Supplementary Information

β-Caryophyllene, a CB2-Selective phytocannabinoid, Differentially Modulates Attention and Inhibitory Control in Low- and High-Performing Young and Aged Mice

Williams MN, Patel NT, Fleischel EJ, Wimmer ME, Ward SJ, Parikh V

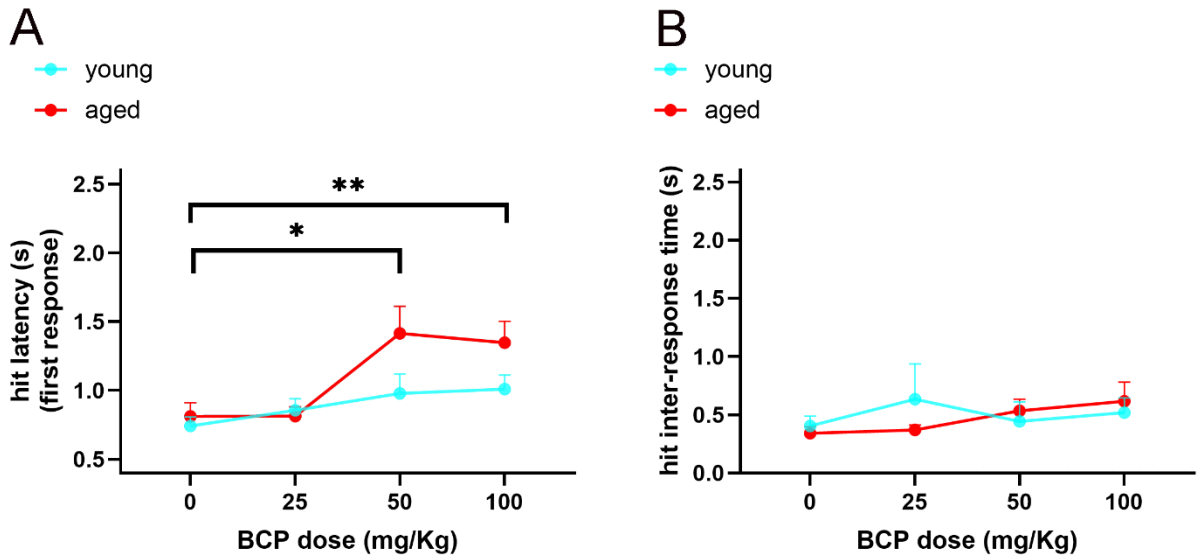

Figure S1. Hit latencies for the first lever press response in young and aged mice show higher reaction times for 50mg and 100mg/Kg BCP doses (A). However, inter-response times between two lever presses for hits did not differ across BCP doses for both young and aged mice. *, ** p<.05, .01

Assessment of locomotor activity:

Another cohort of adult male C57BL/6 mice (Taconic Biosciences, USA; 6–8 weeks old at arrival) were housed in a temperature- and humidity-controlled vivarium on a reverse 12:12 h light/dark cycle with ad libitum access to food and water and were allowed to habituate for at least 2 weeks prior to experimentation. On the test day, mice received an intraperitoneal injection of β-caryophyllene (BCP; dissolved in cremophor-based vehicle, 1:1:19 ETOH, Cremophor, saline) or vehicle alone and were placed in the locomotor activity chambers (Omnitech SuperFlex Open Field System system, Columbus Ohio) 30 min later. Ambulatory activity was recorded in 5-min bins over a 30-min session using the manufacturer's software. Ambulatory counts were summed across bins and analyzed using two-way ANOVA (treatment × time) in GraphPad Prism 11, GraphPad Software, San Diego, CA), with n = 8 mice per group; no significant main effects or interaction were detected. $F(1,84)=1.893$ for treatment, $F(5,84)=.6159$ for time, and $F(5,84)=.4933$ for interaction; all $p>.05$(see Suppl fig S2 below).

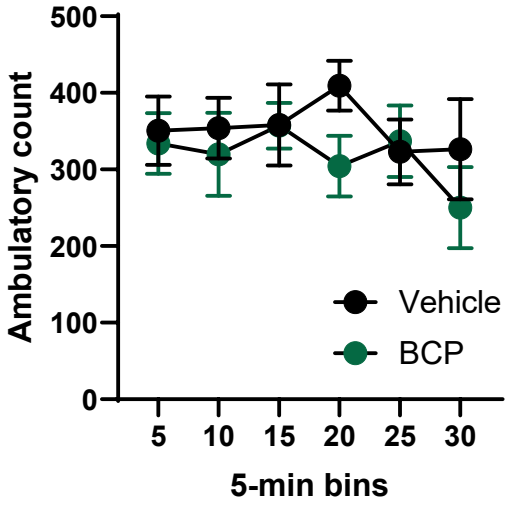

Figure S2. Effect of BCP on locomotor activity in male mice. Vehicle or 30 mg/kg BCP was administered 30 min prior to exposure to the locomotor chambers. Ambulatory counts were recorded in 5 min bins for 30 min. Two-way ANOVA revealed no main effects and no interaction, n=8/group.

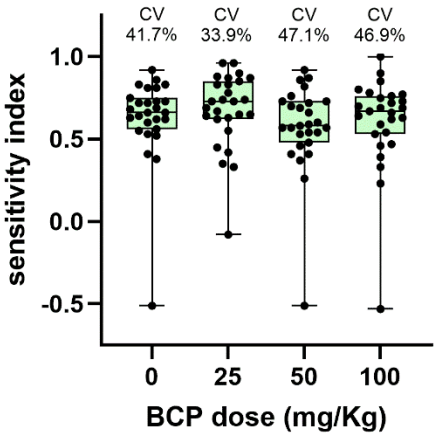

Figure S3. Dispersion in Sensitivity Index measure depicting inter-individual variability in GNG task performance at baseline (BCP 0 or vehicle) and across three BCP doses (25, 50, and 100mg/Kg). The CV ranged from 33.9% to 47.1%.

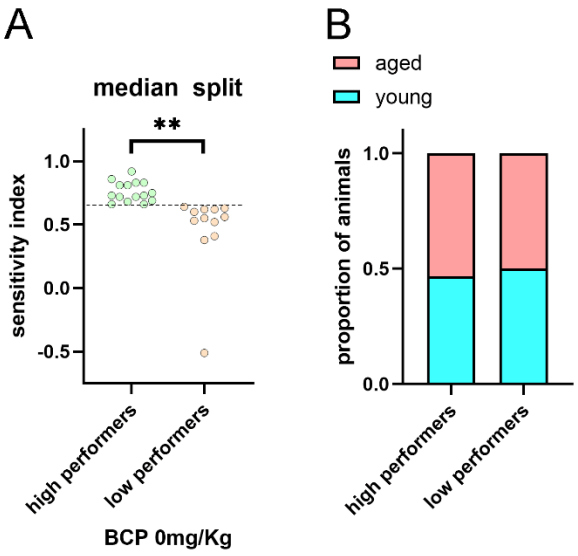

Figure S4. Median split on baseline sensitivity index (vehicle or BCP 0mg/Kg) categorizing animals as high- and low-performers (A). Stacked bars show the proportion of young and aged animal in each performer category remained comparable (χ^2=.03, p-.86). **, p<.01.

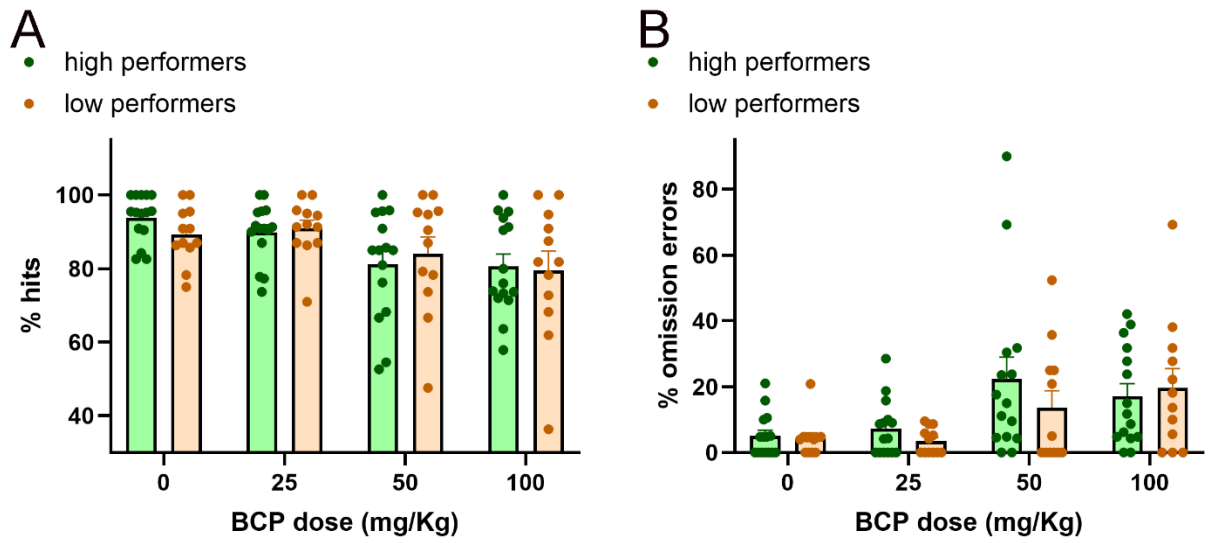

Figure S5. Box plots with individual data points depicting go-trial performance as % hits (A) and % omission errors (B) from high- and low-performers across different BCP doses.

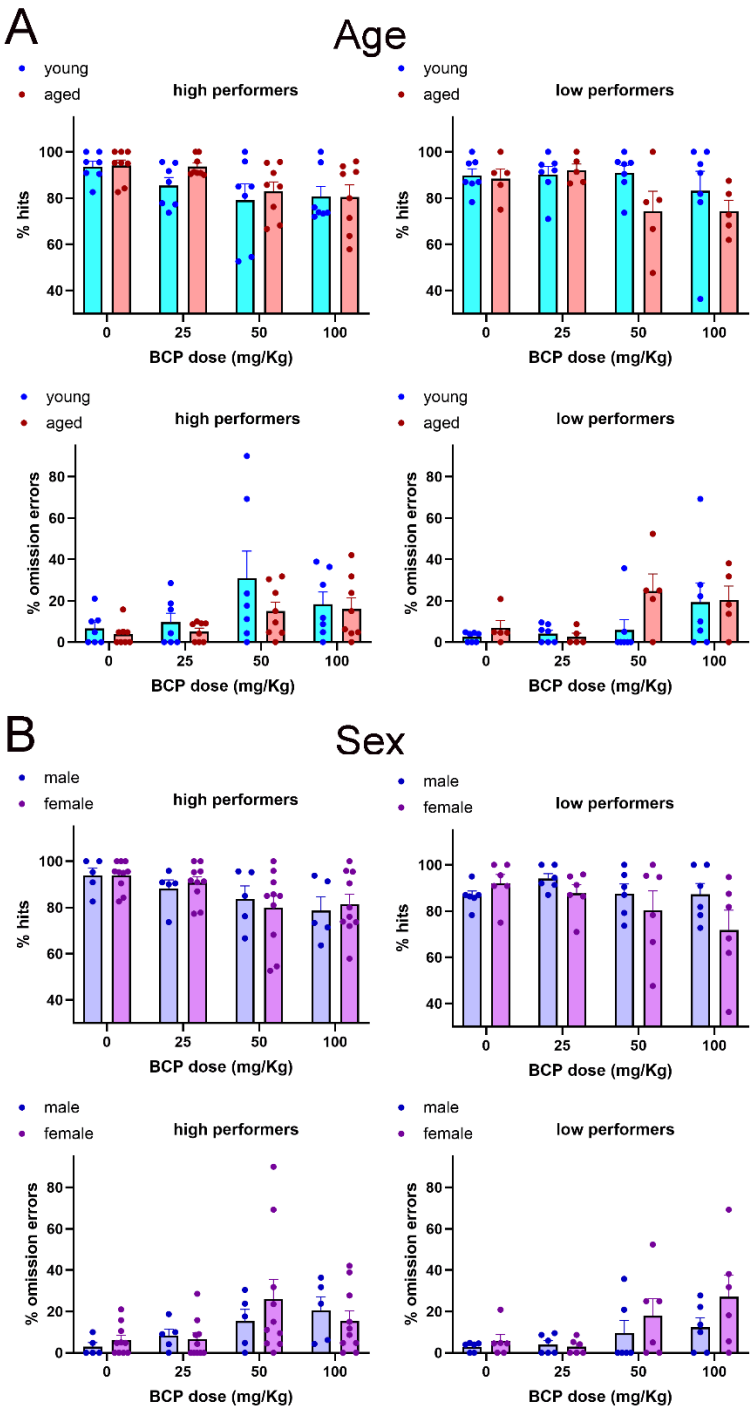

Figure S6. Box plots with individual data points for go-trial performance from high- and low-performers across different BCP doses disaggregated by age (A) and sex (B).

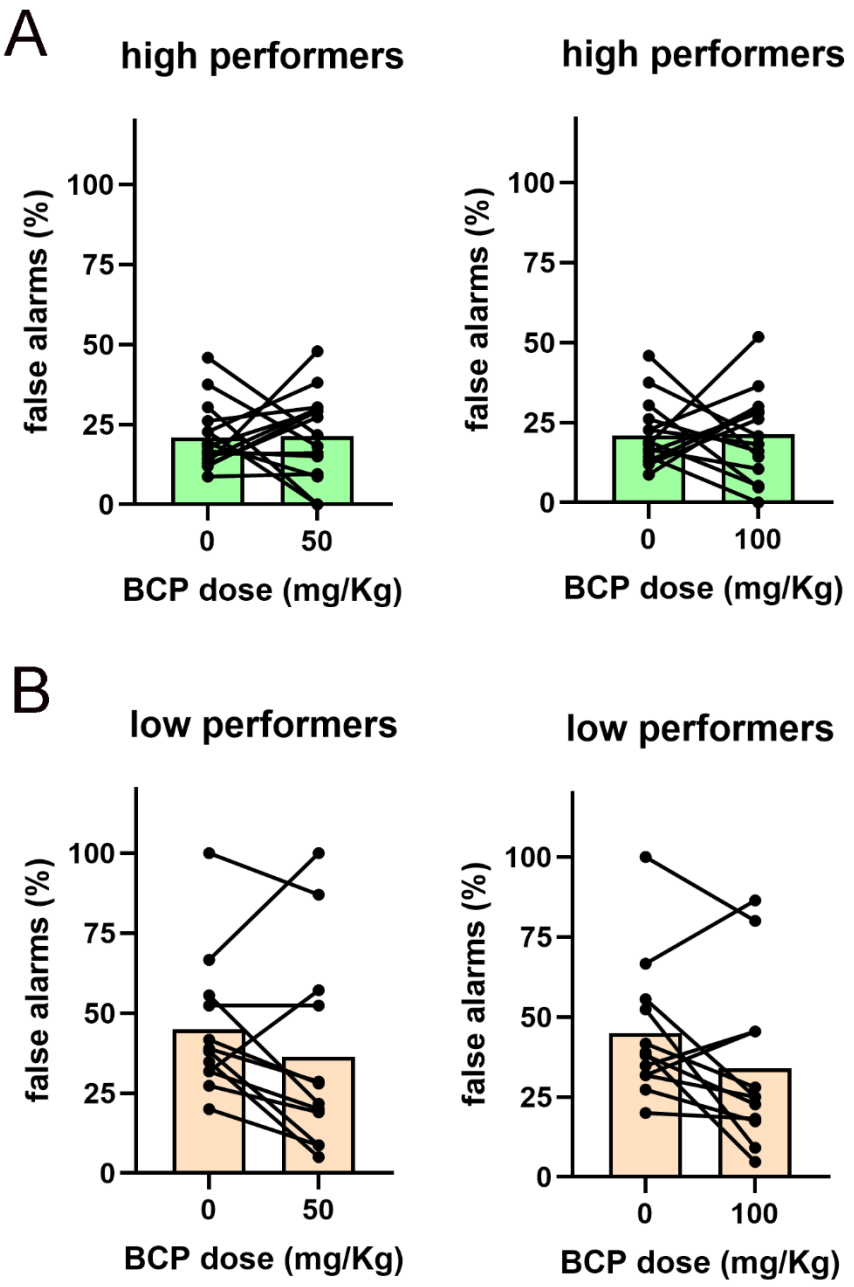

Figure S7. Box plots with individual data points depicting no go-trial performance as % false alarms for comparing vehicle (BCP 0mg/Kg) with BCP 50mg/Kg (A) and BCP 100mg/Kg (B) doses for high-performers (A) and low-performers (B), respectively.