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The neuroprotective actions of dopamine neuron stimulating peptide-11

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Glial cell line-derived neurotrophic factor (GDNF) and other related neurotrophic factors have shown great promise for the protection and restoration of damaged or dying dopamine neurons in animal models and in some Parkinson's disease (PD) clinical trials. However, due to the challenges associated with delivering neurotrophic factors like GDNF to the CNS and the difficulty of protein synthesis and structural modification, smaller neurotrophic-like molecules that are easy to synthesize, modify and with improved bioavailability are needed. We present the neurobiological actions of a small 11-amino acid amidated peptide from the proGDNF domain, named dopamine neuron stimulating peptide-11 (DNSP-11). *In vivo*, increases in resting levels of dopamine and its metabolites are observed at 28 days post injection following a single injection of DNSP-11 into the normal adult rat substantia nigra. Furthermore, in a severe 6-hydroxydopamine rat model of PD, DNSP-11 significantly improves apomorphine-induced rotational behavior and increases dopamine and metabolite tissue levels in the substantia nigra. *In vitro*, DNSP-11 supports the survival and neuritic outgrowth of primary fetal mesencephalic neurons. In the MN9D dopaminergic neuronal cell line, DNSP-11 provides protection against staurosporine and 6-hydroxydopamine-induced cell death, significantly decreasing levels of caspase-3 activity and TUNEL-positive cells. Finally, DNSP-11 pull-down assays suggests similar mechanistic targets of other anti-parkinsonian drugs. Collectively, these data support that this small peptide shows neurotrophic-like effects, thus making it a candidate for further evaluation as a potential PD therapeutic.

Biography

Dr. Luke H. Bradley completed his Ph.D. in biochemistry from Ohio State University. Following a postdoctoral fellowship at Princeton University, Dr. Bradley joined the faculty at the University of Kentucky College of Medicine as an Assistant Professor of Anatomy and Neurobiology. He is also affiliated with the University of Kentucky's Center of Structural Biology and the department of Molecular and Cellular Biochemistry. Dr. Bradley's research interests include the discovery and development of novel, synthetic peptide- and protein-based molecular platforms for downstream bioapplications and PD therapeutics.

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