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Treadmill Running Combined with Microdialysis to Evaluate Motor Deficits and Improvement Following Dopaminergic Grafts in 6-OHDA Lesioned Rats

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To evaluate motor function more quantitatively, we made a treadmill apparatus and investigated the deficits and improvement in locomotion as well as dopamine (DA) turnover using *in vivo* microdialysis after 6-OHDA lesion and DAergic grafts in the rat. Rats were placed on a variable speed conveyer belt (0-1800 cm/min). Control rats ran on the treadmill at any speed but lesioned rats (unilateral lesion in nigrostriatal pathway) could not run at high speed. Grafted rats that showed no methamphetamine-induced rotation following DAergic grafts in the striatum exhibited improved running ability compared to 6-OHDA lesioned rats; however, this functional recovery was not complete. In control rats extracellular DOPAC and HVA were increased by running, and were correlated with the speed (DOPAC: 20-40%, correlation=0.819; HVA: 25-60%, correlation=0.8). DA was also increased by running, but the increase was not correlated with speed (30-40%, correlation=0.29). Increases of DA, DOPAC and HVA were mainly attributed to exercise itself and not to stress. DA, DOPAC and HVA decreased to less than 10% of control in lesioned rats. In grafted rats DA was restored to near control levels, although DOPAC and HVA were restored to 15% of control. In these animals DOPAC and HVA were increased by running; however, their correlations with speed were weaker than in intact rats (DOPAC: 10-30%, correlation=0.552; HVA: 15-50%, correlation=0.542). As in control rats, the increase of DA was not correlated with speed (25-30%, correlation=0.178). In spite of the good recovery of extracellular DA content, DOPAC and HVA levels remained low even following running. These data indicate that the regulation of DA release in the grafted striatum recovers to nearly the same intrinsic level as the intact nigrostriátal DAergic system. This is correlated with the recovery of motor behavior. Treadmill running ability reflects DA turnover in the striatum, and this running test combined with microdialysis is useful for quantitative evaluation of motor function.