

S3_Table: Three-way ANOVA showing the effect of chronic CBD on CB₁R, CB₂R, and GPR55 levels in Tat tg mice.

Brain region	Receptors / Enzymes	Sex effect <i>F, p</i>	Genotype effect <i>F, p</i>	Treatment effect <i>F, p</i>	Sex x Genotype <i>F, p</i>	Sex x Treatment <i>F, p</i>	Genotype x Treatment <i>F, p</i>	Sex x Genotype x Treatment <i>F, p</i>
PFC	CB ₁ R	$F(1,54) = 74.6$ $p < 0.001$ F < M	$F(1,54) = 12.3$ $p < 0.001$ Tat(-) > Tat(+)	$F(1,54) = 0.04$ $p = 0.82$	$F(1,54) = 0.002$ $p = 0.96$	$F(1,54) = 0.73$ $p = 0.39$	$F(1,54) = 2.74$ $p = 0.10$	$F(1,54) = 2.79$ $p = 0.10$ (42%)
	CB ₂ R	$F(1,54) = 35.7$ $p < 0.001$ F < M	$F(1,54) = 3.47$ $p = 0.06$	$F(1,54) = 0.22$ $p = 0.63$	$F(1,54) = 13.0$ $p < 0.001$	$F(1,54) = 0.65$ $p = 0.42$	$F(1,54) = 4.25$ $p = 0.04$	$F(1,54) = 1.46$ $p = 0.23$ (24%)
	GPR55	$F(1,54) = 161.1$ $p < 0.001$ F < M	$F(1,54) = 2.60$ $p = 0.11$	$F(1,54) = 0.71$ $p = 0.40$	$F(1,54) = 9.48$ $p = 0.003$	$F(1,54) = 0.53$ $p = 0.46$	$F(1,54) = 36.1$ $p < 0.001$	$F(1,54) = 19.86$ $p < 0.001$ (99%)
	FAAH	$F(1,54) = 1.39$ $p = 0.24$	$F(1,54) = 27.20$ $p < 0.001$ Tat(-) < Tat(+)	$F(1,54) = 0.08$ $p = 0.77$	$F(1,54) = 6.66$ $p = 0.01$	$F(1,54) = 0.13$ $p = 0.72$	$F(1,54) = 4.83$ $p = 0.03$	$F(1,54) = 2.34$ $p = 0.13$ (36%)
	MAGL	$F(1,54) = 10.41$ $p = 0.002$ F < M	$F(1,54) = 0.66$ $p = 0.41$	$F(1,54) = 1.79$ $p = 0.18$	$F(1,54) = 0.98$ $p = 0.32$	$F(1,54) = 0.44$ $p = 0.83$	$F(1,54) = 0.35$ $p = 0.55$	$F(1,54) = 0.76$ $p = 0.38$ (15%)
Hip	CB ₁ R	$F(1,52) = 120.1$ $p < 0.001$ F < M	$F(1,52) = 0.36$ $p = 0.54$	$F(1,52) = 2.62$ $p = 0.11$	$F(1,52) = 0.82$ $p = 0.36$	$F(1,52) = 4.67$ $p = 0.03$	$F(1,52) = 0.62$ $p = 0.43$	$F(1,52) = 0.46$ $p = 0.49$ (11%)
	CB ₂ R	$F(1,52) = 2.87$ $p = 0.09$	$F(1,52) = 5.99$ $p = 0.01$	$F(1,52) = 0.76$ $p = 0.38$	$F(1,52) = 26.$ $p < 0.001$	$F(1,52) = 1.61$ $p = 0.20$	$F(1,52) = 0.00$ $p = 0.98$	$F(1,52) = 0.80$ $p = 0.37$ (16%)
	GPR55	$F(1,52) = 3.33$ $p = 0.073$	$F(1,52) = 1.72$ $p = 0.19$	$F(1,52) = 1.92$ $p = 0.17$	$F(1,52) = 1.81$ $p = 0.18$	$F(1,52) = 1.98$ $p = 0.16$	$F(1,52) = 2.33$ $p = 0.13$	$F(1,52) = 2.35$ $p = 0.13$ (37%)

	FAAH	$F(1,52) = 98.5$ $p < 0.001$	$F(1,52) = 0.63$ $p = 0.42$	$F(1,52) = 1.23$ $p = 0.27$	$F(1,52) = 45.4$ $p < 0.001$	$F(1,52) = 0.48$ $p = 0.48$	$F(1,52) = 4.30$ $p = 0.04$	$F(1,52) = 0.99$ $p = 0.32$ (19%)
	MAGL	$F(1,52) = 21.1$ $p < 0.001$	$F(1,52) = 13.3$ $p < 0.001$	$F(1,52) = 3.54$ $p = 0.06$	$F(1,52) = 20.5$ $p < 0.001$	$F(1,52) = 2.62$ $p = 0.11$	$F(1,52) = 0.94$ $p = 0.33$	$F(1,52) = 3.68$ $p = 0.06$ (54%)
Amg	CB ₁ R	$F(1,54) = 0.22$ $p = 0.64$	$F(1,54) = 2.34$ $p = 0.13$	$F(1,54) = 0.14$ $p = 0.70$	$F(1,54) = 91.57$ $p < 0.001$	$F(1,54) = 0.33$ $p = 0.56$	$F(1,54) = 0.22$ $p = 0.63$	$F(1,54) = 3.26$ $p = 0.077$ (47%)
	CB ₂ R	$F(1,54) = 6.94$ $p = 0.01$ F < M	$F(1,54) = 5.40$ $p = 0.02$ Tat(-) > Tat(+)	$F(1,54) = 5.87$ $p = 0.01$ Vehicle < CBD	$F(1,54) = 9.27$ $p = 0.004$	$F(1,54) = 12.00$ $p = 0.001$	$F(1,54) = 5.73$ $p = 0.02$	$F(1,54) = 0.24$ $p = 0.622$ (8%)
	GPR55	$F(1,54) = 38.77$ $p < 0.001$ F < M	$F(1,54) = 163.5$ $p < 0.001$ Tat(-) > Tat(+)	$F(1,54) = 1.01$ $p = 0.31$	$F(1,54) = 114.0$ $p < 0.001$	$F(1,54) = 4.13$ $p = 0.04$	$F(1,54) = 0.82$ $p = 0.36$	$F(1,54) = 0.69$ $p = 0.40$ (14%)
	FAAH	$F(1,54) = 0.48$ $p = 0.49$	$F(1,54) = 16.14$ $p < 0.001$ Tat(-) > Tat(+)	$F(1,54) = 0.07$ $p = 0.78$	$F(1,54) = 6.81$ $p = 0.01$	$F(1,54) = 6.73$ $p = 0.01$	$F(1,54) = 1.75$ $p = 0.19$	$F(1,54) = 1.12$ $p = 0.29$ (19%)
	MAGL	$F(1,54) = 107.8$ $p < 0.001$ F > M	$F(1,54) = 10.64$ $p = 0.002$ Tat(-) > Tat(+)	$F(1,54) = 1.09$ $p = 0.30$	$F(1,54) = 22.32$ $p < 0.001$	$F(1,54) = 0.42$ $p = 0.51$	$F(1,54) = 0.07$ $p = 0.78$	$F(1,54) = 0.21$ $p = 0.64$ (7%)
BS	CB ₁ R	$F(1,54) = 54.03$ $p < 0.001$ F < M	$F(1,54) = 0.37$ $p = 0.54$	$F(1,54) = 0.99$ $p = 0.32$	$F(1,54) = 0.76$ $p = 0.38$	$F(1,54) = 0.52$ $p = 0.47$	$F(1,54) = 0.91$ $p = 0.34$	$F(1,54) = 0.04$ $p = 0.83$ (5%)
	CB ₂ R	$F(1,54) = 39.5$ $p < 0.001$ F < M	$F(1,54) = 6.15$ $p = 0.01$ Tat(-) > Tat(+)	$F(1,54) = 0.96$ $p = 0.33$	$F(1,54) = 3.10$ $p = 0.08$	$F(1,54) = 0.02$ $p = 0.87$	$F(1,54) = 1.00$ $p = 0.32$	$F(1,54) = 1.80$ $p = 0.18$ (29%)
	GPR55	$F(1,54) = 120.4$ $p < 0.001$ F > M	$F(1,54) = 0.29$ $p = 0.59$	$F(1,54) = 0.02$ $p = 0.88$	$F(1,54) = 14.5$ $p < 0.001$	$F(1,54) = 2.64$ $p = 0.11$	$F(1,54) = 0.08$ $p = 0.77$	$F(1,54) = 3.96$ $p = 0.05$ (55%)

	FAAH	$F(1,54) = 15.25$ $p < 0.001$ F < M	$F(1,54) = 42.2$ $p < 0.001$ Tat(-) > Tat(+)	$F(1,54) = 1.71$ $p = 0.19$	$F(1,54) = 0.48$ $p = 0.49$	$F(1,54) = 0.57$ $p = 0.45$	$F(1,54) = 9.17$ $p = 0.004$	$F(1,54) = 2.90$ $p = 0.09$ (43%)
	MAGL	$F(1,54) = 0.70$ $p = 0.40$	$F(1,54) = 29.40$ $p < 0.001$ Tat(-) > Tat(+)	$F(1,54) = 2.59$ $p = 0.11$	$F(1,54) = 2.86$ $p = 0.09$	$F(1,54) = 4.93$ $p = 0.03$	$F(1,54) = 4.00$ $p = 0.05$	$F(1,54) = 5.77$ $p = 0.02$ (71%)
SC	CB ₁ R	$F(1,54) = 12.98$ $p < 0.001$ F < M	$F(1,54) = 0.23$ $p = 0.62$	$F(1,54) = 2.03$ $p = 0.15$	$F(1,54) = 0.002$ $p = 0.96$	$F(1,54) = 1.01$ $p = 0.31$	$F(1,54) = 0.00$ $p = 0.99$	$F(1,54) = 0.21$ $p = 0.64$ (7%)
	CB ₂ R	$F(1,54) = 41.05$ $p < 0.001$ F < M	$F(1,54) = 9.22$ $p = 0.004$ Tat(-) > Tat(+)	$F(1,54) = 3.95$ $p = 0.05$ Vehicle < CBD	$F(1,54) = 30.73$ $p < 0.001$	$F(1,54) = 2.28$ $p = 0.13$	$F(1,54) = 16.39$ $p < 0.001$	$F(1,54) = 8.00$ $p < 0.007$ (85%)
	GPR55	$F(1,54) = 14.64$ $p < 0.001$ F < M	$F(1,54) = 0.116$ $p = 0.73$	$F(1,54) = 0.10$ $p = 0.74$	$F(1,54) = 2.65$ $p = 0.10$	$F(1,54) = 0.004$ $p = 0.94$	$F(1,54) = 9.84$ $p = 0.003$	$F(1,54) = 2.55$ $p = 0.11$ (39%)
	FAAH	$F(1,54) = 1.18$ $p = 0.28$	$F(1,54) = 20.82$ $p < 0.001$ Tat(-) > Tat(+)	$F(1,54) = 0.23$ $p = 0.63$	$F(1,54) = 12.63$ $p < 0.001$	$F(1,54) = 2.02$ $p = 0.16$	$F(1,54) = 2.27$ $p = 0.13$	$F(1,54) = 13.30$ $p < 0.001$ (96%)
	MAGL	$F(1,54) = 0.67$ $p = 0.41$	$F(1,54) = 14.40$ $p < 0.001$ Tat(-) > Tat(+)	$F(1,54) = 0.02$ $p = 0.87$	$F(1,54) = 0.03$ $p = 0.85$	$F(1,54) = 3.48$ $p = 0.06$	$F(1,54) = 0.005$ $p = 0.94$	$F(1,54) = 3.57$ $p = 0.06$ (51%)

PFC, prefrontal cortex; Amg, amygdala; BS, brainstem, CB₁R, cannabinoid receptor type 1; CB₂R, cannabinoid receptor type 2; FAAH, fatty acid amide hydrolase; MAGL, monoacylglycerol lipase; SC, spinal cord.