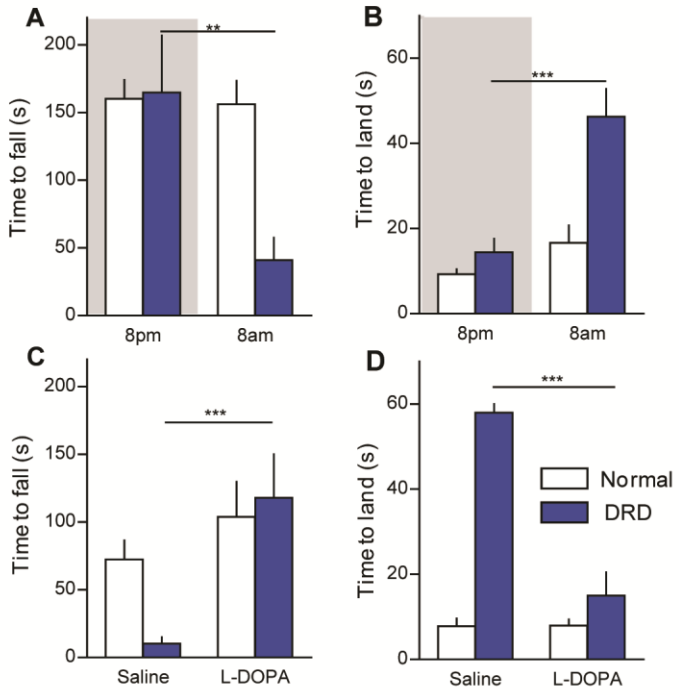
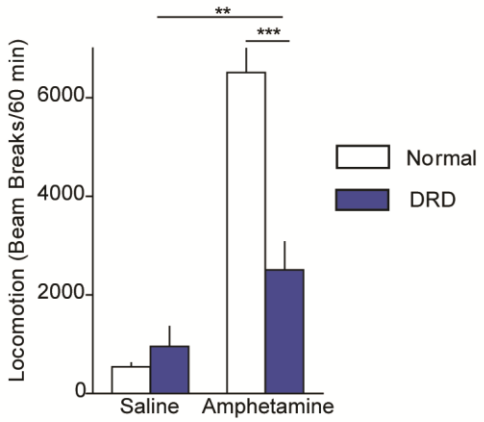


Supplementary Figure 1: Effect of time of day or L-DOPA treatment on rotarod and pole test performance. (A) Rotarod performance was assessed at 8pm and 8am (n=7-8/genotype). DRD mice exhibited poor performance at 8am but not at 8pm (genotype x time of day interaction effect; $F_{1,13}$=15.0, two-way repeated measures ANOVA, p<0.01, Tukey's *post hoc* analysis). (B) Pole test performance was similarly assessed at 8am and 8pm (n=7-8/genotype). DRD mice exhibited poor performance at 8am but not 8pm (genotype x time of day interaction effect; $F_{1,13}$=9.8, two-way repeated measures ANOVA, p<0.01, Tukey's *post hoc* analysis). (C) Rotarod performance was significantly impaired in DRD mice compared to normal mice after saline treatment, but improved significantly after L-DOPA treatment (n=4/condition; $F_{1,23}$=44.1, two-way ANOVA for day 1, p<0.01, Holm-Sidak *post hoc* analysis). (D) DRD mice exhibited a significant deficit in pole test performance compared to normal mice (n=6-7/condition) but L-DOPA treatment significantly improved pole test performance in DRD mice (genotype x treatment interaction effect; $F_{1,23}$=44.1, two-way ANOVA, p<0.001, Holm-Sidak *post hoc* analysis). Values represent mean ± SEM; **p<0.01 ***p<0.001.



Supplementary Figure 2: Effect of 5 mg/kg amphetamine or saline on locomotion in normal (n=8) and DRD mice (n=7) at 2pm. A significant dose x genotype interaction effect was observed ($F_{1,13}$=40.5, two-way repeated measures ANOVA, p<0.001) with amphetamine increasing locomotor activity in DRD mice (p<0.01, Student's *t* test *post hoc*) though less than normal mice (p<0.001, Student's *t* test *post hoc*). Values represent mean ± SEM; **p<0.01 ***p<0.001.

Supplementary Table 1. Regional monoamine concentration.

	DA (ng/mg protein)	DOPAC	DOPAC/DA	NE	5-HT	5-HIAA	5-HIAA/5-HT
Striatum							
Normal	72.1 ± 2.7	7.5 ± 0.3	0.1 ± 0.0	0.2 ± 0.0	3.1 ± 0.2	1.7 ± 0.1	0.6 ± 0.0
Heterozygous	60.1 ± 5.8*	5.7 ± 0.7**	0.1 ± 0.0	0.1 ± 0.0	3.5 ± 0.5	2.2 ± 0.3	0.6 ± 0.0
DRD	0.3 ± 0.1***	0.1 ± 0.0***	0.5 ± 0.1***	0.0 ± 0.0***	3.2 ± 0.2	3.4 ± 0.3***	1.0 ± 0.1***
Midbrain							
Normal	3.4 ± 0.4	1.0 ± 0.1	0.3 ± 0.0	6.0 ± 0.3	8.8 ± 0.4	2.7 ± 0.3	0.3 ± 0.0
Heterozygous	3.5 ± 0.8	0.7 ± 0.1*	0.2 ± 0.0	5.9 ± 0.4	10.0 ± 0.7	3.4 ± 0.3	0.3 ± 0.0
DRD	0.1 ± 0.0***	0.1 ± 0.0***	1.2 ± 0.2***	0.2 ± 0.1***	10.8 ± 0.3	5.4 ± 0.5***	0.5 ± 0.0***
Cortex							
Normal	0.5 ± 0.1	0.1 ± 0.0	0.4 ± 0.1	2.2 ± 0.1	2.6 ± 0.2	1.0 ± 0.1	0.4 ± 0.0
Heterozygous	0.4 ± 0.1	0.1 ± 0.0	0.4 ± 0.1	2.1 ± 0.2	2.9 ± 0.5	1.3 ± 0.2*	0.5 ± 0.1*
DRD	0.1 ± 0.0***	0.0 ± 0.0**	0.6 ± 0.1**	0.1 ± 0.0***	2.5 ± 0.3	1.7 ± 0.1***	0.7 ± 0.0***
Brainstem							
Normal	0.4 ± 0.0	0.3 ± 0.0	0.7 ± 0.0	7.0 ± 0.4	8.1 ± 0.7	5.7 ± 0.5	0.7 ± 0.1
Heterozygous	0.4 ± 0.0	0.2 ± 0.0*	0.5 ± 0.0*	7.4 ± 1.0	9.1 ± 1.7	7.0 ± 0.9	0.8 ± 0.1
DRD	0.3 ± 0.0	0.0 ± 0.0***	0.1 ± 0.0***	0.9 ± 0.1***	14.1 ± 1.6**	17.2 ± 1.4***	1.2 ± 0.1***
Hippocampus							
Normal	N.D.	N.D.	—	3.0 ± 0.3	2.8 ± 0.1	2.1 ± 0.1	0.8 ± 0.0
Heterozygous	N.D.	N.D.	—	2.7 ± 0.3	2.8 ± 0.3	2.2 ± 0.4	0.8 ± 0.1
DRD	N.D.	N.D.	—	0.3 ± 0.0***	3.5 ± 0.7	2.8 ± 0.2**	0.8 ± 0.1
Cerebellum							
Normal	N.D.	N.D.	—	3.2 ± 0.3	1.6 ± 0.2	1.0 ± 0.1	0.6 ± 0.1
Heterozygous	N.D.	N.D.	—	2.6 ± 0.3*	1.9 ± 0.3	1.1 ± 0.1	0.6 ± 0.1
DRD	N.D.	N.D.	—	0.0 ± 0.0***	1.3 ± 0.1	1.2 ± 0.0	1.0 ± 0.1***

Tissue concentrations of monoamines were measured by HPLC in normal (n=9), heterozygous (n=6), and DRD mice (n=6). Effects of genotype were observed for DA ($F_{2,18}$=151, p<0.001), DOPAC ($F_{2,18}$=144, p<0.001), NE ($F_{2,18}$=170, p<0.001), 5-HT ($F_{2,18}$=7.5, p<0.01), 5-HIAA ($F_{2,18}$=66.9, p<0.001), 5-HT/5-HIAA ($F_{2,18}$=31.2, p<0.001). There was a significant genotype x brain region interaction effect for DOPAC/DA ($F_{2,18}$=24.9, p<0.001). Each analyte was tested with two-way repeated measures ANOVA. Significant main effects were tested within each brain region with one-way ANOVA and Holm-Sidak *post hoc* analyses. Values represent mean ± SEM; *p<0.05, **p<0.01, ***p<0.001. N.D. = not detected.

Supplementary Table 2. Effect of L-DOPA or L-DOPS treatment on brain monoamines

	DA	NE	5-HT	5-HIAA	5-HIAA/5-HT
Striatum					
DRD +Saline	0.3 ± 0.1	N.D.	3.2 ± 0.2	3.4 ± 0.3	1.0 ± 0.1
DRD +L-DOPA	15.8 ± 1.1***	0.1 ± 0.1*	2.2 ± 0.2**	1.4 ± 0.1***	0.6 ± 0.1**
DRD +Vehicle	0.1 ± 0.1	0.1 ± 0.0	2.6 ± 0.1	2.1 ± 0.1	0.8 ± 0.0
DRD +L-DOPS	0.8 ± 0.1*	2.4 ± 1.3	2.3 ± 0.4	1.8 ± 0.3	0.8 ± 0.1
Midbrain					
DRD +Saline	0.1 ± 0.0	0.2 ± 0.1	10.8 ± 0.3	5.4 ± 0.5	0.5 ± 0.0
DRD +L-DOPA	5.2 ± 0.9***	2.7 ± 0.4***	12.6 ± 1.0	5.8 ± 0.4	0.5 ± 0.0
DRD +Vehicle	N.D.	0.3 ± 0.0	11.0 ± 0.6	4.5 ± 0.5	0.4 ± 0.0
DRD +L-DOPS	0.3 ± 0.0**	2.4 ± 0.3**	11.6 ± 0.6	4.4 ± 0.4	0.4 ± 0.0
Cortex					
DRD +Saline	0.1 ± 0.0	0.1 ± 0.0	2.5 ± 0.3	1.7 ± 0.1	0.7 ± 0.0
DRD +L-DOPA	2.2 ± 0.6***	2.1 ± 0.5***	2.3 ± 0.5	1.3 ± 0.1*	0.6 ± 0.1
DRD +Vehicle	N.D.	N.D.	7.0 ± 2.0	0.9 ± 0.1	0.9 ± 0.1
DRD +L-DOPS	N.D.	0.7 ± 0.0***	8.5 ± 1.0	0.7 ± 0.0	0.7 ± 0.0
Brainstem					
DRD +Saline	0.3 ± 0.0	0.9 ± 0.1	14.1 ± 1.6	17.2 ± 1.4	1.2 ± 0.1
DRD +L-DOPA	2.4 ± 0.2***	4.7 ± 0.4***	8.1 ± 0.7*	7.3 ± 0.8***	0.9 ± 0.0*
DRD +Vehicle	0.1 ± 0.1	0.4 ± 0.4	5.8 ± 1.0	5.9 ± 0.9	1.1 ± 0.2
DRD +L-DOPS	0.2 ± 0.1	1.0 ± 0.3	6.8 ± 0.5	5.6 ± 1.1	0.8 ± 0.1
Hippocampus					
DRD +Saline	N.D.	0.3 ± 0.0	3.5 ± 0.7	2.8 ± 0.2	0.8 ± 0.1
DRD +L-DOPA	N.D.	1.8 ± 0.2***	3.4 ± 0.1	2.9 ± 0.2	0.8 ± 0.1
DRD +Vehicle	N.D.	0.2 ± 0.1	6.6 ± 0.3	3.0 ± 0.4	0.5 ± 0.1
DRD +L-DOPS	N.D.	0.7 ± 0.1*	7.4 ± 1.6	2.7 ± 0.3	0.4 ± 0.1
Cerebellum					
DRD +Saline	N.D.	N.D.	1.3 ± 0.1	1.2 ± 0.0	0.8 ± 0.1
DRD +L-DOPA	N.D.	2.5 ± 0.7***	1.6 ± 0.4	0.8 ± 0.2*	0.5 ± 0.0**
DRD +Vehicle	N.D.	0.1 ± 0.0	3.9 ± 0.7	0.9 ± 0.2	0.2 ± 0.1
DRD +L-DOPS	N.D.	0.5 ± 0.0***	3.0 ± 0.5	0.4 ± 0.1	0.1 ± 0.0

Tissue concentrations of DA and NE were measured by HPLC 45 min after 10 mg/kg L-DOPA (+2.5 mg/kg benserazide) (n=4) or saline (n=6) or 5 hr after 1 g/kg L-DOPS (+0.25 g/kg benserazide) (n=4) or L-DOPS vehicle (HCl/NaOH) (n=3). There was an effect of L-DOPA on DA concentration ($F_{1,8}$=260, p<0.001) and NE concentration ($F_{1,8}$=789, p<0.001) in all regions. There was an effect of L-DOPS treatment on NE concentration ($F_{1,5}$=8.7, p<0.05), and DA concentration in striatum and midbrain ($F_{1,5}$=14.9, p<0.05). Each analyte was tested with two-way repeated measures ANOVA. Significant main effects were tested *post hoc* within each brain region with Student's *t* tests. Values represent mean ± SEM; *p<0.05, **p<0.01, ***p<0.001. N.D. = not detected.

Supplementary Table 3. DAR mRNA expression.

	D1DAR	D2DAR	D3DAR
Striatum			
Normal	6.1 ± 0.3	5.8 ± 0.3	12.2 ± 0.4
DRD	5.4 ± 0.4	5.1 ± 0.5	12.3 ± 0.7
Midbrain			
Normal	not tested	5.9 ± 0.3	not tested
DRD		5.6 ± 0.2	

Tissue mRNA abundance was determined with qRT-PCR and normalized to 18s rRNA. No difference between genotypes was observed for any mRNA ($p>0.1$, Student's *t* tests for each measure). Values represent mean ± SEM.

Supplementary Table 4. DAR binding studies in normal and DRD mice

	[^{3}H]SCH 23390		[^{3}H]spiperone	
	B_{max} (fmol/mg)	K_d (nM)	B_{max}	K_d
Normal	62.0 ± 12.0	1.4 ± 0.6	12.9 ± 4.4	0.26 ± 0.1
DRD	62.4 ± 3.3	1.6 ± 0.1	13.1 ± 4.0	0.22 ± 0.1

Striatal densities (B_{max}) and affinities (K_d) of D1DARs and D2DARs were determined using [^{3}H]SCH 23390 and [^{3}H]spiperone, respectively (n=6/genotype). No differences between genotypes were observed in D1DAR or D2DAR density or affinity ($p>0.1$, Student's *t* tests for each measure). Values represent mean ± SEM.

Supplementary Video 1: This video provides a representative example of typical hindlimb movements exhibited by DRD mice. Ambulation is limited, with exaggerated flexion of the trunk. The frequent jerky movements of the trunk and neck reflect normal sniffing behavior and are not abnormal. However, the right rear limb is held in a flexed posture, which dynamically changes, with intermittent abnormal flaring of the toes. As the animal turns away from the camera, the abnormal body position becomes more obvious, and it becomes clearer that the right rear limb is not in contact with the floor. At one point, the abnormal right rear limb position becomes much

worse. Then, the animal turns towards the left, and there is abnormal flexed posture of the left rear limb instead.

Supplementary Video 2: This video clip provides a representative example of action-induced worsening of the abnormal movements in DRD mice. The animal ambulates quickly across the cage, and the only obvious abnormality is excessive truncal flexion and short stride length. When the animal defends itself from a stick, it develops transient action-induced abnormal flexion postures of the forelimbs and paws, along with twisting of the neck and trunk to the left. After a brief period of rest, these abnormal postures abate.