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Prenatal and Postnatal Exposures to 1-Methyl-4-phenyl-1,2,3,6-tetra Hydropyridine (MPTP) Impaired Mouse Midbrain Dopamine System and May Produce a Predisposing and Inducing Model for Parkinson ' s Disease

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ABSTRACT

Dopamine cell bodies in the substantia nigra of the midbrain and with their terminals projecting to the neostriatum form the nigrostriatum and these dopamine neurons degenerate in Parkinson ' s disease (PD). Based on metabolic and func- tional specialization of the cell bodies versus the axon terminals, the level and disposition of dopamine, its metabolites and enzymes are different in both regions and are likely to be affected differently in PD. We examined changes in the midbrain dopamine system following 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), to test the hypothesis that a predisposing/sensitization stage and a inducing/precipitating stage underlie PD. Pregnant mice were treated with a low dose of MPTP during gestation days 8 - 12 to model the predisposing/sensitization stage, by interrupting the fetal mid- brain dopamine system during its neurogenesis. For the inducing/precipitating stage, the 12-weeks offspring were ad- ministered MPTP. The prenatal-MPTP offspring appear normal, but midbrain dopamine, 3,4-di-hydroxy-phenyl-acetic- acid, 3-methoxytyramine, tyrosine-hydroxylase and L-aromatic-amino-acid-decarboxylase, were reduced by 49.6%, 48%, 54%, 20.9% and 25%. Postnatal-MPTP of 10, 20, 30 mg/kg administered to the prenatal-PBS vs prenatal-MPTP offspring reduced midbrain dopamine by 43.6%, 47.2%, 70.3% vs 85.4%, 89.1%, 95.2%; tyrosine-hydroxylase by 30%, 63%, 81% vs 30.7%, 70.4%, 91.4%; L-aromatic-amino-acid-decarboxylase by 0%, 2%, 40% vs 32%, 40%, 58%. The prenatal-MPTP may render the DA system sensitive by causing sub-threshold reduction of DA, its metabolites and en- zymes, enabling postnatal-MPTP to reduce dopamine above the 70% - 80% PD-inducing threshold. Thus, the study may produce a prenatal predisposing/sensitization and postnatal inducing/precipitation model of PD. It also indicates that some cases of PD may have a fetal basis, in which sub-threshold nigrostriatal impairments occur early in life and PD-symptoms are induced during aging by further insults to the dopaminergic system that would not cause PD symptoms in normal indi-viduals.

KEYWORDS

Parkinson ' s Disease; Midbrain; 1-Methyl-4-Phenyl-1,2,3,6-Tetrahydropyridine (MPTP); Dopamine; Tyrosine Hydroxylase; L-aromatic Amino Acid Decarboxylase; Sensitization; Precipitation

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References

[1] R. E. Heikkila and P. K. Sonsalla, " The MPTP Treated Mouse as a Model of Parkinsonism: How Good Is It? " Neurochemistry International, Vol. 20, 1992, pp. 299-303. doi:10.1016/0197-0186(92)90256-Q

[2] P. Grandjean and P. J. Landrigan, " Developmental Neurotoxicity of Industrial Chemicals. " Lancet, Vol. 368, No. 9553, 2006, pp. 2167-2178. doi:10.1016/S0140-6736(06)69665-7

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[3] H. R. Andersen, J. B. Nielsen and P. Grandjean, "Toxicologic Evidence of Developmental Neurotoxicity of Environmental Chemicals," Toxicology, Vol. 144, No. 1-3, 2000, pp. 121-127. doi:10.1016/S0300-483X(99)00198-5

[4] L. G. Costa. M. Aschner, A. Vitalone, T. Syversen and O. P. Soldin, "Developmental Neuropathology of Environmental Agents," Annual Review of Pharmacology and Toxicology, Vol. 44, No. 1, 2004, pp. 87-110. doi:10.1146/annurev.pharmtox.44.101802.121424

[5] Z. Ling, D. A, Gayle, S.Y. Ma, J. W. Lipton, C. W. Tong, J. S. Hong and P. M. Carvey, "In Utero Bacterial Endotoxin Exposure Causes Loss of Tyrosine Hydroxylase Neurons in the Postnatal Rat Midbrain," Movement Disorders, Vol. 17, No. 1, 2002, pp. 116-124. doi:10.1002/mds.10078

[6] D. B. Calne and J. W. Langston, "Etiology of Parkinson's Disease," Lancet, Vol. 322, No. 8365, 1983, pp. 1457- 1459. doi:10.1016/S0140-6736(83)90802-4

[7] P. H. V. Jenner, A. Shapira and C. D. Marsden, "New Insight in to the Cause of Parkinson's Disease". Neurology, Vol. 42, No. 12, 1992, pp. 2241-2250. doi:10.1212/WNL.42.12.2241

[8] K. Aoyama, M. Matsubara, Y. Kondo, M. Murakawa, K. Suno and S. Yamaguchi, "N-Methylation Ability for Azaheterocyclic Amines in Higher in Parkinson's Disease: Nicotinamide Loading Test," Journal of Neural Transmission, Vol. 107, No. 8-9, 2000, pp. 985-995. doi:10.1007/s007020070047

[9] D. A. Di Monte, "The Environment and Parkinson's Disease: Is the Nigrostriatal System Preferentially Targeted by Neurotoxins," The Lancet Neurology, Vol. 2, No. 9, 2003, pp. 531-538.

[10] J. L. Kennedy, L. A. Farrer, N. C. Andreason, R. Mayeux and P. St. George Hyslop, "The Genetics of Adult-Onset Neuropsychiatric Disease: Complexities and Conundra?" Science, Vol. 302, No. 5646, 2003, pp. 822-826. doi:10.1126/science.1092132

[11] G. Anderson, A. R. Noorian, G. Taylor, M. Anitha, D. Bernhrd, S. Srinivasan and J. G. Greene, "Loss of Enteric Dopaminergic Neurons and Associated Changes in Colon Mortility in an MPTP Mouse Model of Parkinson's Disease," Experimental Neurology, Vol. 207, No. 1, 2007, pp. 4-12. doi:10.1016/j.expneurol.2007.05.010

[12] G. Natale, O. Kastsiushenka, F. Fulceri, S. Ruggieri, A. Paparelli and F. Fornai, "MPTP-Induced Parkinsonism Extends to a Subclass of TH-Positive Neurons in the Gut," Brain Research, Vol. 1355, No. 8, 2010, pp. 195-206. doi:10.1016/j.brainres.2010.07.076

[13] A. G. Kanthasamy, M. Kitazawa, A. Kanthasamy and V. Anantharaman, "Dieldrin-Induced Neuro Toxicity: Relevance to Parkinson's Disease Pathogenesis," Neurotoxicology, Vol. 26, No. 4, 2005, pp. 701-719.

[14] S. A. Lloyd, C. Faherty and R. J. Smeyne, "Adult and in Utero Exposure to Cocaine Alters Sensitivity to the Parkinsonian Toxin 1-Methyl-4-phenyl-1,2,3,6-tetrahy-dropyridine," Neuroscience, Vol. 137, No. 3, 2006, pp. 905-913. doi:10.1016/j.neuroscience.2005.09.035

[15] C. G. Charlton, "A Parallel Relationship between Parkinson's Disease and Excess of S Adenosylmethionine dependent Biological Methylation in the Brain," Basic, Clinical and Therapeutic Aspects of Alzheimer's and Parkinson's Disease, Vol. 1, Cpt. 65, 1990, pp. 333-339.

[16] C. G. Charlton and B. Crowell, "Parkinson's Disease like Effects of S Adenosyl methionine: Effects of L dopa," Pharmacology Biochemistry and Behavior, Vol. 43, No. 2, 1992, pp. 423 431. doi:10.1016/0091-3057(92)90172-C

[17] L. Axelrod and J. Tomchick. "Enzymatic-O-methylation of Epinephrine and Other Catechols," Journal of Biological Chemistry, Vol. 233, No. 3, 1958, pp. 702-705.

[18] C. G. Charlton and B. Crowell, "Striatal Dopamine Depletion, Tremors and Hypokinesia Following the Intracranial Injection of S Adenosylmethionine," Molecular and Chemical Neuropathology, Vol. 26, No. 3, 1995, pp. 269- 284. doi:10.1007/BF02815143

[19] C. G. Charlton and J. Mack, "Substantia Nigra Degeneration and Tyrosine Hydroxylase Depletion Caused by Excess S Adenosylmethionine in the Rat Brain: Support for an Excess Methylation Hypothesis for Parkinsonism," Molecular Neurobiology, Vol. 9, No. 1-3, 1994, pp. 149 161. doi:10.1007/BF02816115

[20] G. Muthian, V. Mackey and C. G. Charlton, "Modeling a Sensitization Stage and a Precipitation Stage for Parkinson's Disease Using Prenatal and Postnatal 1-Methyl-4- phenyl-1,2,3,6-tetrahydropyridine (MPTP) Administration," Neuroscience, Vol. 169, No. 3, 2010, pp. 1085-1093. doi:10.1016/j.neuroscience.2010.04.080

[21] C. G. Charlton, "Depletion of Nigrostriatal and Forebrain Tyrosine Hydroxylase by S-Adenosylmethionine: A Model That May Explain the Occurrence of Depression in Parkinson's Disease," Life Sciences, Vol. 61, No. 5, 1997, pp. 495-502. doi:10.1016/S0024-3205(97)00409-8