

# Sustained Relief of Refractory Restless Leg Syndrome with Cannabinoids

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## Case Presentation

Patient is 60 years old with restless leg syndrome (RLS) diagnosed at age 40 and having near daily symptoms since.

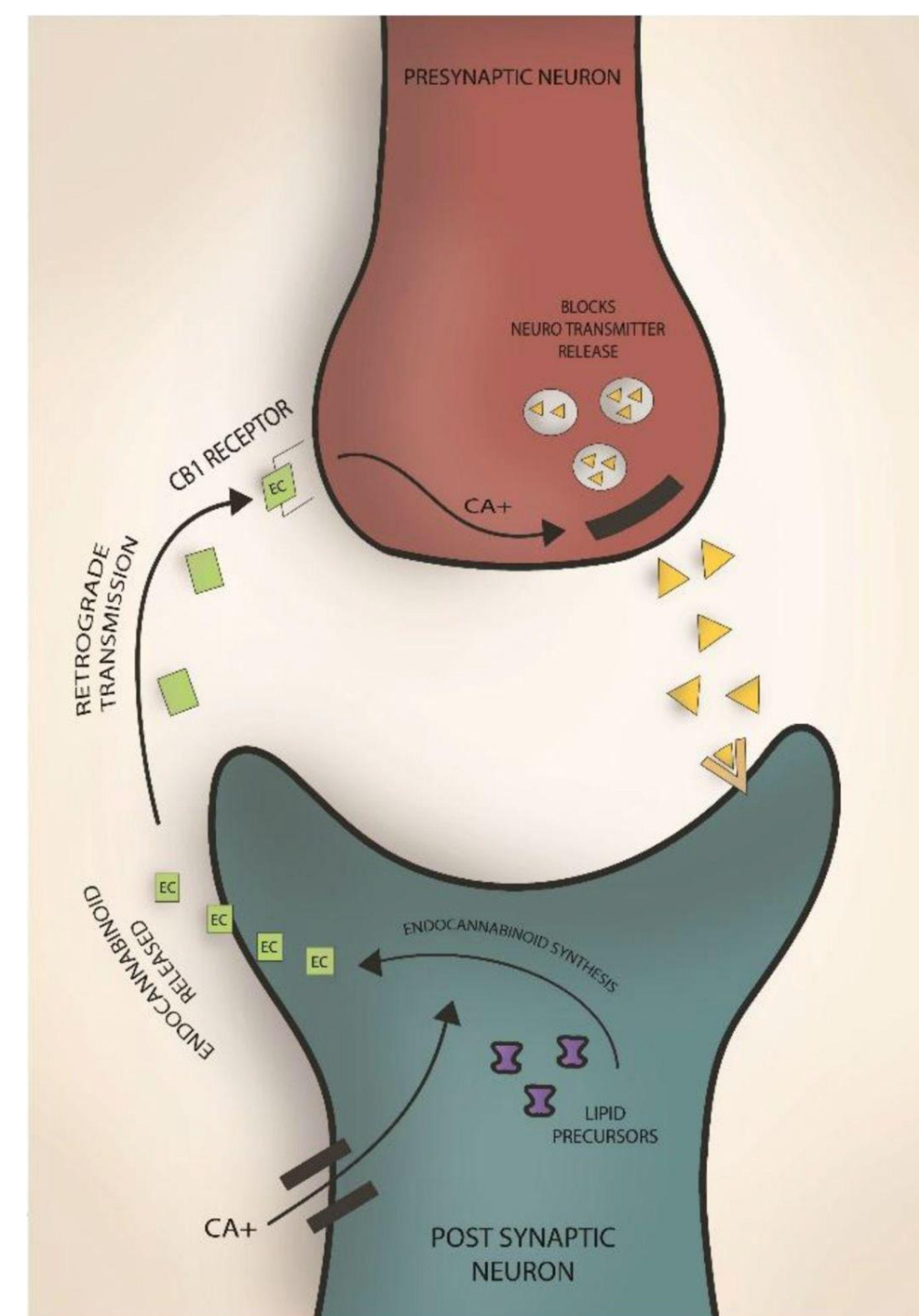
- Symptoms begin around 5 pm - irresistible urge to move her legs and “excruciating” 10/10 pain - and worsen throughout the night, not stopping until around 5 am. She no longer sleeps in bed with her partner, but on a mat in the living room.
- Exam revealed normal tone and strength, no rigidity, and a mild resting tremor.
- Iron studies were normal.
- She has tried many medications which either gave no benefit (Pergolide, Clonazepam) or caused worsening symptoms (Pramipexole, Rotigotine). She had previously had some limited success with Baclofen and Gabapentin - but only for 1-2 weeks before symptoms recurred.

She says that she was “at her wit’s end” in terms of insomnia, pain, and mood. The next option recommended to her was opiates, but she was reluctant and instead wanted to try medical cannabis.

She received education by a cannabis nurse and started a regimen of cannabidiolic acid (CBDA) drops, vaporized Δ9-tetrahydrocannabinol (THC) / cannabiol (CBN) / cannabigerol (CBG) / cannabichromene (CBC) / cannabidiol (CBD), and oral gummies with 1:1 THC/CBG.

Since starting this regimen she reports that she “feels like a new woman” and has achieved total remission of her RLS symptoms for more than 5 months, far longer than any prior period of respite. She reports significant improvement to her quality of life, is sleeping through the night, and denies any significant intoxicating side effects.

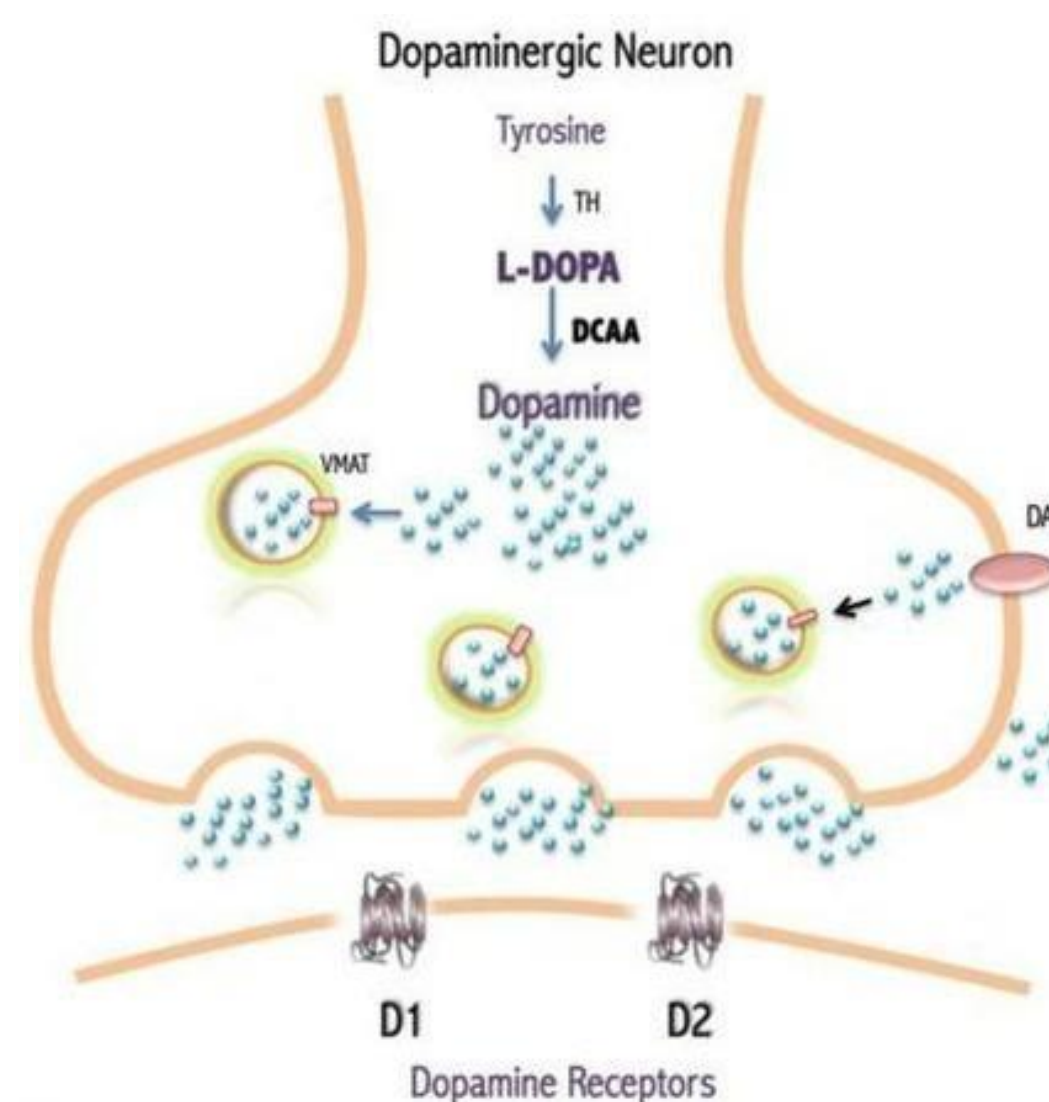
## Endocannabinoid System



- The natural endocannabinoid system consists of many receptors, including cannabinoid type 1 (CB1R) and type 2 (CB2R) and endogenous cannabinoid ligands such as anandamide and 2-AG (1).
- CB1 receptors are located throughout the nervous system where cannabinoids likely maintain homeostasis and induce analgesia by inhibiting presynaptic neurotransmitter release and modulating post-synaptic neuron excitability (2).

## Restless Leg Syndrome Pathophysiology

The mechanism underlying Restless Leg Syndrome is not fully understood, but likely a combination of (3-4):



- Genetic factors
- Alteration of homeostasis resulting in brain tissue iron deficiency, leading to decreased synthesis of tyrosine hydroxylase
- Complex interaction with the dopaminergic system (binding dysfunction, increased dopamine turnover, ? hyperdopaminergic state)
- Decreased inhibition of descending spinal tracts to the periphery

## Discussion

- Moderate to severe RLS affects 2-3% of the North American and European population - leading to significant morbidity and reduced quality of life. Many patients can be treated with a combination of dopamine agonists, anticonvulsants, and opiates; however, a subset of patients either remain refractory or develop significant side effects - such as poor impulse control or augmentation, a worsening of RLS symptoms.
- The antinociceptive effects of cannabinoids for chronic and neuropathic pain has been widely documented - via interaction with CB1 and TRPV1 receptors, among others (5) - but the effectiveness in treating RLS in particular has not been well studied. However, there are reports of patients spontaneously using cannabis and then achieving significant relief of RLS symptoms (6).
- Cannabinoids modulate post synaptic excitability and other cell messaging to maintain homeostasis, and have also been shown to regulate release of serotonin and noradrenaline, and to modulate dopamine synthesis (6).

## Conclusion

A patient with RLS refractory to conventional treatment options found significant and sustained relief using medical cannabis. Endocannabinoid signaling in the nervous system has a variety of mechanisms by which it may exert antinociceptive and anxiolytic effects, and the potential benefit for cannabis to treat RLS symptoms should be explored in robust clinical trials.

## References

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