

Supplementary Materials: Effects of Chronic 100 mg/kg Cannabidiol Treatment in Male Double Transgenic *APP_{Swe}/PS1ΔE9* Mice

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Supplementary Table S1. Western blot results for IBA1 and PPAR γ isoforms.

Treatment Genotype	Vehicle		CBD	
	WT	<i>APP/PS1</i>	WT	<i>APP/PS1</i>
IBA1	1.2 $\pm$ 0.2	1.3 $\pm$ 0.2	1.5 $\pm$ 0.3	1.9 $\pm$ 0.6
PPAR γ 1	0.6 $\pm$ 0.2	0.6 $\pm$ 0.1	0.4 $\pm$ 0.1	0.4 $\pm$ 0.1
PPAR γ 2	0.8 $\pm$ 0	0.9 $\pm$ 0.1	0.7 $\pm$ 0.1	0.8 $\pm$ 0.1

Cortical protein levels of IBA1 and PPAR γ isoforms for male *APP_{Swe}/PS1ΔE9* (*APP/PS1*) transgenic mice and non-transgenic wild type-like (WT) littermates treated with 100 mg/kg cannabidiol (CBD) or vehicle (WT-VEH *n* = 13; *APP/PS1*-VEH *n* = 11; WT-CBD *n* = 13; *APP/PS1*-CBD *n* = 10). Data are presented as mean $\pm$ SEM.

Supplementary Table S2. Statistical outcomes for all behavioural and molecular tests.

	Genotype (<i>p</i> value)	Treatment (<i>p</i> value)	Genotype x Treatment (<i>p</i> value)
Elevated plus maze			
Total distance travelled [m]	0.553	0.932	0.747
Distance in the open arms [%]	0.482	0.415	0.887
Time spent in the open arms [%]	0.679	0.592	0.676
Time spent in the first half of the open arms [%]	0.339	0.761	0.813
Time spent in the second half of the open arms [%]	0.077	0.123	0.193
Novel object recognition task			
Time spent <i>nosing</i> the novel object [%]	0.833	0.389	0.849
Social preference test			
Time spent in mouse chamber [%]	0.835	0.045	0.748
Time spent in novel mouse chamber [%]	0.47	0.348	0.909
Time spent <i>nosing</i> the novel mouse [%]	0.548	0.829	0.338
Resident-intruder task			
Total time spent interacting with standard opponent [s]	0.701	0.601	0.903
Time spent exhibiting aggressive behaviours [s]	0.032	0.445	0.65
Time spent exhibiting socio-positive behaviours [s]	0.001	0.638	0.406
Time spent <i>sniffing</i> [s]	< 0.0001	0.869	0.883
Time spent <i>anogenital sniffing</i> [s]	0.059	0.3	0.043
Time spent <i>following</i> [s]	0.677	0.287	0.079
Time spent <i>wrestling</i> [s]	0.024	0.614	0.828
Time spent <i>tail rattling</i> [s]	0.631	0.032	0.413
Time spent <i>aggressive grooming</i> [s]	0.247	0.493	0.509
Frequency of <i>sniffing</i> [n]	0.115	0.92	0.381
Frequency of <i>anogenital sniffing</i> [n]	0.048	0.356	0.713
Frequency of <i>following</i> [n]	0.677	0.287	0.341
Frequency of <i>wrestling</i> [n]	0.037	0.792	0.714
Frequency of <i>tail rattling</i> [n]	0.397	0.076	0.504
Frequency of <i>aggressive grooming</i> [n]	0.127	0.679	0.362

Neuroinflammation-relevant markers			
TNF- α hippocampal levels	0.017	0.091	0.919
IL-1 β hippocampal levels	0.022	0.254	0.909
IBA1 cortical levels	0.472	0.31	0.188
PPAR γ 1 cortical levels	0.965	0.074	0.789
PPAR γ 2 cortical levels	0.273	0.19	0.951
Neurodegeneration-relevant markers			
proBDNF cortical levels	0.056	0.883	0.02
mature BDNF cortical levels	0.756	0.378	0.066

P-values for all two-way ANOVAs conducted for behavioural tests, western blots and ELISAs for male *APP^{Swe}/PS1 Δ E9* (*APP/PS1*) transgenic mice and non-transgenic wild type-like (WT) littermates treated with 100 mg/kg cannabidiol (CBD) or vehicle are shown; significant results ($p < 0.05$) are highlighted in bold.