S1.

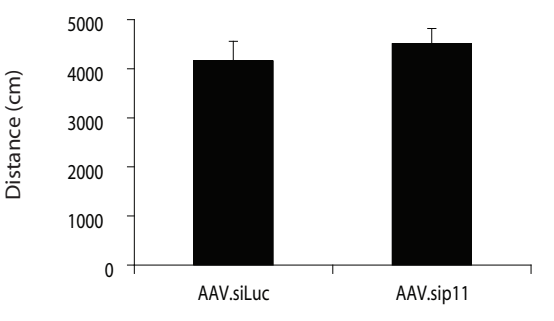

Fig S1. Locomotor activity in an open-field setting.
Mice receiving virus containing p11 RNAi in the NAcc traveled a similar distance during a 30-minute open field test as mice receiving control virus.

S2.

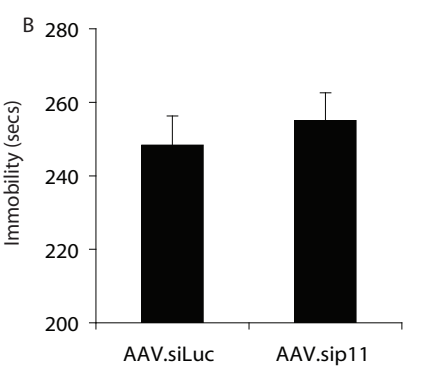

Fig S2. p11 RNAi virus in the mouse anterior cingulate.
(A) YFP immunohistochemistry confirms local transduction of virus in the anterior cingulate in coronal brain section of 3 month old male mouse injected with p11 siRNA virus that co-expresses YFP.
(B) TST reveals no effect of p11 gene transfer to the Acing on duration of immobility.

S3.

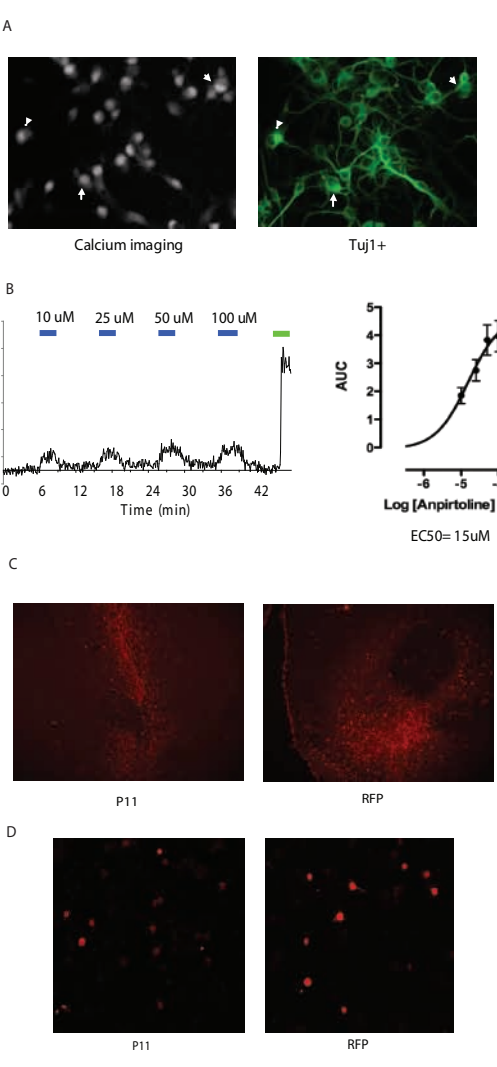

Fig. S3. Images of neonatal striatal sections and cultures after gene transfer and quantification of dose-dependent anpirtoline response.
(A) Fluorescent microscope images of striatal neurons loaded with the Fluor4 calcium-sensitive dye and exposed to anpirtoline (left panel). Immunostaining with Tuj1 confirms that these are neurons (right panel). Two arrowheads and one arrow mark specific neurons.
(B) Quantification of the dose-response of ventral striatal neurons to anpirtoline identifies the range of response and the EC50 at 15mM (Blue bar=anpirtoline, green bar=glutamate positive control)
(C) Immunostaining of sections of rat brain one week following intra-striatal injection of AAV.p11 (left) or AAV.RFP (right) at post-natal day 2.
(D) Primary cultures of ventral striatal neurons reveal efficient expression of either p11 (left) or control RFP (right) in neurons harvested 7-10 days after intrastriatal injection of AAV vectors in vivo on post-natal day 2.

S4.

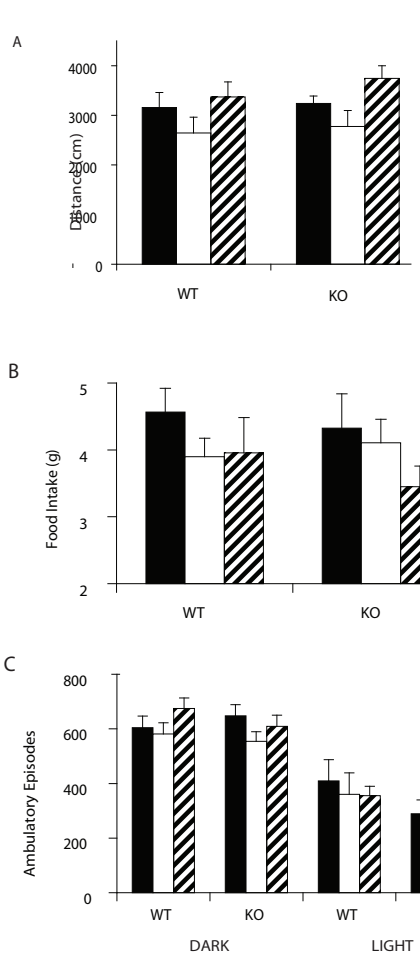

Fig S4. Motor and feeding behaviors of p11 KO mice and WT controls following gene therapy in the NAcc.
(A) Locomotor activity testing yielded no significant difference between groups.
(B) All experimental groups, regardless of viral treatment, consumed comparable amounts of food over the testing period.
(C) Transgenic p11 KO mice did not exhibit any disturbance of normal activity during their dark (awake) or light (sleep) cycles compared to WT control littermates, and this was unaffected by control or p11 virus injection in both groups of mice (closed bar=no surgery, open bar=control AAV YFP, hatched bar=AAVp11).

S5.

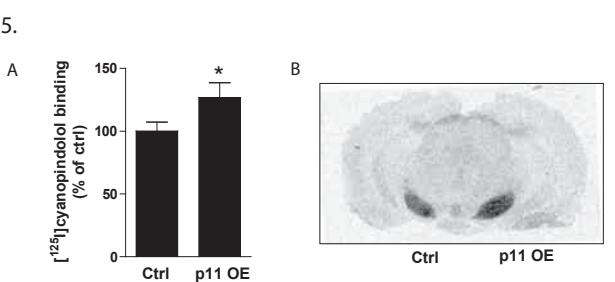

Fig S5. 5-HT1B receptor ligand autoradiography.
(A) Quantification of ligand binding in the subtantia nigra/VTA in each hemisphere in animals injected with AAV vectors expressing YFP (control hemisphere; ctrl) or p11 (p11 overexpressing hemisphere; p11 OE).
(B) Representative autoradiograph of radioligand binding in the substantia nigra/VTA.

Table S1. Characteristics of brain tissue specimens for human nucleus accumbens tissue used for protein analysis.
(PMI, post mortem interval; RIN, RNA integrity number)

	CONTROL			
age	PMI	RIN	pH	gender
16	16	8.3	6.63	M
19	20	9	6.64	M
20	21	8.2	6.8	M
31	16	8.1	6.923	M
32	22	9.7	6.9	M
43	15	6.1	6.89	M
49	12	9.5	6.61	M
49	24	9.5	6.825	M
51	9	8.2	6.864	M
52	20	5.3	6.6	F
57	7	8.3	6.7	M
59	14.3	8.4	6.8	M
60	20	8.5	6.63	M
65	11	8.4	6.84	F
77	13.4	8.9	n.d.	M
80	8	8.7	7.02	F
83	30	8.5	6.31	F
49.59	16.39	8.33	6.75	13M/4F

	DEPRESSION			
age	PMI	RIN	pH	gender
15	28	8.1	6.812	M
19	27	9.3	6.96	M
24	23	9.1	6.446	M
31	14	9	7.129	M
33	18	8.5	6.937	M
41	13	8.2	n.d	F
46	11	8.3	6.439	F
50	23	8.8	6.89	M
50	27	8.9	6.904	F
51	27	7.5	6.808	M
54	11.4	8.8	n.d.	M
54	6	8.9	6.835	M
57	16	6.6	6.44	F
57	9	7	n.d.	F
61	20	8.6	6.85	M
69	22	8.8	6.734	M
90	18	4.9	6.45	M
47.18	18.44	8.19	6.76	12M/5F