A PROPOSED NEW MODEL of RESTLESS LEGS SYNDROME PERIPHERAL ORIGIN, INTEROCEPTIVE PERCEPTION, and AII MODULATION CITED WORKS

1. Ekbom KA. Asthenia crurum paraesthetica (irritable legs). Acta Med Scand. 1944;118:197–209.
2. Allen RP, Picchietti D, Hening WA, Trenkwalder C, Walters AS, Montplaisi J. Restless legs syndrome: diagnostic criteria, special considerations, and epidemiology: a report from the restless legs syndrome diagnosis and epidemiology workshop at the National Institutes of Health. Sleep medicine. 2003 Mar 1;4(2):101-19. DOI: https://doi.org/10.1016/S1389-9457(03)00010-8
3. Manconi M, Garcia-Borreguero D, Schormair B, et al. Restless legs syndrome. Nat Rev Dis Primers. 2021;7:80. DOI: https://doi.org/10.1038/s41572-021-00311-z
4. Clemens S, Rye D, Hochman S. Restless legs syndrome: revisiting the dopamine hypothesis from the spinal cord perspective. Neurology. 2006;67:125–30. DOI: https://doi.org/10.1212/01.wnl.0000223316.53428.c9
5. Trenkwalder C, Allen R, Högl B, et al. Comorbidities, treatment, and pathophysiology in restless legs syndrome. Lancet Neurol. 2018;17:994–1005. DOI: https://doi.org/10.1016/S1474-4422(18)30311-9
6. Hayes CA, Kingsley JR, Hamby KR, Carlow J. The effect of endovenous laser ablation on restless legs syndrome. Phlebology. 2008;23:112–17. DOI: https://doi.org/10.1258/phleb.2007.007051
7. Salminen AV, Rimpilä V, Polo O. Peripheral hypoxia in restless legs syndrome (Willis-Ekbom disease). Neurology. 2014;82:1856–61. DOI: https://doi.org/10.1212/WNL.0000000000000454
8. Strigo IA, Craig AD. Interoception, homeostatic emotions and sympathovagal balance. Philos Trans R Soc Lond B Biol Sci. 2016;371(1708):20160010. DOI: https://doi.org/10.1098/rstb.2016.0010
9. Evrard HC. The Isle of Craig: Neuroanatomical and Functional Evidence for a Role of the Insular Cortex in Subjective Feelings. The Bodily Self, Emotion, and Subjective Time: Exploring Interoception through the Contributions of AD (Bud) Craig. 2025 May 28:33-61. DOI: https://doi.org/10.1007/7854_2025_590
10. Casar JC, Idiaquez J, Benarroch E. What are the functions of interoception and allostasis and their contribution to neurologic symptoms? Neurology. 2025. DOI: https://doi.org/10.1212/WNL.0000000000214366
11. Manconi M, Govoni V, De Vito A, et al. Restless legs syndrome and pregnancy. Neurology. 2004;63:1065–9.DOI: https://doi.org/10.1212/01.WNL.0000138427.83574.A6

12. Trenkwalder C, Allen R, Högl B, Paulus W, Winkelmann J. Restless legs syndrome associated with major diseases: a systematic review and new concept. Neurology. 2016;86(14):1336–43. DOI: https://doi.org/10.1212/WNL.0000000000002542
13. Benarroch EE. Ion channels in nociceptors: recent developments. Neurology. 2015;84(11):1140–9. DOI: https://doi.org/10.1212/WNL.0000000000001382
14. Bennett DL, Woods CG. Painful and painless channelopathies. Lancet Neurol. 2014;13(6):587–99. DOI: https://doi.org/10.1016/S1474-4422(14)70024-9
15. Benarroch EE. Dorsal horn circuitry: complexity and implications for mechanisms of neuropathic pain. Neurology. 2016;86(11):1060–9. DOI: https://doi.org/10.1212/WNL.0000000000002478
16. Tsagareli MG, Nozadze I, Tsiklauri N, et al. Thermal hyperalgesia and mechanical allodynia elicited by histamine and non-histaminergic itch mediators: respective involvement of TRPV1 and TRPA1. Neuroscience. 2020;449:35–45. DOI: https://doi.org/10.1016/j.neuroscience.2020.09.048
17. Kim BS, Inan S, Ständer S, et al. Role of kappa-opioid and mu-opioid receptors in pruritus: peripheral and central itch circuits. Exp Dermatol. 2022;31(12):1900–7. DOI: https://doi.org/10.1111/exd.14669
18. Light AR, Hughen RW, Zhang J, et al. Dorsal root ganglion neurons innervating skeletal muscle respond to physiological combinations of protons, ATP, and lactate mediated by ASIC, P2X, and TRPV1. J Neurophysiol. 2008;100(3):1184–201. DOI: https://doi.org/10.1152/jn.01344.2007
19. Crisafulli A, Marongiu E, Ogoh S. Cardiovascular reflexes activity and their interaction during exercise. Biomed Res Int. 2015;2015:394183. DOI: https://doi.org/10.1155/2015/394183
20. Walters AS, Li Y, Koo BB, et al. Review of the role of the endogenous opioid and melanocortin systems in the restless legs syndrome. Brain. 2024;147(1):26–38. DOI: https://doi.org/10.1093/brain/awad283
21. Redolfi S, Yumino D, Ruttanaumpawan P, et al. Relationship between overnight rostral fluid shift and obstructive sleep apnea in nonobese men. Am J Respir Crit Care Med. 2009;179(3):241–6. DOI: https://doi.org/10.1164/rccm.200807-1076OC
22. Lettieri CJ, Eliasson AH. Pneumatic compression devices are an effective therapy for restless legs syndrome: a prospective, randomized, double-blinded, sham-controlled trial. Chest. 2009;135(1):74–80. DOI: https://doi.org/10.1378/chest.08-1665
23. Dopierała M, Schwermer K, Hoppe K, Kupczyk M, Pawlaczyk K. Benefits of preserving residual urine output in patients undergoing maintenance haemodialysis. International Journal of Nephrology and Renovascular Disease. 2023 Dec 31:231-40. DOI: https://doi.org/10.2147/IJNRD.S421533
24. Winkelmann J, Stautner A, Samtleben W, Trenkwalder C. Long-term course of restless legs syndrome in dialysis patients after kidney transplantation. Movement disorders: official

journal of the Movement Disorder Society. 2002 Sep;17(5):1072-6.DOI: https://doi.org/10.1002/mds.10231

25. Craig AD. Interoception: the sense of the physiological condition of the body. Curr Opin Neurobiol. 2003;13(4):500–5. DOI: https://doi.org/10.1016/S0959-4388(03)00090-4
26. Ku J, Lee YS, Kim KT, Chang H, Cho YW. Alterations in salience network functional connectivity in individuals with restless legs syndrome. Sci Rep. 2020;10(1):7643. DOI: https://doi.org/10.1038/s41598-020-64641-w
27. Astrakas LG, Konitsiotis S, Margariti P, et al. T2 relaxometry and fMRI of the brain in late-onset restless legs syndrome. Neurology. 2008;71(12):911–6. DOI: https://doi.org/10.1212/01.wnl.0000325914.50764.a2
28. Kim TJ, Cha KS, Lee S, et al. Brain regions associated with periodic leg movements during sleep in restless legs syndrome. Sci Rep. 2020;10(1):1615. DOI: https://doi.org/10.1038/s41598-020-58365-0