We have previously shown that the intracranially injected nontoxic carboxy-terminal domain of the tetanus toxin heavy-chain (Hc-TeTx) protects the dopaminergic system and improves motor behavior in hemiparkinsonian rats (Mendieta et al., 2009). However, the Hc-TeTx effects by peripheral administration have not been yet investigated. In our study we have investigated the effects of intramuscular administration of Hc-TeTx fragment in the motor asymmetry and its relation to the dopaminergic system in the rat's hemi-Parkinsonism model. Adult male Wistar rats were intramuscularly treated with the Hc-TeTx fragment at 20 µg/kg i.m. or with only vehicle three days before dopaminergic denervation with 6-Hydroxydopamine (6-OHDA) (16 µg/2 µL) into the left striatum. The motor function was evaluated by the turning behavior, stepping test, and the cylinder test. The Hc-TeTx group had a significant improvement in the motor behavior tests, with improvements close to 90%, 30%, and 45% found in turning behavior, the stepping test, and the cylinder test. After the motor behavior tests, encephalic structures were dissected and tyrosine hydroxylase from the substantia nigra pars compacta (SNpc) was assessed by an immunohistochemical method obtaining significant increases in positive immunostaining from the SNpc in the Hc-TeTx - 6-OHDA treated-animals. In addition, the DA and its metabolites DOPAC and HVA in the striatum were measured by HPLC. We found an increase of 49% of DA levels for the Hc-TeTx - 6-OHDA-treated group compared to 6-OHDA group. These results suggest that the Hc-TeTx improves the motor behavior and protects the dopaminergic system of rats.