

Iron deficiency

Iron delivery to the developing brain is essential for energy and metabolic support needed for processes such as myelination and neuronal development.

Anemia is frequent and an independent risk factor for morbidity and mortality in patients undergoing surgery. Iron deficiency (ID) is the main cause of anemia and can be corrected by intravenous (IV) iron. Supplementation of IV iron to increase Hb concentration preoperatively may be most effective if administered at least ten days before surgery ¹⁾.

May be associated with idiopathic intracranial hypertension.

“Hair-On-End” appearance in the skull

An updated meta-analysis shows that patients with anemia appear to have a nearly 1.39-fold risk of developing overall cognitive impairment (OCI) than those without anemia. The magnitude of this risk underscores the importance of improving anemia patients' health outcomes, particularly in elderly patients ²⁾.

Iron deficiency, especially in the developing brain, can result in a number of long-term neurological deficits that persist into adulthood. There is considerable debate that excess access to iron during development may result in iron overload in the brain and subsequently predispose individuals to age-related neurodegenerative diseases. There is a significant gap in knowledge regarding how the brain acquires iron during development and how biological variables such as development, genetics and sex impact brain iron status.

In a study, Chiou et al. used a mouse model expressing a mutant form of the iron homeostatic regulator protein HFE, (Hfe H63D), the most common gene variant in Caucasians, to determine impact of the mutation on brain iron uptake. Iron uptake was assessed by using ⁵⁹Fe bound to either transferrin or H-ferritin as the iron carrier proteins. We demonstrate that at postnatal day 22, mutant mice brains take up greater amounts of iron compared to wildtype. Moreover, we introduce H-ferritin as a key protein in brain iron transport during development and identify a sex and genotype effect demonstrating female mutant mice take up more iron by transferrin while male mutant mice take up more iron from H-ferritin at PND22. Furthermore, we begin to elucidate the mechanism for uptake using immunohistochemistry to profile the regional distribution and temporal expression of transferrin receptor and Tim-2, the latter is the receptor for H-ferritin. These data demonstrate that sex and genotype have significant effects on iron uptake and that regional receptor expression may play a large role in the uptake patterns during development ³⁾.

Case reports

A 2-year-old girl presenting with non-specific symptoms, who was found to be iron-deficient and anaemic, in the context of excessive cow's milk consumption. We explore the patient's diagnostic journey, including a neurological deterioration and the link between her iron deficiency and the final diagnosis. ⁴⁾.

A young Chinese woman with untreated iron deficiency anemia presented with fatigue and pain in her thigh muscles for 3 days and tea-colored urine for 1 day, after cycling and subsequently receiving percussion gun treatment by her coach for the purpose of massage and relaxing tired muscles. Muscle tenderness and multiple hematomas were found on her thighs, and her urinalysis indicated hemoglobinuria. Her serum creatine kinase was reported as “undetectably high,” a hallmark of serious muscle damage leading to a diagnosis of severe rhabdomyolysis. Aggressive intravenous fluid resuscitation, urine alkalinization via intravenous alkaline solution, assessment of urine output, and maintenance of electrolyte balance were administered during hospitalization.

Results: The patient's clinical presentation gradually improved with the decline of creatine kinase, and she recovered well during follow-up.

Conclusion: A case of severe rhabdomyolysis after percussion massage should alert caregivers, sports professionals, and the public to suspect and recognize the potentially serious adverse effects of percussion guns and to ensure that percussion massage guns be used appropriately and safely in rehabilitation therapy, especially in individuals with an underlying disease or condition. Research is needed to examine the benefits, indications, contraindications, and adverse reactions of percussion guns⁵⁾.

5: Tremblay-Laganière C, Kaiyrzhanov R, Maroofian R, Nguyen TTM, Salayev K, Chilton IT, Chung WK, Madden JA, Phornphutkul C, Agrawal PB, Houlden H, Campeau PM. PIGH deficiency can be associated with severe neurodevelopmental and skeletal manifestations. *Clin Genet*. 2021 Feb;99(2):313-317. doi: 10.1111/cge.13877. Epub 2020 Nov 27. PMID: 33156547; PMCID: PMC7839508.

6: Shin JW, Lee JH, Kim H, Lee DH, Baek KH, Sunwoo JS, Byun JI, Kim TJ, Jun JS, Han D, Jung KY. Bioinformatic analysis of proteomic data for iron, inflammation, and hypoxic pathways in restless legs syndrome. *Sleep Med*. 2020 Nov;75:448-455. doi: 10.1016/j.sleep.2020.09.002. Epub 2020 Sep 13. PMID: 32992101.

7: Shih JH, Li IH, Pan KT, Wang CH, Chen HC, Fann LY, Tseng JH, Kao LT. Association between Anemia and Auditory Threshold Shifts in the US Population: National Health and Nutrition Examination Survey. *Int J Environ Res Public Health*. 2020 Jun 1;17(11):3916. doi: 10.3390/ijerph17113916. PMID: 32492846; PMCID: PMC7312977.

8: Shigekiyo T, Yagi H, Sekimoto E, Shibata H, Ozaki S, Tamura T. Cerebral infarction and iron deficiency anemia due to uterine myoma in two middle-aged women with histidine-rich glycoprotein deficiency. *Thromb Res*. 2020 Jul;191:30-33. doi: 10.1016/j.thromres.2020.04.027. Epub 2020 Apr 23. PMID: 32361514.

9: Connor JR, Duck K, Patton S, Simpson IA, Trotti LM, Allen R, Earley CJ, Rye D. Evidence for communication of peripheral iron status to cerebrospinal fluid: clinical implications for therapeutic strategy. *Fluids Barriers CNS*. 2020 Apr 16;17(1):28. doi: 10.1186/s12987-020-00190-8. PMID: 32295615; PMCID: PMC7161256.

10: Vila Cuenca M, Marchi G, Barqué A, Esteban-Jurado C, Marchetto A, Giorgetti A, Chelban V, Houlden H, Wood NW, Piubelli C, Dorigatti Borges M, Martins de Albuquerque D, Yotsumoto Fertrin K, Jové-Buxeda E, Sanchez-Delgado J, Baena-Díez N, Burnyte B, Utkus A, Busti F, Kaubrys G, Suku E, Kowalczyk K, Karaszewski B, Porter JB, Pollard S, Eleftheriou P, Bignell P, Girelli D, Sanchez M. Genetic

and Clinical Heterogeneity in Thirteen New Cases with Aceruloplasminemia. Atypical Anemia as a Clue for an Early Diagnosis. *Int J Mol Sci*. 2020 Mar 30;21(7):2374. doi: 10.3390/ijms21072374. PMID: 32235485; PMCID: PMC7178074.

11: Hsiung KC, Liu KY, Tsai TF, Yoshina S, Mitani S, Chin-Ming Tan B, Lo SJ. Defects in C1SD-1, a mitochondrial iron-sulfur protein, lower glucose level and ATP production in *Caenorhabditis elegans*. *Biomed J*. 2020 Feb;43(1):32-43. doi: 10.1016/j.bj.2019.07.009. Epub 2020 Feb 27. PMID: 32200954; PMCID: PMC7090286.

12: Nguyen KL, Yoshida T, Kathuria-Prakash N, Zaki IH, Varallyay CG, Semple SI, Saouaf R, Rigsby CK, Stoumpos S, Whitehead KK, Griffin LM, Saloner D, Hope MD, Prince MR, Fogel MA, Schiebler ML, Roditi GH, Radjenovic A, Newby DE, Neuwelt EA, Bashir MR, Hu P, Finn JP. Multicenter Safety and Practice for Off-Label Diagnostic Use of Ferumoxytol in MRI. *Radiology*. 2019 Dec;293(3):554-564. doi: 10.1148/radiol.2019190477. Epub 2019 Oct 22. PMID: 31638489; PMCID: PMC6884068.

13: Varshneya K, Medress ZA, Jensen M, Azad TD, Rodrigues A, Stienen MN, Desai A, Ratliff JK, Veeravagu A. Trends in Anterior Lumbar Interbody Fusion in the United States: A MarketScan Study From 2007 to 2014. *Clin Spine Surg*. 2020 Jun;33(5):E226-E230. doi: 10.1097/BSD.0000000000000904. PMID: 31609798.

14: Ravi V, Madhankumar AB, Abraham T, Slagle-Webb B, Connor JR. Liposomal delivery of ferritin heavy chain 1 (FTH1) siRNA in patient xenograft derived glioblastoma initiating cells suggests different sensitivities to radiation and distinct survival mechanisms. *PLoS One*. 2019 Sep 6;14(9):e0221952. doi: 10.1371/journal.pone.0221952. PMID: 31491006; PMCID: PMC6730865.

15: Inada T, Sadamasa N, Motoie R, Yamana N, Taki W. Cerebral Venous Thrombosis after Red Blood Cell Transfusion for the Treatment of Iron Deficiency Anemia. *J Stroke Cerebrovasc Dis*. 2019 Nov;28(11):104338. doi: 10.1016/j.jstrokecerebrovasdis.2019.104338. Epub 2019 Aug 21. PMID: 31444045.

16: Chiou B, Neely EB, Mcdevitt DS, Simpson IA, Connor JR. Transferrin and H-ferritin involvement in brain iron acquisition during postnatal development: impact of sex and genotype. *J Neurochem*. 2020 Feb;152(3):381-396. doi: 10.1111/jnc.14834. Epub 2019 Aug 22. PMID: 31339576; PMCID: PMC6980902.

17: Gromova OA, Torshin IY, Kobalava ZD, Nazarenko AG. [Systematic Analysis of the Roles of Trace Elements in the Prevention and Treatment of Chronic Heart Failure]. *Kardiologiya*. 2019 Jun 5;59(6):26-34. Russian. doi: 10.18087/cardio.2019.6.n683. PMID: 31242838.

18: Wade QW, Chiou B, Connor JR. Iron uptake at the blood-brain barrier is influenced by sex and genotype. *Adv Pharmacol*. 2019;84:123-145. doi: 10.1016/bs.apha.2019.02.005. Epub 2019 Mar 22. PMID: 31229168.

19: Fluss R, Zguri L, Rahme R, Fulger I. Iron-deficiency Anemia Causes an Ischemic Stroke in a Young Man. *Cureus*. 2019 Mar 11;11(3):e4218. doi: 10.7759/cureus.4218. PMID: 31106101; PMCID: PMC6506274.

20: Grochowski C, Blicharska E, Baj J, Mierzwińska A, Brzozowska K, Forma A, Maciejewski R. Serum iron, Magnesium, Copper, and Manganese Levels in Alcoholism: A Systematic Review. *Molecules*. 2019 Apr 7;24(7):1361. doi: 10.3390/molecules24071361. PMID: 30959950; PMCID: PMC6480471.

21: Zhou X, Xu W, Xu Y, Qian Z. Iron Supplementation Improves Cardiovascular Outcomes in Patients with Heart Failure. *Am J Med*. 2019 Aug;132(8):955-963. doi: 10.1016/j.amjmed.2019.02.018. Epub

2019 Mar 7. PMID: 30853478.

22: Chen P, Totten M, Zhang Z, Bucinca H, Erikson K, Santamaría A, Bowman AB, Aschner M. Iron and manganese-related CNS toxicity: mechanisms, diagnosis and treatment. *Expert Rev Neurother*. 2019 Mar;19(3):243-260. doi: 10.1080/14737175.2019.1581608. Epub 2019 Feb 21. PMID: 30759034; PMCID: PMC6422746.

23: Chiou B, Connor JR. Emerging and Dynamic Biomedical Uses of Ferritin. *Pharmaceuticals (Basel)*. 2018 Nov 13;11(4):124. doi: 10.3390/ph11040124. PMID: 30428583; PMCID: PMC6316788.

24: Trenkwalder C, Allen R, Högl B, Clemens S, Patton S, Schormair B, Winkelmann J. Comorbidities, treatment, and pathophysiology in restless legs syndrome. *Lancet Neurol*. 2018 Nov;17(11):994-1005. doi: 10.1016/S1474-4422(18)30311-9. Epub 2018 Sep 21. PMID: 30244828.

25: Chiou B, Neal EH, Bowman AB, Lippmann ES, Simpson IA, Connor JR. Endothelial cells are critical regulators of iron transport in a model of the human blood- brain barrier. *J Cereb Blood Flow Metab*. 2019 Nov;39(11):2117-2131. doi: 10.1177/0271678x18783372. Epub 2018 Jun 18. PMID: 29911470; PMCID: PMC6827128.

26: Xiang D, Wang X, Liu P, Pan Y, Zhang Q, Chi X, Jing Y, Duan X, Wei Q, Wang J, Li M, Wang C. Increased NGAL level associated with iron store in chronic kidney disease with anemia. *Clin Exp Med*. 2018 Nov;18(4):563-568. doi: 10.1007/s10238-018-0507-4. Epub 2018 Jun 16. PMID: 29909502.

27: Chiou B, Neal EH, Bowman AB, Lippmann ES, Simpson IA, Connor JR. Pharmaceutical iron formulations do not cross a model of the human blood-brain barrier. *PLoS One*. 2018 Jun 11;13(6):e0198775. doi: 10.1371/journal.pone.0198775. PMID: 29889872; PMCID: PMC5995392.

28: Altinoz MA, Elmaci I, Cengiz S, Emekli-Alturfan E, Ozpinar A. From epidemiology to treatment: Aspirin's prevention of brain and breast-cancer and cardioprotection may associate with its metabolite gentisic acid. *Chem Biol Interact*. 2018 Aug 1;291:29-39. doi: 10.1016/j.cbi.2018.05.016. Epub 2018 Jun 7. PMID: 29885857.

29: Riboldi GM, Anstett K, Jain R, Lau H, Swope D. Aceruloplasminemia and putaminal cavitation. *Parkinsonism Relat Disord*. 2018 Jun;51:121-123. doi: 10.1016/j.parkreldis.2018.03.003. Epub 2018 Mar 7. PMID: 29534945.

30: Varga E, Pandur E, Abrahám H, Horváth A, Ács P, Komoly S, Miseta A, Sipos K. Cuprizone Administration Alters the Iron Metabolism in the Mouse Model of Multiple Sclerosis. *Cell Mol Neurobiol*. 2018 Jul;38(5):1081-1097. doi: 10.1007/s10571-018-0578-5. Epub 2018 Feb 20. PMID: 29464444.

31: Chiou B, Lucassen E, Sather M, Kallianpur A, Connor J. Semaphorin4A and H-ferritin utilize Tim-1 on human oligodendrocytes: A novel neuro-immune axis. *Glia*. 2018 Jul;66(7):1317-1330. doi: 10.1002/glia.23313. Epub 2018 Feb 19. PMID: 29457657; PMCID: PMC7009020.

32: Eloqayli H, Al-Yousef A, Jaradat R. Vitamin D and ferritin correlation with chronic neck pain using standard statistics and a novel artificial neural network prediction model. *Br J Neurosurg*. 2018 Apr;32(2):172-176. doi: 10.1080/02688697.2018.1436691. Epub 2018 Feb 15. PMID: 29447493.

33: Allen RP, Picchietti DL, Auerbach M, Cho YW, Connor JR, Earley CJ, Garcia- Borreguero D, Kotagal S, Manconi M, Ondo W, Ulfberg J, Winkelmann JW; International Restless Legs Syndrome Study Group (IRLSSG). Evidence-based and consensus clinical practice guidelines for the iron treatment of restless legs syndrome/Willis-Ekbom disease in adults and children: an IRLSSG task force report. *Sleep Med*. 2018 Jan;41:27-44. doi: 10.1016/j.sleep.2017.11.1126. Epub 2017 Nov 24. PMID: 29425576.

- 34: Peters DG, Pollack AN, Cheng KC, Sun D, Saido T, Haaf MP, Yang QX, Connor JR, Meadowcroft MD. Dietary lipophilic iron alters amyloidogenesis and microglial morphology in Alzheimer's disease knock-in APP mice. *Metallomics*. 2018 Mar 1;10(3):426-443. doi: 10.1039/c8mt00004b. Epub 2018 Feb 9. PMID: 29424844.
- 35: Peters DG, Purnell CJ, Haaf MP, Yang QX, Connor JR, Meadowcroft MD. Dietary lipophilic iron accelerates regional brain iron-load in C57BL6 mice. *Brain Struct Funct*. 2018 Apr;223(3):1519-1536. doi: 10.1007/s00429-017-1565-1. Epub 2017 Nov 22. PMID: 29168009.
- 36: Trenkwalder C, Winkelmann J, Oertel W, Virgin G, Roubert B, Mezzacasa A; FCM-RLS Study Investigators. Ferric carboxymaltose in patients with restless legs syndrome and nonanemic iron deficiency: A randomized trial. *Mov Disord*. 2017 Oct;32(10):1478-1482. doi: 10.1002/mds.27040. Epub 2017 Jun 23. PMID: 28643901; PMCID: PMC5655783.
- 37: Schieffer KM, Connor JR, Pawelczyk JA, Sekhar DL. The Relationship Between Iron Deficiency Anemia and Sensorineural Hearing Loss in the Pediatric and Adolescent Population. *Am J Audiol*. 2017 Jun 13;26(2):155-162. doi: 10.1044/2017_AJA-16-0093. PMID: 28492865; PMCID: PMC5544359.
- 38: Connor JR, Patton SM, Oexle K, Allen RP. Iron and restless legs syndrome: treatment, genetics and pathophysiology. *Sleep Med*. 2017 Mar;31:61-70. doi: 10.1016/j.sleep.2016.07.028. Epub 2016 Nov 10. PMID: 28057495; PMCID: PMC5334282.
- 39: Schieffer KM, Chuang CH, Connor J, Pawelczyk JA, Sekhar DL. Association of Iron Deficiency Anemia With Hearing Loss in US Adults. *JAMA Otolaryngol Head Neck Surg*. 2017 Apr 1;143(4):350-354. doi: 10.1001/jamaoto.2016.3631. PMID: 28033450; PMCID: PMC5787694.
- 40: Bastian TW, Duck KA, Michalopoulos GC, Chen MJ, Liu ZJ, Connor JR, Lanier LM, Sola-Visner MC, Georgieff MK. Eltrombopag, a thrombopoietin mimetic, crosses the blood-brain barrier and impairs iron-dependent hippocampal neuron dendrite development. *J Thromb Haemost*. 2017 Mar;15(3):565-574. doi: 10.1111/jth.13602. Epub 2017 Feb 16. PMID: 28005311; PMCID: PMC5334144.
- 41: Zanganeh S, Hutter G, Spitler R, Lenkov O, Mahmoudi M, Shaw A, Pajarinen JS, Nejadnik H, Goodman S, Moseley M, Coussens LM, Daldrup-Link HE. Iron oxide nanoparticles inhibit tumour growth by inducing pro-inflammatory macrophage polarization in tumour tissues. *Nat Nanotechnol*. 2016 Nov;11(11):986-994. doi: 10.1038/nnano.2016.168. Epub 2016 Sep 26. PMID: 27668795; PMCID: PMC5198777.
- 42: Ono K, Murata K, Arai T, Kino T, Onaka K, Takahashi S, Sato H, Kuwahara H. Posterior reversible encephalopathy syndrome after iron administration in a patient with chronic severe anemia. *J Neurol Sci*. 2016 Aug 15;367:333-4. doi: 10.1016/j.jns.2016.06.042. Epub 2016 Jun 21. PMID: 27423614.
- 43: Shishido H, Toyota Y, Hua Y, Keep RF, Xi G. Role of lipocalin 2 in intraventricular haemoglobin-induced brain injury. *Stroke Vasc Neurol*. 2016 Jun 24;1(2):37-43. doi: 10.1136/svn-2016-000009. PMID: 28959462; PMCID: PMC5435192.
- 44: Wang LF, Yokoyama KK, Lin CL, Chen TY, Hsiao HW, Chiang PC, Hsu C. Knockout of ho-1 protects the striatum from ferrous iron-induced injury in a male- specific manner in mice. *Sci Rep*. 2016 May 20;6:26358. doi: 10.1038/srep26358. PMID: 27198537; PMCID: PMC4873828.
- 45: 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 Apr 5;86(14):1336-1343. doi: 10.1212/WNL.0000000000002542. Epub 2016 Mar 4. PMID: 26944272; PMCID: PMC4826337.

46: Schieffer KM, Peters DG, Richter CK, Loc WS, Pawelczyk JA. Incorporating Informatics for Integrating Biology and the Bedside (i2b2) into Predoctoral Trainee Curriculum to Evaluate Student-Generated Hypotheses. *Clin Transl Sci*. 2015 Dec;8(6):729-33. doi: 10.1111/cts.12357. Epub 2015 Dec 14. PMID: 26663505; PMCID: PMC4703454.

47: Lawton C, Acosta S, Watson N, Gonzales-Portillo C, Diamandis T, Tajiri N, Kaneko Y, Sanberg PR, Borlongan CV. Enhancing endogenous stem cells in the newborn via delayed umbilical cord clamping. *Neural Regen Res*. 2015 Sep;10(9):1359-62. doi: 10.4103/1673-5374.165218. PMID: 26604879; PMCID: PMC4625484.

48: Zhao L, Hadziahmetovic M, Wang C, Xu X, Song Y, Jinnah HA, Wodzinska J, Iacovelli J, Wolkow N, Krajacic P, Weissberger AC, Connelly J, Spino M, Lee MK, Connor J, Giasson B, Harris ZL, Dunaief JL. Cp/Heph mutant mice have iron- induced neurodegeneration diminished by deferiprone. *J Neurochem*. 2015 Dec;135(5):958-74. doi: 10.1111/jnc.13292. Epub 2015 Sep 29. PMID: 26303407; PMCID: PMC4943332.

49: Leitner DF, Stoute JA, Landmesser M, Neely E, Connor JR. The HFE genotype and a formulated diet controlling for iron status attenuate experimental cerebral malaria in mice. *Int J Parasitol*. 2015 Oct;45(12):797-808. doi: 10.1016/j.ijpara.2015.07.003. Epub 2015 Aug 19. PMID: 26296689.

50: Trenkwalder C, Winkelmann J, Inoue Y, Paulus W. Restless legs syndrome- current therapies and management of augmentation. *Nat Rev Neurol*. 2015 Aug;11(8):434-45. doi: 10.1038/nrneurol.2015.122. Epub 2015 Jul 28. PMID: 26215616.

51: Muntean ML, Sixel-Döring F, Trenkwalder C. Serum Ferritin Levels in Parkinson's Disease Patients with and without Restless Legs Syndrome. *Mov Disord Clin Pract*. 2015 Jun 4;2(3):249-252. doi: 10.1002/mdc3.12165. PMID: 30363529; PMCID: PMC6178747.

52: Siler DA, Berlow YA, Kukino A, Davis CM, Nelson JW, Grafe MR, Ono H, Cetas JS, Pike M, Alkayed NJ. Soluble Epoxide Hydrolase in Hydrocephalus, Cerebral Edema, and Vascular Inflammation After Subarachnoid Hemorrhage. *Stroke*. 2015 Jul;46(7):1916-22. doi: 10.1161/STROKEAHA.114.008560. Epub 2015 May 19. PMID: 25991416; PMCID: PMC4480190.

53: Connor JR, Zhang X, Nixon AM, Webb B, Perno JR. Comparative evaluation of nephrotoxicity and management by macrophages of intravenous pharmaceutical iron formulations. *PLoS One*. 2015 May 14;10(5):e0125272. doi: 10.1371/journal.pone.0125272. PMID: 25973894; PMCID: PMC4431721.

54: Ni W, Zheng M, Xi G, Keep RF, Hua Y. Role of lipocalin-2 in brain injury after intracerebral hemorrhage. *J Cereb Blood Flow Metab*. 2015 Sep;35(9):1454-61. doi: 10.1038/jcbfm.2015.52. Epub 2015 Apr 8. PMID: 25853903; PMCID: PMC4640334.

55: Yokota H, Ida Y, Sugiura S, Sasaki K, Itoh H. Cerebral venous sinus thrombosis with increased factor VIII activity in an adult with iron deficiency anemia. *Neurol India*. 2014 Nov-Dec;62(6):674-5. doi: 10.4103/0028-3886.149403. PMID: 25591684.

56: Doyle KP, Quach LN, Arceuil HE, Buckwalter MS. Ferumoxytol administration does not alter infarct volume or the inflammatory response to stroke in mice. *Neurosci Lett*. 2015 Jan 1;584:236-40. doi: 10.1016/j.neulet.2014.10.041. Epub 2014 Nov 1. PMID: 25449870; PMCID: PMC4268374.

57: Choe Y, Lee JB, Kim YJ, Choi IS. Cerebral venous sinus thrombosis and venous hemorrhagic infarction in a young woman. *Ann Rehabil Med*. 2014 Oct;38(5):698-701. doi: 10.5535/arm.2014.38.5.698. Epub 2014 Oct 30. PMID: 25379501; PMCID: PMC4221400.

- 58: Simpson IA, Ponnuru P, Klinger ME, Myers RL, Devraj K, Coe CL, Lubach GR, Carruthers A, Connor JR. A novel model for brain iron uptake: introducing the concept of regulation. *J Cereb Blood Flow Metab.* 2015 Jan;35(1):48-57. doi: 10.1038/jcbfm.2014.168. Epub 2014 Oct 15. PMID: 25315861; PMCID: PMC4294394.
- 59: Earley CJ, Connor J, Garcia-Borreguero D, Jenner P, Winkelman J, Zee PC, Allen R. Altered brain iron homeostasis and dopaminergic function in Restless Legs Syndrome (Willis-Ekbom Disease). *Sleep Med.* 2014 Nov;15(11):1288-301. doi: 10.1016/j.sleep.2014.05.009. Epub 2014 Jun 16. PMID: 25201131.
- 60: Strahle JM, Garton T, Bazzi AA, Kilaru H, Garton HJ, Maher CO, Muraszko KM, Keep RF, Xi G. Role of hemoglobin and iron in hydrocephalus after neonatal intraventricular hemorrhage. *Neurosurgery.* 2014 Dec;75(6):696-705; discussion 706. doi: 10.1227/NEU.0000000000000524. PMID: 25121790; PMCID: PMC4237659.
- 61: Nishioka K, Tanaka R, Tsutsumi S, Yamashiro K, Nakahara M, Shimura H, Hattori N, Urabe T. Cerebral dural sinus thrombosis associated with adenomyosis: a case report. *J Stroke Cerebrovasc Dis.* 2014 Aug;23(7):1985-7. doi: 10.1016/j.jstrokecerebrovasdis.2014.01.027. Epub 2014 May 1. PMID: 24794947.
- 62: Nagae M, Morita-Matsumoto K, Arai S, Wada I, Matsumoto Y, Saito K, Hashimoto Y, Yamaguchi Y. Structural change of N-glycan exposes hydrophobic surface of human transferrin. *Glycobiology.* 2014 Aug;24(8):693-702. doi: 10.1093/glycob/cwu033. Epub 2014 Apr 28. PMID: 24780636.
- 63: Ristić AJ, Sokić D, Baščarević V, Spasić S, Vojvodić N, Savić S, Raičević S, Kovačević M, Savić D, Spasojević I. Metals and electrolytes in sclerotic hippocampi in patients with drug-resistant mesial temporal lobe epilepsy. *Epilepsia.* 2014 May;55(5):e34-7. doi: 10.1111/epi.12593. Epub 2014 Mar 27. PMID: 24673751.
- 64: Iyer A, Rathnasabapathi D, Elson L, Mutch K, Terlizzo M, Footitt D, Jacob A. Transverse myelitis associated with an itchy rash and hyperckemia: neuromyelitis optica associated with dermatitis herpetiformis. *JAMA Neurol.* 2014 May;71(5):630-3. doi: 10.1001/jamaneurol.2013.6277. PMID: 24637913.
- 65: Lee JH, Park KJ, Chung YG, Kang SH. Isolated lateral sinus thrombosis presenting as cerebellar infarction in a patient with iron deficiency anemia. *J Korean Neurosurg Soc.* 2013 Jul;54(1):47-9. doi: 10.3340/jkns.2013.54.1.47. Epub 2013 Jul 31. PMID: 24044081; PMCID: PMC3772287.
- 66: Yang H, Yang M, Guan H, Liu Z, Zhao S, Takeuchi S, Yanagisawa D, Tooyama I. Mitochondrial ferritin in neurodegenerative diseases. *Neurosci Res.* 2013 Sep- Oct;77(1-2):1-7. doi: 10.1016/j.neures.2013.07.005. Epub 2013 Jul 31. PMID: 23916831.
- 67: Allary J, Soubirou JF, Michel J, Amiel I, Silins V, Brasher C, Oury JF, Nivoche Y, Dahmani S. An individual scoring system for the prediction of postpartum anaemia. *Ann Fr Anesth Reanim.* 2013 Jan;32(1):e1-7. doi: 10.1016/j.annfar.2012.11.002. Epub 2012 Dec 17. PMID: 23253154.
- 68: Marin LF, Felicio AC, Santos WA, Prado LB, Prado GF. Clinical correlates of the restless legs syndrome. *Arq Neuropsiquiatr.* 2012 Jul;70(7):529-31. doi: 10.1590/s0004-282x2012000700011. PMID: 22836460.
- 69: Miao X, Liu X, Yue Q, Qiu N, Huang W, Wang J, Xu Y, Zhang Y, Yang J, Chen X. [Deferoxamine suppresses microglia activation and protects against secondary neural injury after intracerebral hemorrhage in rats]. *Nan Fang Yi Ke Da Xue Xue Bao.* 2012 Jun;32(7):970-5. Chinese. PMID:

22820580.

70: Patton SM, Ponnuru P, Snyder AM, Podskalny GD, Connor JR. Hypoxia-inducible factor pathway activation in restless legs syndrome patients. *Eur J Neurol*. 2011 Nov;18(11):1329-35. doi: 10.1111/j.1468-1331.2011.03397.x. Epub 2011 Apr 5. PMID: 21985026.

71: Connor JR, Ponnuru P, Lee BY, Podskalny GD, Alam S, Allen RP, Earley CJ, Yang QX. Postmortem and imaging based analyses reveal CNS decreased myelination in restless legs syndrome. *Sleep Med*. 2011 Jun;12(6):614-9. doi: 10.1016/j.sleep.2010.10.009. Epub 2011 May 12. PMID: 21570342; PMCID: PMC3110510.

72: Todorich B, Zhang X, Connor JR. H-ferritin is the major source of iron for oligodendrocytes. *Glia*. 2011 Jun;59(6):927-35. doi: 10.1002/glia.21164. Epub 2011 Mar 28. PMID: 21446040.

73: Connor JR, Ponnuru P, Wang XS, Patton SM, Allen RP, Earley CJ. Profile of altered brain iron acquisition in restless legs syndrome. *Brain*. 2011 Apr;134(Pt 4):959-68. doi: 10.1093/brain/awr012. Epub 2011 Mar 11. PMID: 21398376; PMCID: PMC3069701.

74: Snyder AM, Neely EB, Levi S, Arosio P, Connor JR. Regional and cellular distribution of mitochondrial ferritin in the mouse brain. *J Neurosci Res*. 2010 Nov 1;88(14):3133-43. doi: 10.1002/jnr.22462. PMID: 20722075.

75: Yoneyama-Sarnecky T, Olivas AD, Azari S, Ferriero DM, Manvelyan HM, Noble-Haeusslein LJ. Heme oxygenase-2 modulates early pathogenesis after traumatic injury to the immature brain. *Dev Neurosci*. 2010 Mar;32(1):81-90. doi: 10.1159/000258700. Epub 2010 Mar 25. PMID: 20389079; PMCID: PMC2866583.

76: Snyder AM, Wang X, Patton SM, Arosio P, Levi S, Earley CJ, Allen RP, Connor JR. Mitochondrial ferritin in the substantia nigra in restless legs syndrome. *J Neuropathol Exp Neurol*. 2009 Nov;68(11):1193-9. doi: 10.1097/NEN.0b013e3181bdc44f. PMID: 19816198; PMCID: PMC3024883.

77: Mollan SP, Ball AK, Sinclair AJ, Madill SA, Clarke CE, Jacks AS, Burdon MA, Matthews TD. Idiopathic intracranial hypertension associated with iron deficiency anaemia: a lesson for management. *Eur Neurol*. 2009;62(2):105-8. doi: 10.1159/000222781. Epub 2009 Jun 12. PMID: 19521086.

78: Connor JR, Wang XS, Allen RP, Beard JL, Wiesinger JA, Felt BT, Earley CJ. Altered dopaminergic profile in the putamen and substantia nigra in restless leg syndrome. *Brain*. 2009 Sep;132(Pt 9):2403-12. doi: 10.1093/brain/awp125. Epub 2009 May 25. PMID: 19467991; PMCID: PMC2732265.

79: Todorich B, Zhang X, Slagle-Webb B, Seaman WE, Connor JR. Tim-2 is the receptor for H-ferritin on oligodendrocytes. *J Neurochem*. 2008 Dec;107(6):1495-505. doi: 10.1111/j.1471-4159.2008.05678.x. Epub 2008 Nov 5. PMID: 19014383.

80: Todorich B, Pasquini JM, Garcia CI, Paez PM, Connor JR. Oligodendrocytes and myelination: the role of iron. *Glia*. 2009 Apr 1;57(5):467-78. doi: 10.1002/glia.20784. PMID: 18837051.

81: Snyder AM, Connor JR. Iron, the substantia nigra and related neurological disorders. *Biochim Biophys Acta*. 2009 Jul;1790(7):606-14. doi: 10.1016/j.bbagen.2008.08.005. Epub 2008 Aug 20. PMID: 18778755.

82: Connor JR, Wang XS, Neely EB, Ponnuru P, Morita H, Beard J. Comparative study of the influence of Thy1 deficiency and dietary iron deficiency on dopaminergic profiles in the mouse striatum. *J Neurosci Res*. 2008 Nov 1;86(14):3194-202. doi: 10.1002/jnr.21758. PMID: 18615641.

- 83: Geguchadze RN, Coe CL, Lubach GR, Clardy TW, Beard JL, Connor JR. CSF proteomic analysis reveals persistent iron deficiency-induced alterations in non-human primate infants. *J Neurochem*. 2008 Apr;105(1):127-36. doi: 10.1111/j.1471-4159.2007.05113.x. Epub 2007 Nov 6. PMID: 17996030.
- 84: Magaki S, Mueller C, Yellon SM, Fox J, Kim J, Snissarenko E, Chin V, Ghosh MC, Kirsch WM. Regional dissection and determination of loosely bound and non- heme iron in the developing mouse brain. *Brain Res*. 2007 Jul 16;1158:144-50. doi: 10.1016/j.brainres.2007.05.004. Epub 2007 May 8. PMID: 17560557; PMCID: PMC1959335.
- 85: Fisher J, Devraj K, Ingram J, Slagle-Webb B, Madhankumar AB, Liu X, Klinger M, Simpson IA, Connor JR. Ferritin: a novel mechanism for delivery of iron to the brain and other organs. *Am J Physiol Cell Physiol*. 2007 Aug;293(2):C641-9. doi: 10.1152/ajpcell.00599.2006. Epub 2007 Apr 25. PMID: 17459943.
- 86: Clardy SL, Wang X, Zhao W, Liu W, Chase GA, Beard JL, True Felt B, Connor JR. Acute and chronic effects of developmental iron deficiency on mRNA expression patterns in the brain. *J Neural Transm Suppl*. 2006;(71):173-96. doi: 10.1007/978-3-211-33328-0_19. PMID: 17447428.
- 87: Zhao H, Zhu W, Pan T, Xie W, Zhang A, Ondo WG, Le W. Spinal cord dopamine receptor expression and function in mice with 6-OHDA lesion of the A11 nucleus and dietary iron deprivation. *J Neurosci Res*. 2007 Apr;85(5):1065-76. doi: 10.1002/jnr.21207. PMID: 17342757.
- 88: Kinoshita Y, Taniura S, Shishido H, Nojima T, Kamitani H, Watanebe T. Cerebral venous sinus thrombosis associated with iron deficiency: two case reports. *Neurol Med Chir (Tokyo)*. 2006 Dec;46(12):589-93. doi: 10.2176/nmc.46.589. PMID: 17185884.
- 89: Ill AM, Mitchell TR, Neely EB, Connor JR. Metabolic analysis of mouse brains that have compromised iron storage. *Metab Brain Dis*. 2006 Sep;21(2-3):77-87. doi: 10.1007/s11011-006-9022-5. Epub 2006 Jul 20. PMID: 16855871.
- 90: Patton SM, Piñero DJ, Surguladze N, Beard J, Connor JR. Subcellular localization of iron regulatory proteins to Golgi and ER membranes. *J Cell Sci*. 2005 Oct 1;118(Pt 19):4365-73. doi: 10.1242/jcs.02570. Epub 2005 Sep 6. PMID: 16144863.
- 91: Bouly S, Le Bayon A, Blard JM, Touzé E, Leys D, Mas JL, Neau JP, Dauzat M, Gautier V, Delhaume O, Castelnovo G, Labauge P. Thrombus endoluminal de l'artère carotide sans lésion sous-jacente. Etude rétrospective de 8 patients [Spontaneous thrombosis of lesion-free carotid arteries: a retrospective analysis of eight patients]. *Rev Neurol (Paris)*. 2005 Jan;161(1):61-6. French. doi: 10.1016/s0035-3787(05)84974-4. PMID: 15678002.
- 92: Pandolfo M. Friedreich's ataxia: clinical aspects and pathogenesis. *Semin Neurol*. 1999;19(3):311-21. doi: 10.1055/s-2008-1040847. PMID: 12194387.
- 93: Matz PG, Fujimura M, Lewen A, Morita-Fujimura Y, Chan PH. Increased cytochrome c-mediated DNA fragmentation and cell death in manganese-superoxide dismutase-deficient mice after exposure to subarachnoid hemolysate. *Stroke*. 2001 Feb;32(2):506-15. doi: 10.1161/01.str.32.2.506. PMID: 11157190.
- 94: Gerszten PC, Gerszten E, Allison MJ. Diseases of the skull in pre-Columbian South American mummies. *Neurosurgery*. 1998 May;42(5):1145-51; discussion 1151-2. doi: 10.1097/00006123-199805000-00114. PMID: 9588561.
- 95: Takenaka N, Mine T, Takada Y, Uematsu Y, Okuno T, Enomoto K. [A case of pseudotumor cerebri

associated with colon cancer]. *No To Shinkei*. 1989 Aug;41(8):825-9. Japanese. PMID: 2803839.

96: Aoki N, Sakai T. Cerebral sinus thrombosis in patients with severe iron deficiency anaemia due to myoma uteri. *Acta Neurochir (Wien)*. 1989;97(3-4):131-4. doi: 10.1007/BF01772824. PMID: 2718805.

97: Navone R, Azzoni L, Valente G. Immunohistochemical assessment of ferritin in bone marrow trephine biopsies: correlation with marrow hemosiderin. *Acta Haematol*. 1988;80(4):194-8. doi: 10.1159/000205636. PMID: 2464264.

98: Morikawa E, Sasaki T, Basugi N, Hashimoto K, Iwata J. [Chondromyxoid fibroma of the skull base extending from the middle fossa to the posterior fossa—case report]. *No Shinkei Geka*. 1987 Nov;15(11):1233-8. Japanese. PMID: 3437932.

99: Najem AZ, Cheung NK, Spillert CR, Ghuman SS, Lazaro EJ. Von Haberer-Finney gastrectomy revisited. *Am Surg*. 1984 Feb;50(2):112-5. PMID: 6703516.

100: Thomas WE, Thompson MH, Williamson RC. The long-term outcome of Billroth I partial gastrectomy for benign gastric ulcer. *Ann Surg*. 1982 Feb;195(2):189-95. doi: 10.1097/00000658-198202000-00012. PMID: 7034660; PMCID: PMC1352441.

101: Siim C, Lublin HK, Jensen HE. Selective gastric vagotomy and drainage for duodenal ulcer: a 10-13-year follow-up study. *Ann Surg*. 1981 Dec;194(6):687-91. doi: 10.1097/00000658-198112000-00004. PMID: 7305480; PMCID: PMC1345378.

102: Liavåg I, Roland M. A seven-year follow-up of proximal gastric vagotomy. Clinical results. *Scand J Gastroenterol*. 1979;14(1):49-56. doi: 10.3109/00365527909179845. PMID: 424688.

103: Rösch W. Moderne Ulkuschirurgie aus der Sicht des Internisten: Vagotomie versus Resektion [Current ulcer surgery from the internist's view point: vagotomy versus resection]. *Fortschr Med*. 1977 Aug 11;95(30):1851-4. German. PMID: 903061.

104: Quik M, Sourkes TL. The effect of chronic iron deficiency on adrenal tyrosine hydroxylase activity. *Can J Biochem*. 1977 Jan;55(1):60-5. doi: 10.1139/o77-011. PMID: 13918.

105: Bhoola RL, Moshal MG, Joubert SM. Basal serum gastrin levels in normal subjects and in various gastro-intestinal conditions. *S Afr Med J*. 1976 Apr 10;50(16):630-2. PMID: 1224275.

106: Magnusson BE. Iron absorption after antrectomy with gastroduodenostomy. Studies on the absorption from food and from iron salt using a double radioiron isotope technique and whole-body counting. *Scand J Haematol Suppl*. 1976;26:1-111. PMID: 1064895.

107: Wheldon EJ, Venables CW, Johnston ID. The relationship of anaemia to gastric secretion more than 15 years after vagotomy and gastro-enterostomy. *Br J Surg*. 1975 May;62(5):356-9. doi: 10.1002/bjs.1800620508. PMID: 1139130.

108: Svensson A. Vagotomy with antrum resection. *Acta Chir Scand*. 1974;140(1):50-6. PMID: 4819023.

109: Williams JA. The effects of gastric operations. *Ann R Coll Surg Engl*. 1971 Jan;48(1):54-62. PMID: 4929343; PMCID: PMC2387857.

110: Johnston ID. The management of side-effects of surgery for peptic ulceration. *Br J Surg*. 1970 Oct;57(10):787-90. doi: 10.1002/bjs.1800571025. PMID: 5476761.

111: Prasad AS, Oberleas D, Wolf P, Horwitz JP. Effect of growth hormone on nonhypophysectomized zinc-deficient rats and zinc on hypophysectomized rats. *J Lab Clin Med*. 1969 Mar;73(3):486-94. PMID: 5766193.

1)

Neef V, Baumgarten P, Noone S, Piekarski F, Triphaus C, Kleinerüschkamp A, Helmer P, Messroghli L, Zacharowski K, Choorapoikayil S, Meybohm P. The impact of timing of intravenous iron supplementation on preoperative haemoglobin in patients scheduled for major surgery. *Blood Transfus*. 2021 May 26. doi: 10.2450/2021.0058-21. Epub ahead of print. PMID: 34059194.

2)

Kung WM, Yuan SP, Lin MS, Wu CC, Islam MM, Atique S, Touray M, Huang CY, Wang YC. Anemia and the Risk of Cognitive Impairment: An Updated Systematic Review and Meta-Analysis. *Brain Sci*. 2021 Jun 11;11(6):777. doi: 10.3390/brainsci11060777. PMID: 34208355; PMCID: PMC8231247.

3)

Chiou B, Neely EB, Mcdevitt DS, Simpson IA, Connor JR. Transferrin and H-ferritin involvement in brain iron acquisition during postnatal development: impact of sex and genotype. *J Neurochem*. 2019 Jul 24. doi: 10.1111/jnc.14834. [Epub ahead of print] PubMed PMID: 31339576.

4)

Machta J, Trompeter S, Yamamoto AK, Eisen S. Iron-deficiency anaemia: the perils of excessive milk-drinking. *Arch Dis Child Educ Pract Ed*. 2021 May 27;edpract-2020-320687. doi: 10.1136/archdischild-2020-320687. Epub ahead of print. PMID: 34045288.

5)

Chen J, Zhang F, Chen H, Pan H. Rhabdomyolysis After the Use of Percussion Massage Gun: A Case Report. *Phys Ther*. 2021 Jan 4;101(1):pzaa199. doi: 10.1093/ptj/pzaa199. PMID: 33156927; PMCID: PMC7846179.

From:

<https://neurosurgerywiki.com/wiki/> - **Neurosurgery Wiki**

Permanent link:

https://neurosurgerywiki.com/wiki/doku.php?id=iron_deficiency

Last update: **2024/06/07 02:57**

