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Nanodelivery of cerebrolysin induces neuroprotection in Parkinson's disease

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Parkinson's disease (PD) affects over 80 thousand Americans every year for which no suitable therapy is available till date. PD induces severe disability in victims and so far no suitable strategies have been developed resulting an urgent need to explore novel therapeutic strategies to treat PD for the benefit of the mankind. Recently, nanodrug delivery of therapeutic compounds has been shown to induce superior neuroprotective effects than the parent compounds in central nervous system (CNS) diseases. There are evidences that increased oxidative stress and neurotoxic elements in the CSF and in the brain appears to be responsible for PD pathology and decline in cognitive and motor functions. Recent research suggests that increased alpha-synuclein (α-synuclein, ASNC) in the CSF and in several brain areas together with oxidative stress correlates well with the brain pathology and cognitive decline in human cases of PD. Thus, a possibility exists that drugs that are capable to reduce the levels of oxidants and/or ASNC could be useful for novel therapeutic tools in PD. Previous reports from our laboratory showed that intraperitoneal injections of 1-metyl-4-fenyl-1,2,3,6-tetrahydropyridin (MPTP, 20 mg/kg) daily within 2-h intervals for 5 days in mice induce PD like symptoms on the 8th day. This model is well-characterized biochemically, histologically and functionally for PD like symptoms. Thus, marked decrease in the number of tyrosine hydroxylase (TH) positive cells in the Substantia Nigra Pars Compacta (SNpc) and striatum (STr) as well as decrease in dopamine (DA) and its metabolites 3,4-Dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA) with marked behavioral dysfunctions e.g., Rota-Rod performances, walking on an inclined mesh grid and gait deficits was seen on the 8th day. Cerebrolysin (CBL) is a well-balanced composition of several neurotrophic factors and active peptide fragments. Thus, this multimodal drug may have an added value on therapeutic strategies in PD. In present investigations we examined timed release of CBL using titanate nanospheres (TiNS) in treating PD in our mouse model. In this investigation, timed release of CBL using titanate nanospheres (TiNS) treatment results in significant neuroprotection and behavioral improvements. Thus, it would be interesting to examine whether this model of PD is also associated with increased ASNC and free radical nitric oxide in the CSF and brain areas of mice and cerebrolysin treatment could modulate these elements in our model. ASNC was measures using commercial ELISA kit in the CSF and in brain whereas neuronal nitric oxide synthase (nNOS) was examined using immunohistochemistry on paraffin sections. Our results showed a significant increase in ASNC by 2- to 4-fold in the CSF and in various brain areas from normal control group (control: SNpc 1.78±0.08 ng/µg, STr 6.34±0.21 ng/µg, frontal cortex 8.24±0.32 ng/µg; CSF 1.21±0.07 pg/µl). In these brain areas nNOS expression was also increased by 4- to 8-fold as compared to control group. Nanodelivery of cerebrolysin (3 ml/kg, i.v. 2 days after MPTP for 5 days) significantly reduced ASNC levels in the CSF and in all the brain areas examined. In the treated PD mice downregulation of nNOS was also seen in the above brain regions. These results are the first to show that nanodelivery of cerebrolysin induces neuroprotection in PD by reducing ASNC and nNOS expression. However, further research is needed to explore TiNS in clinical situations, a feature that requires additional investigations.

Biography

Aruna Sharma, MD is currently Secretary of Research at Uppsala University Hospital, Uppsala University, Sweden. She obtained her Bachelor of Science in 1971 and trained in Indian Medicine up to 1977 and engaged in medical research from 1978 to 1986 in India on hyperthermia induced brain dysfunction in the lab of Hari Sharma and Prasanta Kumar Dey under University Grants Commission and Indian Council of Medical Research Programs. She is a qualified experimental Neurpathologist and received her training at Karl Marx University Leipzig, Institute of Neurobiology (1987-1988); Semmelweis University Medical School, Department of Human Morphology and Developmental Biology, Budapest, Hungary (1988-1989), Free University Berlin, Germany (1989-1991) and Neuropathology Institute Uppsala (1992-1995). Dr Sharma is member of various Distinguished American Organizations and elected to receive the prestigious award "Women of the Years Representing Sweden Award 2009" for her outstanding contributions towards society by American Biographical Research Institute, USA; and "Best Professional Business Women Award 2010" For Setting Standard to Motivate, Excel and Inspire Others, Raleigh, North Carolina, USA. She has published over 50 original research papers in Reputed Neuroscience Journals and is currently Acquisition Editor of American Journal of Neuroproetction and Neuroregenartion.

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