



Official Journal of the
Neuroscience Society of Nigeria
(NSN)

ISSN 1116-4182

AMELIORATIVE EFFECT OF VITAMIN C AND UV-B RAYS ON NIGROSTRIATAL AND CORTICOSTRIATAL DEGENERATION IN HALOPERIDOL INDUCED PARKINSONISM IN WISTAR RATS

Mujittapha U. Sirajo¹, Lukman F. Owolabi², Musa Abubakar¹,
Azeez O. Ishola³, Abdu I. Tela¹, Kabir Shehu⁴, Esther O. Oyeleke⁵

¹Department of Anatomy, Faculty of Basic Health sciences, Bayero University Kano

²Department of Medicine, Bayero University Teaching Hospital, Kano

³Department of Anatomy, College of Medicine and Health Sciences, Afe Babalola University, Ado Ekiti

⁴Department of Anatomy, Faculty of Basic Medical Sciences, Federal University, Kebbi

⁵Department of Anatomy, College of Medicine and Health Sciences, University of Lagos, Lagos

Received: April 2019

Accepted: August 2019

ABSTRACT

Prolonged inhibition of dopamine-2 receptor (D₂R) is shown to cause degeneration of dopamine neurons leading to parkinsonism. Previously we have shown that vitamin D₃ receptor stimulation improved motor–cognitive functions in dopamine-2 receptor (D₂R) parkinsonian mice model. Presently, we examined the ameliorative effect of vitamin C and UV-B rays on nigrostriatal and corticostriatal degeneration in drug induced parkinsonism in Wistar rats. Twenty male Wistar rats with average weight of 120 g were distributed into four groups (NS, -D₂, -D₂+UV-B and -D₂+Vit.C). Parkinsonism was induced by administering 10 mg/kg b.wt. of haloperidol for 14 days (intraperitoneally) without and with treatment of 125 mg/kg b.wt. of vitamin C or 2 hours of exposure to morning sunlight between 8-10 am. The animals were subjected to cylinder, pole and stepping test for motor functions. Motor cortex (M1), substantia nigra pars compacta (SNc) and striatum (CPu) were processed and stained using haematoxylin and eosin and Cresyl violet stains. Cell count was done using ImageJ software (version 5). Data were presented as mean ± standard error of mean; analysed using one-way analysis of variance and Tukey's multiple comparison test, and significant level was determined at 0.05 (p < 0.05*). Haloperidol induced parkinsonism caused significant bradykinesia (*p < 0.05), rigidity (** p < 0.01), neuron lost (**p < 0.01) and expressions of degeneration hallmarks in SNc and M1. UV-B or Vit. C treatment showed ameliorative potentials in reducing motor deficit experience in parkinsonism, but not regenerating the already lost neurons.

Key words: Parkinsonism, Vitamin C, UV-B rays, Dopamine-2 receptor blocker, Substantia nigra (SN), Striatum (CPu), Motor cortex (M1)

INTRODUCTION

Several studies have shown that prolonged inhibition of dopamine-2 receptor (-D₂R) causes loss of dopamine neurons, resulting in to parkinsonism (Shirayama et al. 2000; Iderberg et al. 2015). These dopamine neurons project from substantia nigra to striatum (nigrostriatal tract), and are also found in the

cortex (corticostriatal tract) (Singh 2009). It is known that haloperidol has the ability to centrally block dopamine-2 receptors (Seeman and Tallerico 2003;

Correspondence: Mujittapha U. Sirajo, MSc, Department of Anatomy, Faculty of Basic Health Sciences, Bayero University, PMB 3011, Kano, Nigeria. mujittaphasurajo@gmail.com; +2348101682449

REFERENCES

- Angelow, S. Haselbach, M. and Galla, H.J. (2003) Functional characterisation of the active ascorbic acid transport into cerebrospinal fluid using primary cultured choroid plexus cells. *Brain Research*. 98(8):105-113.
- Bankole, O.O., Babafemi, J.L., Mujittapha, U.S., Azeez, O.I., Damilola, E.O., Wasiu, G.B., Amin, A., Ansa, E.C., Ibukun, D. A. and Olalekan M. O. (2015) Vitamin D3 receptor activation rescued corticostriatal neural activity and improved motor function in -d2r tardive dyskinesia mice model. *Journal of Biomedical Science and Engineering*. 8:520-530.
- Berardelli, A., Rothwell, J.C. and Thompson, P.D. (2001) Pathophysiology of Bradykinesia in Parkinson's disease. *Brain*. 124:2131-2146.
- Booth, T.C. Nathan M. Waldman A.D. Quigley A.M. Schapira, A.H. and Buscombe, J. (2014) The role of functional dopamine-transporter SPECT imaging in parkinsonian syndromes, *Journal of Neurology*. 23: 354-359.
- Broussolle, E. Krack, P. and Thobois, S. (2007) Contribution of Jules Froment to the study of parkinsonian rigidity. *Movement Disorders*. 22:909-914
- Calero, C.I. Vickers, E. Moraga Cid, G. Aguayo, L.G. V.H. and Calvo, D.J. (2011) Allosteric modulation of retinal GABA receptors by ascorbic acid. *Journal of Neuroscience*. 31: 9672-9682.
- Castellani, B.A. Alexiev, B.A. Philips, D. Perry, G. and Smith, M.A. (2007). Microscopic investigation in neurodegenerative diseases. *Modern research and educational topics in microscopy*. 1:171-182
- Dawson, T.M. and Dawson, V.L. (2003) Rare genetic mutations shed light on the pathogenesis of Parkinson's Disease. *Journal of Clinical Investigation*. Pp. 11(1):145-151.
- Graff-Guerrero, A. Mamo D. Shammi, C.M. Mizrahi, R. Marcon, H. Barsoum, P. Rusjan, P. Houle, S. Wilson A.A. and Kapur, S. (2009). The effect of antipsychotics on the high-affinity state of D2 and D3 receptors: a positron emission tomography study with [¹¹C]-(+)-PHNO. *Archives of General Psychiatry*. 66(6):606-615.
- Grant, M.M., Barber, V.S. and Griffiths, H.R. (2005) The presence of ascorbate induces expression of brain derived neurotrophic factor in SH-SY5Y neuroblastoma cells after peroxide insult, which is associated with increased survival. *Proteomics*. 5:534-540.
- Holick, M.F. (2006) Resurrection of vitamin D deficiency and rickets. *Journal of Clinical Investigation*. 2006;116:2062-2072.
- Iderberg, H., Maslava, N. Thompson, A.D. Bubser, M. Niswender, C.M., Hopkins, C.R., Lindsley, C.W., Conn, P.J., Jones, C.K. and Cenci, M.A. (2015) Pharmacological stimulation of metabotropic glutamate receptor type 4 in a rat model of Parkinson's disease and L-DOPA-induced dyskinesia: Comparison between a positive allosteric modulator and an orthosteric agonist. *Neuropharmacology*. 4(95):121-129.
- Singh, I. (2009) *Textbook of Human Neuroanatomy (Fundamental and Clinical)*. 8th ed., Haryana: Jaypee Brothers Medical Publishers (p) Ltd.
- Ishola, A.O., Laoye, B.J., Oyeleke, D.E., Bankole O.O., Sirajo, M.U., Cobham, A.E. Balogun, W.O., Abdulbasit, A., Akinrinade, I.D. and Ogundele, O.M. (2015) Vitamin D3 receptor activation rescued corticostriatal neural activity and improved motor-cognitive function in -D2R parkinsonian mice model. *Journal Biomedical Science and Engineering*. 8:601-615.
- Jai, S.N., Hyo, J., Kang, E.Y., Kim, S.S., Young, K.C., Seung, U.K. and Byoung, J.G. (2000) Haloperidol Induced neuronal apoptosis: role of p38 and c-Jun-NH2-terminal protein kinases. *Journal of Neurochemistry*. 75: 2327-2334
- Jung, U.J., Leem, E. and Kim, S.R. (2014) Naringin: a protector of the nigrostriatal dopaminergic projection. *Expression Neurobiology*. 23(2):124-129. doi: 10.5607/en.2014.23.2.124.
- Karl, T., Duffy, L., O'brien, E., Matsumoto, I. and Dedova, I. (2006) Behavioural effects of chronic haloperidol and risperidone treatment in rats. *Behavioral Brain Research*. 171(2):286-294.
- Kozina, E.A., Khakimova, G.R., Khaindrava, V.G., Kucheryanu, V.G., Vorobyeva, N.E., Krasnov, A.N., Georgieva, S.G., Kerkerian-Le, G.L. and Ugrumov, M.V. (2014) Tyrosine hydroxylase expression and activity in nigrostriatal dopaminergic neurons of MPTP-treated mice at the presymptomatic and symptomatic stages of parkinsonism. *Journal of Neurology*. 15:198-207.
- Lorenc-Koci, E. Wolfarth S. and Ossowska, K. (1996) Haloperidol-Increased muscle tone in rats as a model of parkinsonian rigidity. *Expression of Brain Research*. 109(2):268-276.
- Meltzer, H.Y., Li Z., Kaneda, Y. and Ichikawa J. (2003) Serotonin receptors: their key role in drugs to treat schizophrenia. *Progress in Neuropsychopharmacological Biological Psychiatry*. 27:1159-1172.
- Muthane, U.B., Swamy, H.S., Satishchandra, P., Subhash, M.N. and Rao, S. (1994) Early onset Parkinson's disease: are juvenile and young-onset different? *Journal of Movement Disorders*. 9(5):539-544. <https://doi.org/10.1002/mds.870090506>
- Ogundele, O.M. Okunnuga, A.A., Fabiyi, T.D., Olajide, O.J., Akinrinade, I.D. and Ojo, A.A. (2014) NMDA receptor inhibition and potentiation affects cellular process formation in melanocytes; a model for synaptic denervation in parkinsonism. *Metabolic Brain Disease*: 29:541-555. doi 10.1007/s11011-013-9447-6.
- Olsson, M., Nikkiah, G., Bentlage, C. and Bjorklund, A. (1995) Forelimb akinesia in the rat Parkinson model: differential effects of dopamine agonists and

- nigral transplants as assessed by a new stepping test. *The Journal of Neuroscience*. 15(5):3863-3875.
- Padayatty, S.J. Katz, A. Wang, Y. Eck, P. Kwon, O. Lee, J.H. Chen, S., Chen, S., Corpe, S., Dutta, A., Dutta, S.K. and Levine, M. (2003) Vitamin C as an antioxidant: evaluation of its role in disease prevention. *Journal of American College of Nutrition*. 22(1):18-35.
- Paviour, D.C., Surtees, R.A.H. and Lees, A.J. (2004) Diagnostic considerations in juvenile parkinsonism. *Journal of Movement Disorders* 19(2):123-135. <https://doi.org/10.1002/mds.10644>
- Peiying, L (2012) Morphological assessment of global cerebral ischemia: viable cells. 1st ed. Springer Protocol Handbook. 14-16
- Periquet, M, Latouche, M., Lohmann, E., Rawal, N. and De Michele, G, (2003) Parkin mutations are frequent in patients with isolated early-onset parkinsonism. *Brain*. 126(Pt 6):1271-1278. <https://doi.org/10.1093/brain/awg136>
- Piffl, C., Rajput, A., Reither, H., Blesa, J., Cavada, C., Obeso, J.A., Rajput, A.H. and Hornykiewicz, O. (2014) Is Parkinson's disease a vesicular dopamine storage disorder? Evidence from a study in isolated synaptic vesicles of human and nonhuman primate striatum. *Journal of Neuroscience*. 11: 82-83.
- Pioli, E.Y., Meissner, W., Sohr, R., Gross, C.E., Bezard, E. and Bioulac, B.H. (2008) Differential behavioral effects of partial bilateral lesions of ventral tegmental area or substantia nigra pars compacta in rats. *Neuroscience*. 153(4):1213-1224.
- Polydoro, M., Schroder, N., Lima, M.N., Caldana, F., Laranja, D.C., Bromberg, E., Roesler R., Quevedo, J., Moreira, J.C. and Dal-Pizzol, F. (2004) Haloperidol and clozapine induced oxidative stress in the rat brain. *Pharmacology Biochemistry and Behavior*. 78(4):751-756. DOI:10.1016/j.pbb.2004.05.018.
- Rathish, N. and Arun, M. (2012) Vitamin D: The "sunshine" vitamin. *Journal of Pharmacology and Pharmacotherapy*. 3(2):118-126. doi: 10.4103/0976-500X.95506
- Robert, H. (2011) Histology of central nervous system. *Toxicologic Pathology*. 39:22-35. doi: 10.1177/0192623310389621
- Schrag, A., Ben-Shlomo, B., Brown, R., Marsden, C.D., Quinn, N. (1998). Young-onset Parkinson's disease revisited: clinical features, natural history, and mortality. *Journal of Movement Disorders*. 13(6):885-894. <https://doi.org/10.1002/mds.870130605>.
- Seeman, P. and Tallerico, T. (2003) Link between dopamine D1 and D2 receptors in rat and human striatal tissues. *Synapse*. 47(4):250-254.
- Shirayama, Y., Mitsushio, H., Takahashi, K. and Nishikawa, T. (2000) Differential effects of haloperidol on phencyclidine-induced reduction in substance P contents in rat brain regions. *Synapse*. 35(4):292-299.
- Silver, G.A., Vuong, K. and Jankovic, J. (2004) Young-onset versus late-onset Parkinson's disease: clinical features and disease progression. *Movement Disorders*. 19(9):S264.
- Yers, H.R. Maheshwary, S. Amodeo, D.M. and Dykstra, S.G. (2013) VDR potentiation. *Journal of Investigative Dermatology*. 121:813-820.