to unlearn it.

5. Peripheral amplifiers: fascia, small fibres and connective tissue

A technical Somatica piece cannot become brain-only.

The body matters.

Peripheral input matters.

Connective tissue matters.

Fascia matters.

Small fibres matter.

Mechanical instability matters.

Small fibre pathology is especially important because it gives a concrete peripheral route into pain and autonomic symptoms. A meta-analysis reported that the pooled prevalence of small fibre pathology in fibromyalgia was around 49%, although with heterogeneity between

studies [9]. This does not mean all fibromyalgia is small fibre neuropathy. It means a substantial subset may have peripheral nerve involvement that can feed central sensitisation and autonomic instability.

This is especially relevant for hypermobility and hEDS-style presentations.

The clean Somatica wording is:

EDS and hypermobility act as structural amplifiers. They do not simply add pain; they increase the amount of continuous correction the body and nervous system must perform to maintain ordinary stability.

That means the baseline cost of posture, circulation and proprioception may be higher. Joints are less passively stable. Vessels may be more compliant. Proprioceptive feedback may be noisier. Muscles and fascia may brace more often. The autonomic system may have to work harder just to keep the person upright and coherent.

Miller et al. found that 31% of a POTS sample met clinical criteria for hypermobile Ehlers-Danlos syndrome, with an additional 24% showing generalised joint hypermobility [10]. That does not prove hEDS causes POTS, but it supports the idea that connective-tissue state and autonomic regulation frequently overlap.

That changes the meaning of "activity."

For one person, standing is background.

For another, standing is a continuous regulatory task.

For one person, sitting upright is rest.

For another, it is low-grade exertion.

Same visible action.

Different internal cost.

6. Neuroimmune priming: inflammation without a single inflammatory disease

The immune system is another place where people get trapped between extremes.

Either inflammation is treated as everything, or normal blood tests are

used to imply nothing inflammatory is happening.

The reality is more complicated.

Neuroimmune signalling can influence pain, fatigue, sleep and cognition without behaving like a simple high-CRP inflammatory disease. Microglia and astrocytes can contribute to sensitisation and altered neural processing, while systemic immune signals can affect brain function through multiple routes.

This is not the same as claiming “chronic encephalitis” as a blanket explanation.

It is more careful:

immune signalling may shift thresholds, prime pain and vigilance circuits, and make the system easier to destabilise.

The practical consequence is that a person can feel inflamed, poisoned or flu-like while routine markers remain unimpressive. That does not prove neuroinflammation in that individual, but it does mean the symptom pattern should not be dismissed simply because standard blood tests fail to capture the relevant dynamics.

Static markers are not always enough for dynamic illness.

7. Energy restriction and PEM: the late protective state

This is the deepest layer.

ME/CFS should not be placed early in the chain as “fatigue that causes other problems.”

In the Somatica progression, the myalgic/ME-CFS phenotype sits late as a protective low-power state.

That is a stronger model.

ME/CFS is not “tiredness.”

It is anti-throughput.

The system no longer prices exertion normally.

A task may seem possible during performance because compensation hides the deficit. Later, the debt appears. That is PEM. The activity was not free. It was borrowed.

When the debt arrives, the system clamps output: cognition narrows, pain increases, sensory tolerance drops, sleep may worsen, orthostatic symptoms rise and the person loses access to normal capacity.

NICE describes PEM as symptom worsening after activity that is often delayed by hours or days, disproportionate to the activity, and associated with prolonged recovery [2]. That is fundamentally different from ordinary tiredness.

This is why generic graded expansion can be dangerous when applied without state awareness. NICE explicitly warns against fixed incremental graded exercise therapy for ME/CFS when activity is increased regardless of symptoms [2].

The Somatica rule is:

expansion only makes sense after stabilisation.

Otherwise, you are not training the system.

You are proving to it that ordinary output is unsafe.

8. Long COVID as a lower-entry insult

Most staged-collapse models move downward gradually.

Priming.

High-gain alarm.

Autonomic spillover.

Recovery failure.

Sensitisation.

Low-power state.

But Long COVID complicates this because a major post-viral insult may enter lower in the system.

That means the person may not slowly descend through every visible stage. Infection can potentially create early immune, vascular, autonomic or bioenergetic disturbance, pushing the system toward PEM-dominant dysfunction faster.

The careful wording is:

Long COVID may act as a lower-entry systems insult by impairing metabolic, immune, vascular or autonomic stability early, producing a PEM-dominant state that then back-propagates into cognition, sleep, pain and autonomic regulation.

Not every Long COVID case does this.

Not every Long COVID case is ME/CFS.

But Long COVID provides a powerful example of non-linear chronic illness trajectories after an identifiable trigger. Reviews increasingly discuss mitochondrial dysfunction and altered cellular energy metabolism as candidate contributors to Long COVID symptoms, including fatigue and reduced cellular energy availability [11].

This matters because Long COVID makes the "similar room, different door" model harder to ignore.

A person can be pushed into system instability by a biological event.

Once there, persistence may be governed by loops rather than the original trigger alone.

9. The modelling layer: DMN, prediction and cognitive cost

The mind is not floating above physiology.

Thinking costs energy.

Prediction costs energy.

Masking costs energy.

Monitoring body signals costs energy.

Trying to remain coherent while the body produces unstable interoceptive data costs energy.

The Default Mode Network is relevant because it is involved in internally focused cognition, including self-referential thought, autobiographical memory and future simulation [12]. In Somatica language, this makes it part of the modelling layer: the brain's internal simulation system.

This does not mean the DMN "causes" chronic illness.

It means cognitive symptoms should not be reduced to attitude or mood. Brain fog, zoning out, intrusive loops, threat-weighted prediction and

difficulty switching between rest and task states can be understood as network-regulation problems interacting with sleep, arousal, autonomic state and metabolic capacity.

A useful line:

the mind does not escape the body's state.

If the body is noisy, sleep is poor, pain is amplified and autonomic signals are unstable, the modelling system has worse data and less energy. It must work harder to produce coherence.

That is why people can be intelligent and still unable to think on command.

The capacity is not gone.

Access is impaired.

10. Neurodivergence and trauma as modulators, not causes

This part has to be handled cleanly.

Neurodivergence is not pathology in itself.

Trauma is not a magic explanation for everything.

Neither should be used to reduce biological illness to psychology.

But both can alter load, signalling and recovery.

Neurodivergent systems may process more sensory data, carry higher switching cost, require more structured recovery, or use more energy for masking and environmental translation. Trauma-shaped physiology may bias the system toward threat detection, hypervigilance, dissociation or altered stress response.

The technical point is:

they change the starting conditions.

They do not automatically cause collapse.

They alter margin.

Under supportive conditions, these configurations can be stable or advantageous. Under prolonged mismatch, they can increase baseline

load and reduce recovery room.

A useful phrase:

not causes, but parameter shifts.

They change how quickly the system reaches instability under sustained pressure.

11. The full progression

The cleanest technical progression is this.

A system begins with a certain margin. That margin may be reduced by trauma load, neurodevelopmental load, connective tissue instability, repeated illness, poor sleep, pain, stress or environmental mismatch.

At first, the person may still function, but ordinary life costs more.

If load persists, the CNS shifts toward high-gain governance. The alarm system stops pulsing and begins idling high.

That high-gain state spills into autonomic regulation. Heart rate, blood pressure, digestion, temperature, posture and sleep become less stable.

The unstable body then feeds back into the brain as more alarming internal signal.

Recovery starts failing. Sleep becomes non-restorative. Pain inhibition weakens. Cognitive reset degrades. Sensory tolerance drops. Repair debt accumulates.

Central sensitisation and neuroimmune priming make the system easier to trigger and harder to calm.

Eventually, the system may enter a low-power protective mode where PEM dominates and ordinary output is restricted.

That is the cone:

1. Primed terrain
2. CNS high-gain
3. ANS destabilisation
4. Recovery failure and sensitisation

5. Myalgic low-power clamp

That is the technical spine of Somatica Mechanistica.

12. What would make this useful clinically?

The point of this model is not to create a new label.

It is to change what we measure.

If the illness is dynamic, static snapshots will miss the point.

A single HRV reading is not autonomic stability.

A normal blood test is not proof of normal recovery.

A good hour is not proof of functional capacity.

A normal scan is not proof that regulation is intact.

Somatica predicts that useful data will often be longitudinal:

recovery curves,

orthostatic response over time,

sleep quality and next-day function,

PEM delay,

symptom variance,

heart-rate recovery,

response to cognitive load,

and whether activity expands capacity or steals from future capacity.

The practical measurement shift is this:

measure the thing that is actually failing: regulation over time.

Not just what the person can do once.

What it costs.

How long recovery takes.

Whether baseline returns.

Whether the system is widening or narrowing.

13. What would break the model?

A good model should be able to fail.

Somatica Mechanistica would weaken if:

PEM did not show delayed recovery debt under controlled load.

Autonomic variability did not correlate with functional impairment in relevant subgroups.

Sleep restoration reliably improved subjective rest without changing recovery, gain or function.

Central sensitisation markers had no relationship to pain, fatigue or sensory amplification.

Longitudinal patterns did not outperform static snapshots.

Baseline modulators such as connective tissue instability, trauma load or neurodevelopmental load had no effect on trajectory when properly controlled.

The aim is not to defend Somatica as doctrine.

The aim is to build a better map, then let measurement sharpen it.

Closing

The first Somatica piece said:

the body can enter martial law.

This piece says:

here is how that state may be built.

Not by one cause.

Not by one organ.

Not by one emotion.

But by coupled regulation: alarm, sleep, immune signalling, pain processing, autonomic control, connective tissue load, metabolism and cognition feeding each other until ordinary recovery no longer works.

The model is not finished.

It should not be treated as settled medicine.

But it gives a structure for something patients have been describing for years:

the body is not simply tired.

It is reactive, unstable, under-recovered, over-amplified, poorly cleared, poorly buffered and increasingly restrictive with output.

That is why the person can still be present while capacity disappears.

That is why Long COVID and ME/CFS need to be discussed together without making them identical.

That is why fibromyalgia should not be reduced to pain, dysautonomia should not be reduced to anxiety, and post-exertional malaise should not be reduced to deconditioning.

A chronic complex illness is not always one broken component.

Sometimes it is a system that has learned the wrong survival state too well.

And once that happens, recovery is not about forcing performance.

It is about restoring the conditions under which the system can safely stand down.

Source note

This piece is mainly drawn from *The Somatica Model*, *Somatica Modelo*, *Integrative Mechanisms Linking Fibromyalgia, Dysautonomia, Chronic Fatigue, and Neurodivergence*, and the Somatica people-first release discussion. The internal documents provide the core structure: chronic multi-system illness as governance reorganisation, body–nervous-system–mind coupling, recovery failure, longitudinal measurement, and state-matched intervention logic. The longer Somatica draft also develops the martial-law framing, predictive modelling cost, sleep/clearance logic, nonlinear coupling, hysteresis and severity gradients. The integrated mechanisms draft supplies the more

biomedical layer: autonomic overdrive, sleep disturbance, glymphatic hypotheses, central sensitisation, neuroimmune activity, myofascial/peripheral amplifiers, EDS/hypermobility, trauma and neurodivergence. The release discussion helped freeze the public/technical bridge, including the five-layer cone, ME/CFS as a late low-power state, EDS as structural amplifier, and Long COVID as a possible lower-entry insult.

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