

## CASE REPORT

# Hypermanganesemia Induced Chorea and Cognitive Decline in a Tea Seller

Ritwik Ghosh\*, Souvik Dubey†, Subhankar Chatterjee‡, Mrinalkanti Ghosh§, Biman Kanti Ray† and Julián Benito-León||,¶,\*\*

**Background:** Manganese associated neurotoxicity and neurodegeneration is quite rare yet established neurological disorder. This neurotoxic element has predilection for depositing in basal ganglia structures, manifesting mainly as parkinsonian and dystonic movement disorders with behavioral abnormalities.

**Case report:** We report a 40-year-old man who presented with a subacute onset bilateral, asymmetric hyperkinetic movement disorder (predominantly left sided chorea) with multi-domain cognitive impairment, dysarthria, and generalized rigidity. Clinical history and examination yielded multiple differential diagnoses including deposition and metabolic disorders, autoimmune and paraneoplastic encephalitis involving basal ganglia, and neurodegenerative disorders with chorea and cognitive impairment. However, magnetic resonance imaging was suggestive of paramagnetic substance deposition, which came out to be manganese after laboratory investigations. History, clinical examinations, and investigation results pointed towards a diagnosis of acquired hypermanganesemia due to over-ingestion of manganese containing substance (i.e., black tea). He was treated symptomatically and with chelation therapy (calcium disodium edetate). At the sixth month of follow-up, complete resolution of chorea, dysarthria and partial amelioration of rigidity were observed. His cognitive decline and behavioral abnormalities improved.

**Discussion:** This is probably the first reported case of acquired hypermanganesemia that presented as a combination of asymmetric chorea and cognitive dysfunction with atypical imaging characteristics. The clinical picture mimicked that of Huntington's disease. We highlight the potential deleterious effects of an apparently "benign" non-alcoholic beverage (i.e., black tea) on cerebral metabolism.

**Keywords:** Hypermanganesemia; Manganese; Chorea; Movement disorder; Dementia; Cognition; Tea

## Introduction

Manganese is an essential trace element having crucial role in cellular metabolism, but, when in excess, can lead to seri-

ous neurotoxicity, which can be accredited to mitochondrial dysfunction, injury to dopaminergic, serotonergic, GABAergic and glutaminergic neurotransmission, free radical damage, and neuroinflammation [1]. Manganese affects neurons of striatum (caudate nucleus, putamen and nucleus accumbens), globus pallidus and substantia nigra, resulting in motor dysfunction with associated psychiatric and cognitive features, collectively known as "manganism" [2–4]. Hypermanganesemia due to mutations in SLC30A10, SLC39A14, and SLC39A8 presents at an early age with predominantly dystonia, gait disturbance, blood dyscrasias, and hepatic dysfunction [5–11]. On the other side, common causes of acquired hypermanganesemia are dietary exposure (food and drinking water), inhalational exposure, total parenteral nutrition and recreational drug use, among others [12–15]. However, magnetic resonance imaging (MRI) features of both types of manganese deposition are similar (i.e. increased signal intensity on T1-weighted images in basal ganglia) [7, 11].

\* Department of General Medicine, Burdwan Medical College and Hospital, Burdwan, West Bengal, IN

† Department of Neuromedicine, Bangur Institute of Neurosciences, Kolkata, IN

‡ Department of General Medicine, Rajendra Institute of Medical Sciences, Ranchi, IN

§ Department of Radiology, Burdwan Medical College, Burdwan, West Bengal, IN

|| Department of Neurology, University Hospital "12 de Octubre", Madrid, ES

¶ Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Madrid, ES

\*\* Department of Medicine, Complutense University, Madrid, ES

Corresponding author: Julián Benito-León, MD, PhD  
([jbenitol67@gmail.com](mailto:jbenitol67@gmail.com))

We herein report a middle-aged man who presented with subacute onset cognitive decline and chorea caused by hypermanganesemia probably due to chronic compulsive over consumption of manganese containing drink (i.e., black tea).

### Case presentation

A 40-year-old right-handed man, who worked as a tea seller and had 12 years of formal education, was admitted to the hospital reporting gradual onset progressive dance-like movements for last 2 months and deterioration of mental status for last 1 month. The patient was unable to provide an accurate timeline of events leading up to his presentation. According to his wife, the patient had conversation difficulties and misplacement of objects associated with recent memory impairment and behavioral abnormalities (aggression, compulsive behavior and disinhibition).

His past medical history and drug history were unrevealing. He had no history of smoking, drug addiction and reported only occasional alcohol use, but had craving for tea. For last 10–15 years he used to drink on an average of 20 cups of black tea [150 ml (5 Oz) of tea per cup] per day. His wife noticed a significant increase in this craving for tea over last few months. Craving for tea became so severe that his family members had to shut down his tea-stall eventually.

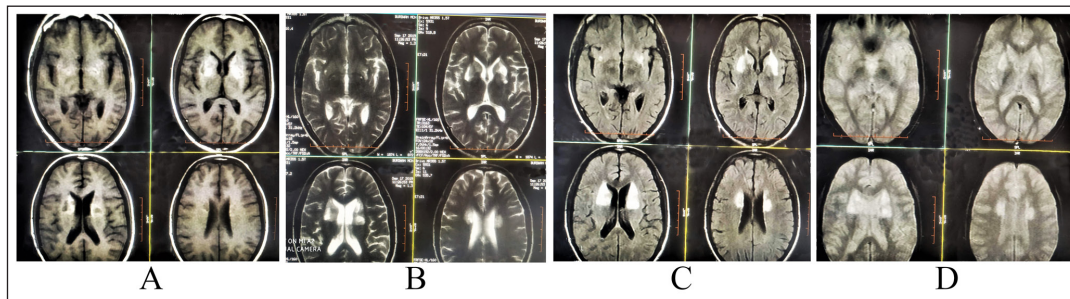
On examination, he had severe dysarthria and impaired verbal fluency with apparently unaffected comprehension. Mini Mental Status Examination (MMSE) total score was 16/30. Complex attention, executive function, social cognition, learning, and memory domains were affected. He had normal power in all four limbs with generalized rigidity and asymmetric chorea (predominantly involving left upper and lower limbs) (**video**). Deep tendon reflexes were normal with bilateral flexor plantar responses. He had walking difficulties due to persistent abnormal movements. Saccades were poorly initiated and hypometric with fractionated smooth pursuit. All other aspects of neurological examination and review of other systems were normal.

Complete blood count, along with peripheral blood smear, renal, liver, thyroid function tests, blood glucose, serum sodium, potassium, calcium, phosphorus,

lactate, and iron profile were within normal limits. Brain MRI revealed non-enhancing, bilateral symmetrical increased signal intensity on T1-weighted, T2-weighted and T2-weighted-fluid-attenuated inversion recovery (FLAIR) images in basal ganglia (particularly involving caudate nucleus and putamen), with areas of gliosis, without any mass effect (**Figure 1**). Electroencephalogram was normal. Deposition and metabolic disorders, autoimmune and paraneoplastic encephalitis, and Huntington's disease were considered as differential diagnoses. HIV serology, autoimmune and paraneoplastic neuronal antibodies panel [NMDA (anti-glutamate receptor against NR1 subunit), AMPA (anti-glutamate)-GluR1, AMPA (anti-glutamate)-GluR2, GABA-B receptor antibody, LGI-1 antibody, CASPR2



**Video: Asymmetric choreic movements in a case of acquired hypermanganesemia.** Video demonstrating involuntary, rapid dance-like movements involving predominantly left upper and lower limbs that flow from one muscle to the other in continuous fashion suggestive of a predominantly left hemichorea (Although the patient had bilateral chorea, left much more than right with motor impersistence, this is not demonstrated in the video).



**Figure 1:** Brain MRI shows non-enhancing bilateral increased signal intensity on axial T1-weighted (**A**), axial T2-weighted (**B**) and axial T2-fluid-attenuated inversion recovery (FLAIR)-weighted (**C**) images in basal ganglia, with scattered areas of gliosis (T1-weighted images). Gradient-echo axial T2\*-weighted image (**D**) shows no evidence of signal blooming (unlike iron or calcium deposition, manganese deposition does not cause blooming on gradient-echo images or susceptibility-weighted imaging).

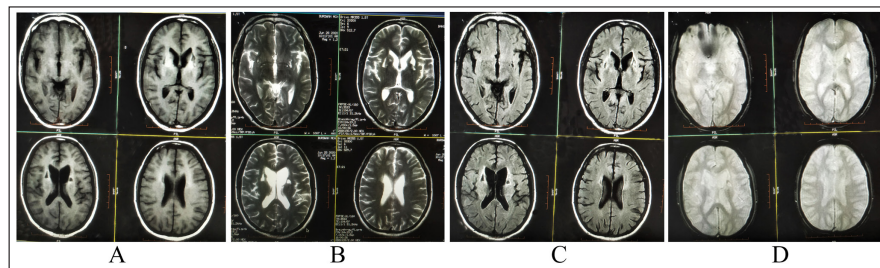
antibody, amphiphysin, anti-CRMP5/CV2, PNMA2 (Ma2/Ta), ANNA-1/Hu, ANNA-2/Ri, and PCA-1/Yo antibodies], amino acid chromatography and routine cerebrospinal fluid (CSF) (cell type, cell count, protein, glucose, bacterial staining, and cultures), assay for protein 14-3-3 in CSF, and genetics for Huntington's disease and Huntington's disease like (HDL) 4/SCA 17 were all normal or negative. Serum ceruloplasmin, copper, 24 hours urinary copper, and test for ATP7B gene were normal. Slit lamp examination ruled out Kayser-Fleischer ring. MR portography was normal.

The serum manganese level was sent, which came out to be 3281 nmol/L (reference value < 320 nmol/L). Although inherited manganism was unlikely, considering the age of the patient and negative family history, screening for mutations for SLC39A14, SLC30A10 and SLC39A8 were done for objective confirmation and expectedly came out to be negative. Personal history revealed he had a compulsive habit of drinking black tea, on an average 20 cups (5 Oz/cup) per day over last 10–15 years. On an average he ingested 26 mg of manganese per day for last 10–15 years.

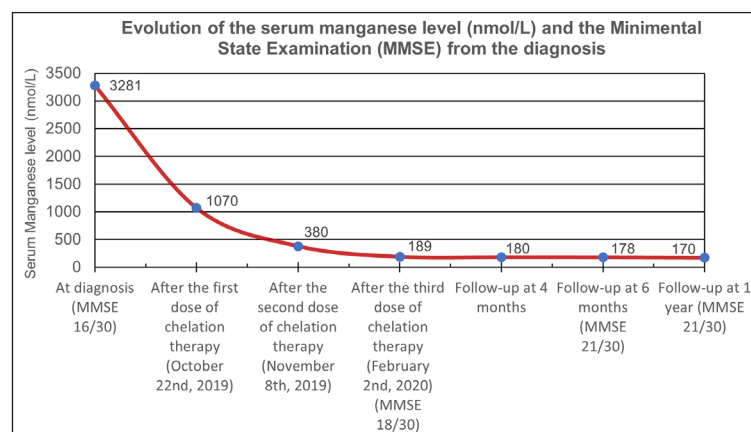
Edetate calcium disodium was administered as a chelation therapy at 1 g/m<sup>2</sup>/day (in 500 ml normal saline) once daily for 5 days. Further, oral tetrabenazine (50 mg/day) was given. On tenth day, the serum manganese level decreased

(1070 nmol/L) and motor symptoms started showing some improvement. Intravenous chelation with edetate calcium disodium was repeated twice in first month (two weeks apart) and once in third month. Metabolic parameters were routinely monitored alongside serum manganese level (**Figure 3**). After three cycles of chelation therapy, his serum manganese level normalized (189 nmol/L) and we then stopped chelation therapy. Tetrabenazine was also stopped at four weeks of follow-up as there was no abnormal movement.

At the sixth month of follow-up, complete resolution of chorea, dysarthria and partial amelioration of rigidity were observed. Serum manganese level remained normal (178 nmol/L). Cognitive function improved in the following domains: complex attention, executive function, social cognition, learning and memory. MMSE score improved by 5 points (i.e. 21/30). Brain MRI, at follow-up, revealed partial resolution of previous findings, but the gliotic areas, which persisted along with resultant dilatation of frontal horns of lateral ventricles due to negative mass effects (**Figure 2**). At the one year of follow-up, the patient's clinical status remained similar and had a normal serum manganese level (170 nmol/L). **Figure 3** summarizes the timeline of events in relation to serum manganese level and MMSE along time.



**Figure 2:** Follow-up brain MRI after 6 months: Axial T1-weighted image (A) shows heterogeneous signal changes (i.e. bilateral increased signal intensity in basal ganglia possibly due to manganese deposition along with hypointense gliotic areas with mild dilatation of frontal horns of both lateral ventricles). Axial T2-weighted (B) and T2-FLAIR-weighted (C) images show iso- to hypointense signal changes at the areas of deposits and scattered gliotic foci with central hypo and peripheral hyperintense signal changes. Gradient-echo axial T2\*-weighted image (D) shows no evidence of signal blooming.



**Figure 3:** Schematic diagram of the timeline of events in relation to serum manganese level and Mini Mental Status Examination (MMSE) along time.

## Discussion

Disruption anywhere in the circuitries between frontal cortex and structures of basal ganglia may lead to neurocognitive and behavioral dysfunction along with movement disorders [16, 17] as evident in the current case. Thus, involvement of basal ganglia and its cortical connections should be suspected in patients with subacute onset chorea followed by multi-domain cognitive decline [16, 17]. Considering age, form of presentation and neuroimaging characteristics, exclusion of deposition disorders was mandatory. With this scenario, calcium, copper, iron, and manganese deposition disorders were considered. Serum calcium was normal and brain CT scan did not reveal any calcium deposition. Tremor, dystonia, and parkinsonism are far more common than pure chorea in Wilson disease [18]. A complex and heterogenous spectrum of inherited neurodegenerative disorders, the neurodegeneration with brain iron accumulation (NBIA) disorders, are characterized by superabundant iron accumulation, particularly in the basal ganglia, movement disorders (usually dystonia and parkinsonism), retinal abnormalities and cognitive impairment [19]. Extensive clinical and laboratory investigations ruled out both Wilson disease and NBIA propelling us to think of some other deposition disorder than copper, iron and calcium.

Subacute onset chorea followed by cognitive impairment warranted investigations for Huntington's disease and HDL disorders. Family history and genetics were negative for Huntington's disease and HDL 4/SCA 17. Relative rarity of HDL in eastern India (permanent residence of the patient), absence of positive family history, age of presentation, and significant response to chelation therapy (in terms of clinical, biochemical and neuroradiological improvements) restrained us from doing costly genetic testing for HDL1,2 and 3. Clinical-radiological manifestations were better explained by an alternative etiology, supported by other investigations (i.e. high serum manganese level).

A neuroacanthocytosis syndrome was a very unlikely possibility by absence of peripheral neuropathy, raised creatinine kinase and acanthocytes in peripheral blood smears. Mitochondrial cytopathies were also an exceedingly rare possibility by normal serum and cerebrospinal fluid lactate and normal lactate-pyruvate ratios. In addition, the clinical picture improved after chelation therapy.

After ruling out possible and relevant differential diagnoses and finding extremely high serum manganese level, deposition of manganese in both basal ganglia was presumed to be the explanation of the clinical picture. Typical movement disorders in manganese deposition are dystonia, dystonic tremor, and parkinsonism [9]. Chorea or choreoathetosis, although uncommon, have been reported [20]. Fell et al. [21], described two children receiving long-term parenteral nutrition with manganese toxicity who developed dystonic limb movements and abnormal posturing. Haug et al. [22], reported an interesting case of Morvan's fibrillary chorea in which chronic manganese intoxication (occupational exposure) seemed to be implicated. Manganese inhibits

acetylcholine esterase and thus could lead to generation of central and peripheral cholinergic activity [22]. In a survey carried out in a dry battery industry with high inhalational exposure to manganese revealed that 2 out of 36 workers had movement disorders (one with left hemi-parkinsonism and other having left hemi-choreoathetosis) [23]. Although among basal ganglia nuclei, globus pallidus is affected preferentially, other areas such as striatum, subthalamic nuclei, substantia nigra and thalami can be affected in majority of the cases of manganism [24, 25]. Classically, hypermanganesemia is associated with bilateral increased signal intensity on T1-weighted images in the basal ganglia and iso- to hyperintense signal changes on T2-weighted images [11, 26]. Increased signal intensity on T2-weighted in basal ganglia, similar to the present case, although rare, has been reported previously [26]. A probable explanation of this fact is astrogliosis and spongiform neurodegeneration due to prolonged manganese neurotoxicity [27]. Moreover, we excluded many other possible causes of bilateral increased signal intensity on T2-weighted images in the basal ganglia basing on clinical grounds and appropriate investigations.

Searching for probable etiologies of manganese deposition, hepatic causes were excluded (normal liver function tests and normal MR portography). Inhalational exposure was not evident. Common genetic causes of hypermanganesemia were also ruled out. Hence, hypermanganesemia of our patient could be due to consumption of manganese containing food or unknown exposure to some toxins containing manganese. History was revisited, which revealed patient had habit of compulsive black tea intake. The serum manganese level in our patient was found to be similarly high compared to other recently reported cases of hypermanganesemia, i.e. above 3000 nmol/L, which was far beyond the reference value (less than 320 nmol/L) [4, 5, 7, 10].

Manganese, an essential trace element, is neurotoxic at high doses [1–4, 28]. Excess dietary intake with food and/or drinking water, and inhalational exposure from working places are considered common sources of environmental exposure [12–15, 28]. Chronic exposure to excess manganese from drinking water ( $\geq 0.2$  mg/L) has been linked to poor scholastic performance, impaired cognitive abilities, neurobehavioral dysfunction, oppositional behavior, hyperactivity and manganism in children [28]. Indian black tea is rich in manganese (range of 56.8–1163.8  $\mu\text{g/g}$ ; manganese levels of 0.4–1.3 mg/cup) [29–33]. Black tea manufactured from young tender shoots of *Camellia sinensis* (L.) O. Kuntze is the most widely consumed non-alcoholic drink in India [29]. Hope et al. [34], concluded that tea drinking is a major source of dietary manganese and intakes commonly exceed proposed adequate intake values of 1.8–2.3 mg manganese per day and, on occasion, exceed upper limits of 10–11 mg/day.

Although neurobehavioral alterations are considered as one of the most sensitive markers of excessive exposure to manganese over long-term, there is no reported minimal

manganese level that points to a chronic intoxication [28]. Hence it is difficult to estimate how much of dietary manganese intake per day and for how much duration will lead to development of neurotoxicity [28]. In addition, several studies refute the effects of dietary intake of manganese on its plasma levels [34] and on neurological functions [35]. Although arrangements for estimation of manganese concentration in drinking water used by the patient and his family were beyond our scope, none of the family members had clinical-radiological or laboratory evidence of manganism or hypermanganesemia and hence this etiology was excluded. Defect in homeostasis of bivalent ions have been associated with cognitive impairment [36–39]. However, we feel that the multi-domain (complex attention, execution, learning and memory, and social cognition) cognitive impairment in this case may be attributed to damage to cortico-striato-thalamo-cortical loop due to manganese toxicity itself [40, 41].

In conclusion, this is the first reported case of acquired hypermanganesemia who presented as a combination of asymmetric chorea and cognitive dysfunction. The clinical picture mimicked that of Huntington's disease. We highlight the potential deleterious effects of an apparently "benign" non-alcoholic beverage (i.e., black tea) on cerebral metabolism.

### Funding Information

R. Ghosh, S. Dubey, S. Chatterjee, M. Ghosh and B.K. Ray report no relevant disclosures. J. Benito-León is supported by the National Institutes of Health, Bethesda, MD, USA (NINDS #R01 NS39422), European Commission (grant ICT-2011-287739, NeuroTREMOR), the Ministry of Economy and Competitiveness (grant RTC-2015-3967-1, NetMD—platform for the tracking of movement disorder), and the Spanish Health Research Agency (grant FIS PI12/01602 and grant FIS PI16/00451).

### Competing Interests

The authors have no competing interests to declare.

### Author Contributions

RG and SD managed the case and wrote the first draft which was critically reviewed and improved by SC, MG, BKR and JBL.

### References

1. **Tuschl K, Mills PB, Clayton PT.** Manganese and the brain. *International review of neurobiology.* 2013; 110: 277–312. DOI: <https://doi.org/10.1016/B978-0-12-410502-7.00013-2>
2. **Racette BA.** Manganism in the 21st century: the Hanninen lecture. *Neurotoxicology.* 2014; 45: 201–207. DOI: <https://doi.org/10.1016/j.neuro.2013.09.007>
3. **Bowler RM, Gysens S, Diamond E, Nakagawa S, Drezgic M, Roels HA.** Manganese exposure: neuropsychological and neurological symptoms and effects

- in welders. *Neurotoxicology.* 2006; 27: 315–326. DOI: <https://doi.org/10.1016/j.neuro.2005.10.007>
4. **Bowler RM, Koller W, Schulz PE.** Parkinsonism due to manganism in a welder: neurological and neuropsychological sequelae. *Neurotoxicology.* 2006; 27: 327–332. DOI: <https://doi.org/10.1016/j.neuro.2005.10.011>
5. **Martí-Sánchez L, Ortigoza-Escobar JD, Darling A,** et al. Hypermanesemia due to mutations in SLC39A14: further insights into Mn deposition in the central nervous system. *Orphanet journal of rare diseases.* 2018; 13: 28. DOI: <https://doi.org/10.1186/s13023-018-0758-x>
6. **Tuschl K, Clayton PT, Gospe SM, Jr.,** et al. Syndrome of hepatic cirrhosis, dystonia, polycythemia, and hypermanganesemia caused by mutations in SLC30A10, a manganese transporter in man. *American journal of human genetics.* 2012; 90: 457–466. DOI: <https://doi.org/10.1016/j.ajhg.2012.01.018>
7. **Zeglam A, Abugrara A, Kabuka M.** Autosomal-recessive iron deficiency anemia, dystonia and hypermanganesemia caused by new variant mutation of the manganese transporter gene SLC39A14. *Acta neurologica Belgica.* 2019; 119: 379–384. DOI: <https://doi.org/10.1007/s13760-018-1024-7>
8. **Avelino MA, Fusão EF, Pedroso JL,** et al. Inherited manganism: the "cock-walk" gait and typical neuroimaging features. *J Neurol Sci.* 2014; 341: 150–152. DOI: <https://doi.org/10.1016/j.jns.2014.03.057>
9. **Stamelou M, Tuschl K, Chong WK,** et al. Dystonia with brain manganese accumulation resulting from SLC30A10 mutations: a new treatable disorder. *Mov Disord.* 2012; 27: 1317–1322. DOI: <https://doi.org/10.1002/mds.25138>
10. **Tavassoli A, Arjmandi Rafsanjani K, Hemmati S, Mojbafan M, Zarei E, Hosseini S.** A case of dystonia with polycythemia and hypermanganesemia caused by SLC30A10 mutation: a treatable inborn error of manganese metabolism. *BMC pediatrics.* 2019; 19: 229. DOI: <https://doi.org/10.1186/s12887-019-1611-7>
11. **Padmanabha H, Krishnamurthy S, Sharath Kumar GG, Chikkanayakana I, Sethuraman A, Mathew T.** Teaching NeuroImages: An imaging clue for treatable early childhood-onset dystonia: Manganism. *Neurology.* 2019; 92: e628–e629. DOI: <https://doi.org/10.1212/WNL.0000000000006881>
12. **Peres TV, Schettinger MR, Chen P,** et al. "Manganese-induced neurotoxicity: a review of its behavioral consequences and neuroprotective strategies". *BMC pharmacology & toxicology.* 2016; 17: 57. DOI: <https://doi.org/10.1186/s40360-016-0099-0>
13. **Khan A, Hingre J, Dhamoon AS.** Manganese Neurotoxicity as a Complication of Chronic Total Parenteral Nutrition. *Case reports in neurological medicine.* 2020; 2020: 9484028. DOI: <https://doi.org/10.1155/2020/9484028>

14. **O'Neal SL, Zheng W.** Manganese Toxicity Upon Over-exposure: a Decade in Review. *Current environmental health reports*. 2015; 2: 315–328. DOI: <https://doi.org/10.1007/s40572-015-0056-x>
15. **Roels HA, Bowler RM, Kim Y,** et al. Manganese exposure and cognitive deficits: a growing concern for manganese neurotoxicity. *Neurotoxicology*. 2012; 33: 872–880. DOI: <https://doi.org/10.1016/j.neuro.2012.03.009>
16. **Mega MS, Cummings JL.** Frontal-subcortical circuits and neuropsychiatric disorders. *J Neuropsychiatry Clin Neurosci*. 1994; 6: 358–370. DOI: <https://doi.org/10.1176/jnp.6.4.358>
17. **Tekin S, Cummings JL.** Frontal-subcortical neuronal circuits and clinical neuropsychiatry: an update. *Journal of psychosomatic research*. 2002; 53: 647–654. DOI: [https://doi.org/10.1016/S0022-3999\(02\)00428-2](https://doi.org/10.1016/S0022-3999(02)00428-2)
18. **Czlonkowska A, Litwin T, Chabik G.** Wilson disease: neurologic features. *Handbook of clinical neurology*. 2017; 142: 101–119. DOI: <https://doi.org/10.1016/B978-0-444-63625-6.00010-0>
19. **Salomão RP, Pedroso JL, Gama MT,** et al. A diagnostic approach for neurodegeneration with brain iron accumulation: clinical features, genetics and brain imaging. *Arquivos de neuro-psiquiatria*. 2016; 74: 587–596. DOI: <https://doi.org/10.1590/0004-282X20160080>
20. **Sue WC, Chen CY, Chen CC.** Dyskinesia from manganese in a hepatic dysfunction patient. *Zhonghua Min Guo Xiao Er Ke Yi Xue Hui Za Zhi*. 1996; 37: 59–64.
21. **Fell JM, Reynolds AP, Meadows N, Khan K, Long SG, Quaghebeur G, Taylor WJ, Milla PJ.** Manganese toxicity in children receiving long-term parenteral nutrition. *Lancet*. 1996 May 4; 347(9010): 1218–21. PMID: 8622451. DOI: [https://doi.org/10.1016/S0140-6736\(96\)90735-7](https://doi.org/10.1016/S0140-6736(96)90735-7)
22. **Haug BA, Schoenle PW, Karch BJ, Bardosi A, Holzgraefe M.** Morvan's fibrillary chorea. A case with possible manganese poisoning. *Clin Neurol Neurosurg*. 1989; 91(1): 53–9. PMID: 2538282. DOI: [https://doi.org/10.1016/S0303-8467\(89\)80008-3](https://doi.org/10.1016/S0303-8467(89)80008-3)
23. **Emara AM, el-Ghawabi SH, Madkour OI, el-Samra GH.** Chronic manganese poisoning in the dry battery industry. *Br J Ind Med*. 1971 Jan; 28(1): 78–82. PMID: 5101169; PMCID: PMC1009195. DOI: <https://doi.org/10.1136/oem.28.1.78>
24. **Criswell SR, Perlmutter JS, Huang JL, Golchin N, Flores HP, Hobson A, Aschner M, Erikson KM, Checkoway H, Racette BA.** Basal ganglia intensity indices and diffusion weighted imaging in manganese-exposed welders. *Occup Environ Med*. 2012 Jun; 69: 437–43. DOI: <https://doi.org/10.1136/oemed-2011-100119>
25. **Ikeda S, Yamaguchi Y, Sera Y, Ohshiro H, Uchino S, Yamashita Y, Ogawa M.** Manganese deposition in the globus pallidus in patients with biliary atresia. *Transplantation*. 2000 Jun 15; 69: 2339–43. DOI: <https://doi.org/10.1097/00007890-200006150-00021>
26. **Klos KJ, Ahlskog JE, Josephs KA, Fealey RD, Cowl CT, Kumar N.** Neurologic spectrum of chronic liver failure and basal ganglia T1 hyperintensity on magnetic resonance imaging: probable manganese neurotoxicity. *Arch Neurol*. 2005; 62: 1385–90. DOI: <https://doi.org/10.1001/archneur.62.9.1385>
27. **Harischandra DS, Ghaisas S, Zenitsky G, Jin H, Kanthasamy A, Anantharam V,** et al. Manganese-Induced Neurotoxicity: New Insights Into the Triad of Protein Misfolding, Mitochondrial Impairment, and Neuroinflammation. *Front Neurosci*. 2019; 13: 654. DOI: <https://doi.org/10.3389/fnins.2019.00654>
28. **Williams M, Todd GD, Roney N, Crawford J, Coles C, McClure PR, Garey JD, Zaccaria K, Citra M.** Toxicological Profile for Manganese. Atlanta, GA: Agency for Toxic Substances and Disease Registry (US); 2012 Sep. PMID: 24049862.
29. **Khanum H, Faiza S, Sulochanamma G, Borse BB.** Quality, antioxidant activity and composition of Indian black teas. *J Food Sci Technol*. 2017 Apr; 54(5): 1266–1272. Epub 2017 Mar 10. PMID: 28416877; PMCID: PMC5380613. DOI: <https://doi.org/10.1007/s13197-017-2506-y>
30. **Aschner JL, Aschner M.** Nutritional aspects of manganese homeostasis. *Mol Aspects Med*. 2005 Aug–Oct; 26(4–5): 353–62. PMID: 16099026; PMCID: PMC6309959. DOI: <https://doi.org/10.1016/j.mam.2005.07.003>
31. **Rezaee E, Mirlohi M, Fallah A, Babashahi M.** A Systematic Review on Exposure to Toxic and Essential Elements through Black Tea Consumption in Iran: Could It be a Major Risk for Human Health? *International journal of preventive medicine*. 2014; 5: 1351–1359.
32. **Schwalfenberg G, Genuis SJ, Rodushkin I.** The benefits and risks of consuming brewed tea: beware of toxic element contamination. *Journal of toxicology*. 2013; 2013: 370460. DOI: <https://doi.org/10.1155/2013/370460>
33. **Ross C, O'Reilly DS, McKee R.** Potentially clinically toxic concentrations of whole blood manganese in a patient fed enterally with a high tea consumption. *Annals of clinical biochemistry*. 2006; 43: 226–228. DOI: <https://doi.org/10.1258/000456306776865151>
34. **Hope S, Daniel K, Gleason KL, Comber S, Nelson M, Powell JJ.** Influence of tea drinking on manganese intake, manganese status and leucocyte expression of MnSOD and cytosolic aminopeptidase P. *Eur J Clin Nutr*. 2006 Jan; 60(1): 1–8. PMID: 16118651. DOI: <https://doi.org/10.1038/sj.ejcn.1602260>
35. **Finley JW, Penland JG, Pettit RE, Davis CD.** Dietary manganese intake and type of lipid do not affect clinical or neuropsychological measures in healthy young women. *J Nutr*. 2003 Sep; 133(9): 2849–56.

- PMID: 12949376. DOI: <https://doi.org/10.1093/jn/133.9.2849>
36. **Sahni V, Léger Y, Panaro L, Allen M, Giffin S, Fury D, Hamm N.** Case report: a metabolic disorder presenting as pediatric manganism. *Environ Health Perspect.* 2007 Dec; 115(12): 1776–9. PMID: 18087599; PMCID: PMC2137101. DOI: <https://doi.org/10.1289/ehp.10421>
37. **Vollet K, Haynes EN, Dietrich KN.** Manganese Exposure and Cognition Across the Lifespan: Contemporary Review and Argument for Biphasic Dose-Response Health Effects. *Curr Environ Health Rep.* 2016; 3(4): 392–404. DOI: <https://doi.org/10.1007/s40572-016-0108-x>
38. **Kawahara M, Tanaka KI, Kato-Negishi M.** Zinc, Carnosine, and Neurodegenerative Diseases. *Nutrients.* 2018 Jan 29; 10(2): 147. PMID: 29382141; PMCID: PMC5852723. DOI: <https://doi.org/10.3390/nu10020147>
39. **Wang L, Yin YL, Liu XZ, Shen P, Zheng YG, Lan XR, Lu CB, Wang JZ.** Current understanding of metal ions in the pathogenesis of Alzheimer's disease. *Transl Neurodegener.* 2020 Apr 3; 9: 10. PMID: 32266063; PMCID: PMC7119290. DOI: <https://doi.org/10.1186/s40035-020-00189-z>
40. **Grahn JA, Parkinson JA, Owen AM.** The cognitive functions of the caudate nucleus. *Progress in neurobiology.* 2008; 86: 141–155. DOI: <https://doi.org/10.1016/j.pneurobio.2008.09.004>
41. **Haber SN.** Corticostriatal circuitry. *Dialogues Clin Neurosci.* 2016 Mar; 18(1): 7–21. PMID: 27069376; PMCID: PMC4826773. DOI: [https://doi.org/10.1007/978-1-4614-6434-1\\_135-1](https://doi.org/10.1007/978-1-4614-6434-1_135-1)

**How to cite this article:** Ghosh R, Dubey S, Chatterjee S, Ghosh M, Ray BK, Benito-León J. Hypermanganesemia Induced Chorea and Cognitive Decline in a Tea Seller. *Tremor and Other Hyperkinetic Movements.* 2020; 10(1): 45, pp.1–7. DOI: <https://doi.org/10.5334/tohm.537>

**Submitted:** 05 June 2020

**Accepted:** 06 October 2020

**Published:** 20 October 2020

**Copyright:** © 2020 The Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC-BY 4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited. See <http://creativecommons.org/licenses/by/4.0/>.

]u[

*Tremor and Other Hyperkinetic Movements* is a peer-reviewed open access journal published by Ubiquity Press.

OPEN ACCESS 