

# Movement Disorders in India

The ancient texts of the Indian system of medicine 'Ayurveda', describes Parkinsonism and tremors as early as 5000-3000 BC.<sup>1</sup>

## Parkinsonism

The Ayurvedic physician, Charaka, was possibly the first to describe Parkinson's disease (PD) in his treatise "Charaka Samhitha" where he called it 'Kampavata', literally meaning 'tremors of neurological origin'. Interestingly, the treatment recommended in Ayurveda for PD is the seeds of *Mucuna Pruriens* whose extract contains levodopa. All this was known much before James Parkinson described this disease in modern times.

The prevalence of PD in Indians is lower than people of European origin. Parsis who immigrated to India centuries ago from Persia have a much higher prevalence of PD than the Indians.<sup>2</sup> A recent epidemiological study from Kolkata showed a low prevalence (Crude Prevalence: 45.8 and Age Adjusted Prevalence: 71.6 per 100,000) of Parkinsonism.<sup>3</sup> On the contrary, the prevalence of PD in Anglo-Indians, a mixed race from marriage between a European man and an Indian woman is about 40% lower than the prevalence in the Caucasian population.<sup>4</sup>

Normal Indians have 40% fewer melanised nigral neurons than British Caucasians and these neurons are not lost with increasing age.<sup>5</sup> The number of melanised nigral neurons between the British and Nigerians did not differ significantly suggesting that factors other than neuronal numbers contribute to differential susceptibility to PD between non-white and white races.<sup>6</sup>

Genetic studies in familial PD have shown that alpha-synuclein,<sup>7</sup> Parkin,<sup>8-11</sup> LRRK2,<sup>10</sup> PINK and DJ-1 mutations occur in a small number of Indian patients. SCA2 commonly causes ataxia in the Indians but Ragothaman et al have described a family with homozygous SCA2 mutation, who presented as levodopa responsive parkinsonism. However, unlike the ataxic phenotype that have slow saccades, they had normal eye movements. These patients develop motor fluctuations and dyskinesia, hence early in the illness they can be mistaken as PD. Furthermore these SCA2 patients with parkinsonism develop slow saccades, psychosis and dementia about six years after disease onset.<sup>12</sup>

Manganese-induced Parkinsonism is common in the manganese mine workers in India. These patients typically walk on their toes and fall frequently as they have severely impaired postural reflexes. They typically have a pathological laughter and deep pigmentation of gums, palate and uvula, and their parkinsonism does not improve with levodopa.<sup>13,14</sup> Bhatt et al reported parkinsonism on exposure to household pesticides.<sup>15</sup> In Japanese encephalitis-endemic regions, parkinsonism occurs in ~80% of patients during the acute illness but a long-term follow up showed that it persists in only a few adults, whilst in children they develop dystonia. JE antibodies and antigen were absent in the CSF of patients who developed these movement disorders, showing that the virus

does not remain in the nervous system. These patients do not improve with levodopa.<sup>16</sup>

Surgery was the treatment of choice for PD before levodopa was introduced. In 1963, Prof Varma attempted to lesion the ventrolateral thalamic nucleus by injecting alcohol via needle inserted through the foramen ovale to control tremors.<sup>17,19</sup> Using this outpatient procedure he stopped advancing the needle when the tremors stopped, thinking he had reached the planned target, the VL thalamic nucleus. However, when these lesions were mapped using the Schaltenbrand atlas, they were located in the subthalamic nucleus. This anatomical localisation was confirmed at autopsy, using a stereotaxic atlas and, recently, using MRI.<sup>18</sup>

In the modern era, surgical treatment for advanced PD has resurfaced as a treatment and Doshi and Bhatt reported depression following deep brain stimulation of the subthalamic nucleus possibly due to spread of the stimulation to the limbic region of this structure. Kishore et al have also observed motor improvement following stereotactic lesions to treat levodopa-induced dyskinesia but this is dependent on the volume of lesions in the ventral globus pallidus and suggested different anatomical substrates might be involved in controlling 'off signs' and dyskinesia.

Behari et al evaluated the quality of life (QoL) in PD patients and observed that female gender, depression, reduced independence, higher levodopa dose (>400 mg/day) and UPDRS scores were associated with worse QoL.<sup>19</sup>

Medicines and surgical interventions have improved the quality of life of PD patients but are still expensive and unaffordable to many living in developing countries. Managing PD in Indians where only 3% have health insurance is a challenge. Indian patients spend nearly 40% of their average gross income to buy medicines and despite the costs of treating PD in India being lower than in developed nations, optimal treatment is still out of reach for many Indian patients.<sup>20</sup>

## Chorea

Rheumatic fever is still common in India and chorea still occurs frequently. The prevalence of Huntington's disease (HD) in Indians is not known, it occurs in 1.75 per 100,000 population of Indians living in the United Kingdom.<sup>21</sup> Salem et al, found that the distribution of alleles (D2642 and D4S127) in Indian HD patients are similar to West European populations and suggest that this admixture possibly occurred when British troops were located in South India during various wars.<sup>22</sup>

Wali et al reported a large South Indian family with autosomal dominant paroxysmal kinesogenic choreathetosis (PKC) and onset in early childhood. Choreathetosis was precipitated by activities such as hyperventilation (46%), swimming (23%), exposure to cold (30.8%) and prolonged exercise (23%). This family has a second PKC mutation localised to the long-arm of chromosome 16q13-q22.1.<sup>23</sup>



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## Dystonia

Naiya et al evaluated DYT1 mutations in patients with primary dystonia from eastern India and found three reported and two novel mutations suggesting these mutations rarely cause dystonia in Indians.<sup>24</sup> Behari et al identified chewing betel nut with tobacco increased the risk of developing Meige syndrome.<sup>25</sup> Ragothaman et al reported task specific dystonia while playing the Indian percussion instruments 'tabla' and wind instrument 'Nadaswaram'.<sup>26</sup> Dystonia due to Niemann-Pick type C, GM1 gangliosidosis and Hallervorden Spatz have been reported.<sup>27-30</sup> GM1 gangliosidosis patients have generalised dystonia with prominent facial dystonia, severe dysarthria and normal eye movements, with Gaucher-like foam cells in the marrow and their MRI shows typical symmetrical putamen lesions. The diagnosis is confirmed by deficiency of beta-galactosidase. Dystonia following Japanese encephalitis occurs in children, and typically develops one to three weeks after the acute illness. Some patients relapse after a partial recovery suggesting a biphasic illness pattern. During the second phase, patients develop behavioural changes, dystonia, peri-oral dyskinesia and drooling.<sup>31</sup>

## Tremors

Infantile tremors syndrome has been described in Indian infants from poor, malnourished families. Tremors are generalised and are prominently seen in distal extremities, appearing suddenly after a brief febrile illness lasting for six weeks. Frontal lobe biopsy showed features of encephalitis and meningoencephalitis but CSF examination is normal and negative for common viruses.

## Wilson's Disease

Wadia and Dastur reported that 30% of Wilson's disease cases in India

present with osteomalacia.<sup>32,33</sup> Wilson's disease is though a common cause of dystonia and other movement disorders in Indians. Patients present with neurological deficits (69%) in the first or second decade of life and ~15% have hepatic dysfunction.<sup>34</sup> Autopsy shows caudate atrophy (100%) or central pontine myelinolysis (83%)<sup>35</sup> and treatment with D-Penicillamine can initially worsen the neurological deficits in ~50% of patients.

## Myoclonus

Subacute Sclerosing Encephalitis (SSE) still unfortunately occurs and is a common cause of myoclonus as measles vaccination is still not mandatory and is often unaffordable. It can occur in children and adults. Adult SSE occurs at a mean age of 20.9 years with the patients presenting with generalised myoclonus, behavioural changes, seizures, cognitive decline, visual impairment and extrapyramidal features like parkinsonism and dystonia. SSE still poses diagnostic challenges for clinicians in India.<sup>36</sup> Neuronal ceroid lipofuscinosis is another cause of myoclonus (83.8%) in children and is associated with regression of milestones (83.3%), chorea (50%), visual impairment (42%), ataxia (33.3%) and abnormal behaviour (17%). Eye examination shows optic atrophy (50%), macular degeneration (33.3%) and retinitis pigmentosa (8.3%). Skin biopsy shows characteristic PAS and Luxol Fast Blue (LFB) positive, autofluorescent intracellular ceroid material in neurons and astrocytes.<sup>37</sup>

## Conclusion

Patients in India present with a wide variety of movement disorders and these pose challenges, especially in terms of treatment, given the therapeutic limitations due to a near total lack of health insurance.

## References

- Muthane UB, Bhatt MH, Wadia NH. *Parkinson's Disease and other Akinetic disorders*. In: Wadia NH, editor. *Neurological Practice: An Indian Perspective*. New Delhi: Elsevier, 2005:353-65.
- Muthane U, Jain S, Gururaj G. *Hunting genes in Parkinson's disease from the roots*. *Medical Hypotheses* 2001; 57(1)(2001):51-5.
- Das SK, Biswas A, Roy T, Banerjee TK, Mukherjee CS, Raut DK et al. *A random sample survey for prevalence of major neurological disorders in Kolkata*. *Indian J Med Res* 2006;124(2):163-72.
- Ragothaman M, Murgod UA, Gururaj G, Kumaraswamy SD, Muthane U. *Lower risk of Parkinson's disease in an admixed population of European and Indian origins*. *Mov Disord* 2003;18(8):912-4.
- Muthane U, Yasha TC, Shankar SK. *Low Numbers and No Loss of Melanized Nigral Neurons with Increasing Age in Normal Human Brains from India*. *Ann Neurol* 1998;43:283-7.
- Muthane UB, Chickabasaviah YT, Henderson J, Kingsbury AE, Kilford L, Shankar SK et al. *Melanized nigral neuronal numbers in Nigerian and British individuals*. *Mov Disord* 2006;21(8):1239-41.
- Nagar S, Juyal RC, Chaudhary S, Behari M, Gupta M, Rao SN et al. *Mutations in the alpha-synuclein gene in Parkinson's disease among Indians*. *Acta Neurol Scand* 2001;103(2):120-2.
- Madegowda RH, Kishore A, Anand A. *Mutational screening of the parkin gene among South Indians with early onset Parkinson's disease*. *J Neurol Neurosurg Psychiatry* 2005;76(11):1588-90.
- Biswas A, Gupta A, Naiya T, Das G, Neogi R, Datta S et al. *Molecular pathogenesis of Parkinson's disease: identification of mutations in the Parkin gene in Indian patients*. *Parkinsonism Relat Disord* 2006;12(7):420-6.
- Punia S, Behari M, Govindappa ST, Swaminath PV, Jayaram S, Goyal V et al. *Absence/rarity of commonly reported LRRK2 mutations in Indian Parkinson's disease patients*. *Neurosci Lett* 2006;409(2):83-8.
- Biswas A, Maulik M, Das SK, Ray K, Ray J. *Parkin polymorphisms: risk for Parkinson's disease in Indian population*. *Clin Genet* 2007; 72(5):484-6.
- Ragothaman M, Muthane U. *Homozygous SCA 2 mutations changes phenotype and hastens progression*. *Movement Disorders* 2008 (In Press).
- Wadia NH. *Manganese intoxication in Indian mines*. In: Bogaert LV, Kafer JP, Poch G, Lopez L, editors. *Tropical Neurology proceedings of the 1st International Symposium Buenos Aires*. Buenos Aires, Argentina: 1962:272-7.
- Veerendrakumar M, Gourie-Devi M, Chandra SV. *Neurological disorders in chronic industrial exposure to manganese*. *Indian Academy of Neurology*. 1990. (Abstract)
- Bhatt MH, Elias MA, Mankodi AK. *Acute and reversible parkinsonism due to organophosphate pesticide intoxication: five cases*. *Neurology* 1999;52:1467-71.
- Murgod UA, Muthane UB, Ravi V, Radhesh S, Desai A. *Persistent movement disorders following Japanese Encephalitis*. *Neurology* 2001;57(12):2313-5.
- Varma RM. *Percutaneous cheomthalamectomy for Parkinsonism*. *Neurology India* 1964;12:54-60.
- Muthane UB, Varma RM, Sundarajan P, Hegde T, Jayakumar PN, Shankar SK. *Percutaneous trans-Foramen Ovale approach to Subthalamic Nucleus (Varma's technique): A shorter route and economical technique in the surgical management of Parkinson's Disease*. *Mov.Disord*. 1998;13(Suppl 2):71. (Abstract)
- Behari M, Srivastava AK, Pandey RM. *Quality of life in patients with Parkinson's disease*. *Parkinsonism Relat Disord* 2005;11(4):221-6.
- Ragothaman M, Govindappa ST, Rattihalli R, Subbakrishna DK, Muthane UB. *Direct costs of managing Parkinson's disease in India: concerns in a developing country*. *Mov Disord* 2006;21(10):1755-8.
- Shiwach RS, Lindenbaum RH. *Prevalence of Huntington's disease among the Indian immigrants from the Indian subcontinent*. *Br J Psychiatry* 1990;157:598-9.
- Saleem Q, Muthane U, Verma IC, Brahmachari SK, Jain S. *Expanding colonies and expanding repeats*. *Lancet* 2002;359(9309):895-6.
- Valente EM, Spacey SD, Wali GM, Bhatia KP, Dixon PH, Wood NW et al. *A second paroxysmal kinesigenic choreoathetosis locus (EKD2) mapping on 16q13-q22.1 indicates a family of genes which give rise to paroxysmal disorders on human chromosome 16*. *Brain* 2000;123:2040-5.
- Naiya T, Biswas A, Neogi R, Datta S, Misra AK, Das SK et al. *Clinical characterization and evaluation of DYT1 gene in Indian primary dystonia patients*. *Acta Neurol Scand* 2006;114(3):210-15.
- Behari M, Sharma AK, Changkakoti S, Sharma N, Pandey RM. *Case-control study of Meige's syndrome. Result of a pilot study*. *Neuroepidemiology* 2000;19(5):275-80.
- Ragothaman M, Sarangmat N, Jayaram S, Swaminath P, Muthane U. *Task-specific dystonia in tabla players*. *Movement Disorders* 2004.
- Muthane UB, Yasha TC, Shankar SK, Christopher R, Cooney AM, Kaneski CR et al. *A new variety of dystonia with a phenotype mimicking Niemann-Pick type C or a new variant of Niemann Pick type C disease? Mov.Disord*. 1998;13(suppl 2):96. Ref Type: Abstract
- Muthane UB, Yasha TC, Kaneski CR, Shankar SK, Gayathri N, Christopher R et al. *Clinical Features of Adult GM1 Gangliosidosis: Report of three Indian patients and Review of 40 cases*. *Movement Disorders*. In press.
- Muthane U, Chickabasaviah Y, Kaneski C, Shankar SK, Narayanappa G, Christopher R et al. *Clinical features of adult GM1 gangliosidosis: report of three Indian patients and review of 40 cases*. *Mov Disord* 2004;19(11):1334-41.
- Muthane UB, Shetty R, Panda K, Yasha TC, Jayakumar PN, Taly AB. *Hallervorden Spatz disease and acanthocytes*. *Neurology* 1999;53(8):32.
- Pradhan S, Gupta RK, Singh MB, Mathur A. *Biphasic illness pattern due to early relapse in Japanese-B virus encephalitis*. *J Neurol Sci* 2001;183(1):13-8.
- Wadia NH, Dastur DK. *Wilson's Disease in four Indian families (Clinical, Genetical and Biochemical aspects)*. *Neurology* 1963;11:1-18.
- Dastur DK, Manghani DK, Wadia NH. *Wilson's disease in India. I. Geographic, genetic, and clinical aspects in 16 families*. *Neurology* 1968;18:21-31.
- Taly AB, Meenakshi-Sundaram S, Sinha S, Swamy HS, Arunodaya GR. *Wilson disease: description of 282 patients evaluated over 3 decades*. *Medicine (Baltimore)* 2007;86(2):112-21.
- Sinha S, Jha DK, Sinha KK. *Wilson's disease in eastern India*. *J Assoc Physicians India* 2001;49:881-4.
- Prashanth LK, Taly AB, Ravi V, Sinha S, Arunodaya GR. *Adult onset subacute sclerosing panencephalitis: clinical profile of 39 patients from a tertiary care centre*. *J Neurol Neurosurg Psychiatry* 2006;77(5):630-3.
- Sinha S, Satischandra P, Santosh V, Gayatri N, Shankar SK. *Neuronal ceroid lipofuscinosis: a clinicopathological study*. *Seizure* 2004;13(4):235-40.