Neurochem Res (2012) 37:358–369
DOI 10.1007/s11064-011-0619-7

ORIGINAL PAPER

Increased Oxidative Damage and Decreased Antioxidant Function in Aging Human Substantia Nigra Compared to Striatum: Implications for Parkinson's Disease

C. Venkateshappa · G. Harish · Rajeswara Babu Mythri · Anita Mahadevan · M. M. Srinivas Bharath · S. K. Shankar

Received: 26 July 2011 / Revised: 9 September 2011 / Accepted: 22 September 2011 / Published online: 5 October 2011

Abstract Parkinson's disease (PD) is characterized by selective degeneration and loss of dopaminergic neurons in the substantia nigra (SN) of the ventral mid brain leading to dopamine depletion in the striatum. Oxidative stress and mitochondrial damage have been implicated in the death of SN neurons during the evolution of PD. In our previous study on human PD brains, we observed that compared to SN, striatum was significantly protected against oxidative damage and mitochondrial dysfunction. To understand whether brain aging contributes to the vulnerability of midbrain to neurodegeneration in PD compared to striatum, we assessed the status of oxidant and antioxidant markers, glutathione metabolic enzymes, glial fibrillary acidic protein (GFAP) expression and mitochondrial complex I(CI) activity in SN (n = 23) and caudate nucleus (n = 24) during physiological aging in human brains. We observed a significant increase in protein oxidation ($P < 0.001$), loss of CI activity ($P = 0.04$) and increased astrocytic proliferation indicated by GFAP expression ($P < 0.001$) in SN compared to CD with increasing age. These changes were attributed to significant decrease in antioxidant function represented by superoxide dismutase (SOD) ($P = 0.03$), glutathione (GSH) peroxidase (GPx) ($P = 0.02$) and GSH reductase (GR) ($P = 0.03$) and a decreasing trend in total GSH and catalase with increasing age. However, these parameters were relatively unaltered in CD. We propose that SN undergoes extensive oxidative damage, loss of antioxidant and mitochondrial function and increased GFAP expression during physiological aging which might make it more vulnerable to neurotoxic insults thus contributing to selective degeneration during evolution of PD.

Keywords Aging · Human brain · Substantia nigra · Caudate nucleus · Oxidative protein damage · Glutathione · Glial fibrillary acidic protein · Parkinson's disease

Abbreviations

PD	Parkinson's disease
SN	Substantia nigra
CI	Mitochondrial complex I
GSH	Glutathione reduced
PMI	Postmortem interval
CD	Caudate nucleus
3-NT	3-Nitrotyrosine
GFAP	Glial fibrillary acidic protein
SOD	Superoxide dismutase
GST	Glutathione-s-transferase
GR	Glutathione reductase
GPx	Glutathione peroxidase

C. Venkateshappa · G. Harish · R. B. Mythri · M. M. Srinivas Bharath (✉)
Departments of Neurochemistry, National Institute of Mental Health and Neurosciences (NIMHANS), No. 2900, Hosur Road, Bangalore, Karnataka 560029, India
e-mail: bharath@nimhans.kar.nic.in; thathachar@rediffmail.com

A. Mahadevan · S. K. Shankar
Departments of Neuropathology, National Institute of Mental Health and Neurosciences (NIMHANS), No. 2900, Hosur Road, Bangalore, Karnataka 560029, India

Introduction

Parkinson's disease (PD) is an age-associated neurodegenerative disease clinically characterized as a movement disorder [1]. The chief pathological hallmark in PD is the gradual loss of dopaminergic neurons in the substantia