Supporting Information

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Fig. S1. (*A*) HPLC analysis of catecholamine metabolites. Upon L-DOPA administration similar increases in 3,4-dihroxyphenyacetic acid (DOPAC), dopamine (DA), 5-hydroxyindoleacetic acid (5-HIAA), and homovanillic acid (HVA) are observed in DDD/WT vs. DDD/ β arr2KO mice. **P* < 0.05, ***P* < 0.01 L-DOPA treatment compared with basal. (*B*) Locomotion and (*C*) dyskinesia activity after 100 mg/kg i.p. acute dose of L-DOPA in DDD/WT mice. (*D*) Representative image of β arr2AAV injection in the striatum of DAT-KO mice. CTX, cortex; STR, striatum; V, ventricle. (*E*) Representative image of 6-OHDA lesioned mouse striatum. (*F*) Representative Western blot of AAV-induced GFP or β arr2 overexpression in 6-OHDA lesioned mice. Myc-tagged β arr2 has higher molecular weight than endogenous β arr2 owing to the myc epitope tag and the p2A sequence.



Fig. S2. (*A*) Loss of striatal TH staining in rats injected with 6-OHDA unilaterally. (*B*) Quantification of striatal TH fiber loss in saline, GFP, or βarr2 overexpression (βarr2 OE) rats. (*C*) Average striatal volume and transduction volume in all rats transduced by GFP or βarr2 AAV in rats. (*D*) Percentage transduction in GFP (green) and βarr2-AAV (red) rats.



Fig. S3. (*A* and *C*) Locomotive score and (*B* and *D*) average ALO AIMs score of saline, GFP infected, or $\beta arr2$ infected (overexpressed, OE) rats on (*A* and *B*) day 3 and (*C* and *D*) day 7 postviral L-DOPA injection. **P* < 0.05 $\beta arr2$ OE compared with saline or GFP rats. (*E*) ALO AIMs score for postviral L-DOPA injection for days 1, 3, and 7. **P* < 0.05 $\beta arr2$ OE compared with saline or °*P* < 0.05 $\beta arr2$ OE compared with GFP rats.



Fig. S4. (A) Transduction efficiency of β arr2-AAV in macaques. (B) Radiologand binding shows levels of D1 and D2 receptors in DAT-KO and DDD (chronic AMPT) mice. **P < 0.01 D1 binding from DAT compared with DDD.



Movie S1. Vertical activity/three-paw dyskinesia in DDD mice. DDD mice were placed in a glass jar after chronic L-DOPA treatment. Mice display persistent vertical positioning with rapid limb movements of three paws accompanied by tongue protrusions.

Movie S1

DNA C