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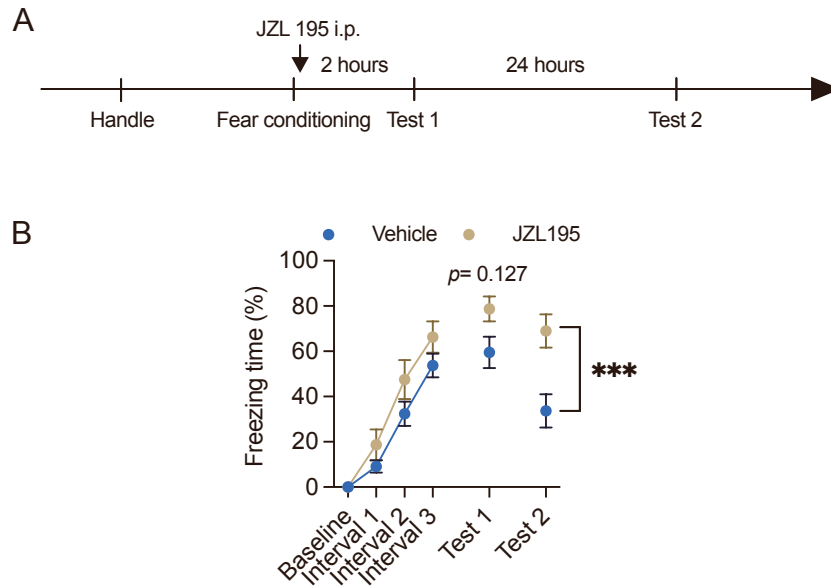
## **Supplemental information**

### **Inhibition of cannabinoid degradation enhances hippocampal contextual fear memory and exhibits anxiolytic effects**

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Supplemental information

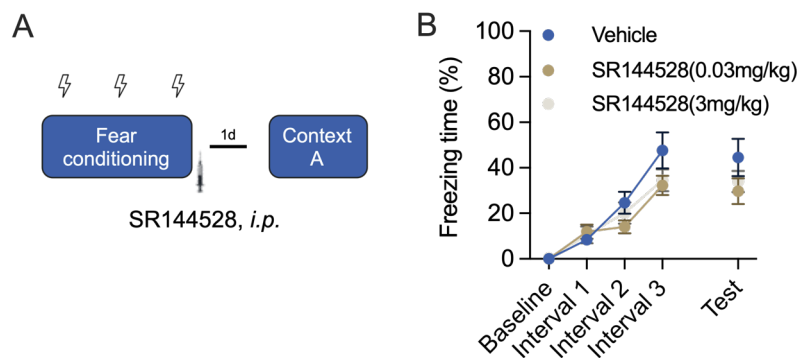
Figure S1-S3.



Supplemental Figure S1, related to Figure 1 - JZL195 treatment has no influence on short term fear memory

(A) The procedure of short term fear memory test ( $n_{\text{Vehicle}}=12$ ,  $n_{\text{JZL195}}=10$ ).

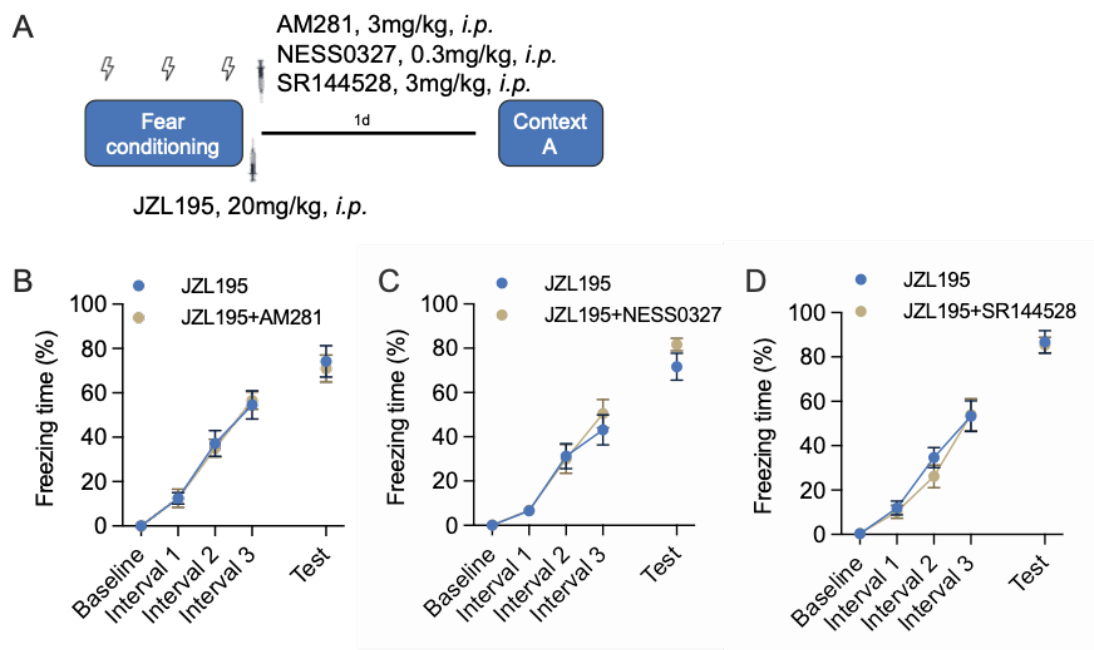
(B) The freezing time of mice during contextual fear conditioning, Test 1 and Test 2 (Two-way ANOVA, the main effect of time:  $F_{(5,95)}=76.280$ ,  $p<0.0001$ ; the main effect of Vehicle vs. JZL195:  $F_{(1,19)}=6.379$ ,  $p=0.021$ ; the interaction effect:  $F_{(5,95)}=3.597$ ,  $p=0.005$ ; Sidak's posthoc test of Vehicle vs. JZL195 at Test 1:  $p=0.127$ , at Test 2:  $p=0.0003$ ).



Supplemental Figure S2, related to Figure 7 - The effect of SR144528 on contextual fear memory consolidation.

(A) The procedure of contextual fear conditioning ( $n=10/\text{group}$ ).

(B) Different doses of SR144528 show no effect on the freezing time of mice (Two-way ANOVA, the main effect of intervals:  $F_{(4,108)}=60.380$ ,  $p<0.001$ ; the main effect of doses:  $F_{(2,27)}=1.489$ ,  $p=0.244$ ; the interaction effect:  $F_{(8,108)}=1.622$ ,  $p=0.127$ ; Sidak's posthoc test of Vehicle vs. SR144528 (0.03mg/kg) at Test:  $p=0.055$ , Vehicle vs. SR144528 (3mg/kg) at Test:  $p=0.226$ , SR144528 (0.03mg/kg) vs. SR144528 (3mg/kg) at Test:  $p=0.781$ ).



**Supplemental Figure S3, related to Figure 7 - Neither CB1R nor CB2R suppressed the promoted contextual fear memory induced by JZL195.**

(A) The procedure of behavioral test.

(B) The freezing time of mice during fear conditioning and contextual test (Two-way ANOVA, the main effect of intervals:  $F_{(4,68)}=119.00$ ,  $p<0.0001$ ; the main effect of JZL195 (n=10) vs. JZL195+AM281 (n=9):  $F_{(1,17)}=0.022$ ,  $p=0.885$ ; the interaction effect:  $F_{(4,68)}=0.136$ ,  $p=0.969$ ; Sidak's posthoc test of JZL195 vs. JZL195+AM281 at Test:  $p=0.993$ ).

(C) Freezing time of mice during fear conditioning and contextual test (Two-way ANOVA, the main effect of intervals:  $F_{(4,68)}=123.900$ ,  $p<0.0001$ ; the main effect of JZL195 (n=10) vs. JZL195+NESS (n=9):  $F_{(1,17)}=0.585$ ,  $p=0.455$ ; the interaction effect:  $F_{(4,68)}=0.818$ ,  $p=0.518$ ; Sidak's posthoc test of JZL195 vs. JZL195+NESS0327 at Test:  $p=0.512$ ).

(D) Freezing time of mice during fear conditioning and contextual test (Two-way ANOVA, the main effect of intervals:  $F_{(4,72)}=180.900$ ,  $p<0.0001$ ; the main effect of JZL195 (n=10) vs. JZL195+SR (n=10):  $F_{(1,18)}=0.229$ ,  $p=0.634$ ; the interaction effect:  $F_{(4,72)}=0.515$ ,  $p=0.725$ ; Sidak's posthoc test of JZL195 vs. JZL195+SR144528 at Test:  $p=0.999$ ).