Neuregulin-1 (Nrg1) is genetically linked to schizophrenia, a disease caused by neurodevelopmental imbalance in dopaminergic function. The Nrg1 receptor ErbB4 is abundantly expressed on midbrain dopaminergic neurons. Nrg1 has been shown to penetrate blood-brain barrier. Peripherally administered Nrg1 activates ErbB4 in neonatal mice and leads to a persistent hyperdopaminergic state. These data prompted us to study the effect of peripheral administration of Nrg1 in the context of Parkinson's disease (PD), a neurodegenerative disorder affecting the dopaminergic system in the adult brain. We observed that systemic injections of the extracellular domain of Nrg1ß1 (Nrg1ß1-ECD) increased dopamine levels in the substantia nigra and striatum of adult mice. Moreover, Nrg1ß1-ECD injections significantly protected the mouse nigrostriatal dopaminergic system morphologically and functionally against 6-hydroxydopamine-induced toxicity in vivo. In the substantia nigra of human PD patients, the percentage of dopaminergic neurons expressing the ErbB4-receptor was increased, and Nrg1ß1-ECD also protected human dopaminergic neurons in vitro against 6-hydroxydopamine, demonstrating that the human nigral dopaminergic neurons are reactive to Nrg1ß1-ECD-treatment. In conclusion, we have identified Nrg1ß1-ECD as a neurotrophic factor for adult mouse and human midbrain dopaminergic neurons with peripheral administrability, warranting further investigation as therapeutic option for PD patients.