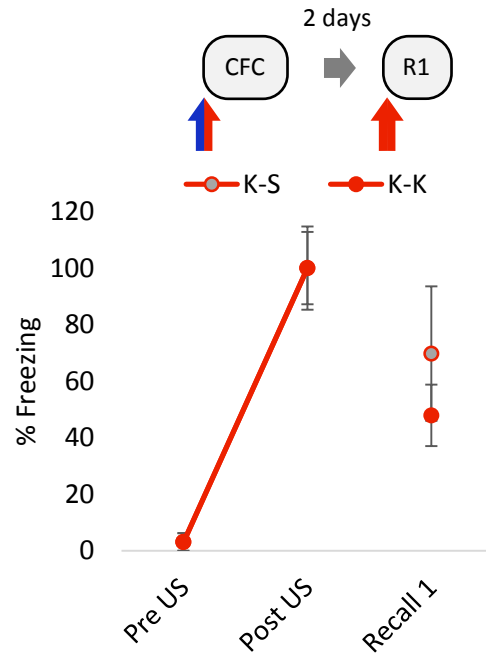


Supplementary Figure 1 The effect of 25 mg/kg ketamine on fear extinction. Experimental groups expanded to show order of treatment. Displayed are the first (Ext Start) and last (Ext End) 2 mins of the extinction trial. 25 mg/kg ketamine or saline vehicle was administered IP 30 min before trials. $n=6$ per group. In recall trials, ketamine-treated rats received either the same (Recall 1) or different (Recall 2) administration to that received prior to conditioning. Data represented by mean \pm SEM of percent freezing response normalised to Post-US. ** $P<0.01$, * $P<0.05$ in one-way ANOVA with Tukey's multiple comparisons test. CFC, contextual fear conditioning; Ext, Extinction trial; R1, Recall 1; US, unconditioned stimulus; S, saline; K, ketamine.



Supplementary Figure 2 8 mg/kg ketamine does not induce a state-dependent contextual fear memory. Ketamine (8 mg/kg) or saline vehicle was administered IP 30 min before conditioning and recall trials. n=4. Data represented by mean \pm SEM of percent freezing response normalised to Post-US. CFC, contextual fear conditioning; R1, Recall 1; K, ketamine; S, saline; US, unconditioned stimulus.

Supplementary Table 1 Group size calculations

| Effect size | Power | Required N per group |
|--------------------|--------------|-----------------------------|
| 1.5 | 0.8 | 9 |
| 2.0 | 0.8 | 6 |
| 2.5 | 0.8 | 4 |
| 3.0 | 0.8 | 4 |

Predicted effect size (Hedges' *g*; based on previous studies) and target power were used to estimate the required number of subjects (N) per group.

Supplementary Table 2 Contextual fear conditioning experiments freezing data

| Group | N | Pre-US (mean±SEM) | Post-US (mean±SEM) | Recall 1 (mean±SEM) | Recall 2 (mean±SEM) | Recall 3 (mean±SEM) |
|--|----------|------------------------------|-------------------------------|--------------------------------|--------------------------------|--------------------------------|
| The effect of 25 mg/kg pre-training ketamine on contextual fear conditioning | | | | | | |
| S-S | 6 | 1.39±1.39 | 69.44±10.02 | 75.00±10.32 | 52.78±10.90 | 50.00±9.13 |
| K-K | 6 | 6.94±3.34 | 63.89±5.12 | 6.94±3.98 | 31.94±12.44 | 18.06±3.98 |
| The effect of 8 mg/kg pre-training ketamine on contextual fear conditioning | | | | | | |
| K-S | 4 | 2.08±2.08 | 62.50±7.98 | 43.75±16.80 | - | - |
| K-K | 4 | 2.08±2.08 | 54.17±7.98 | 27.08±8.59 | - | - |

Mean ± SEM percent freezing without normalisation to post-US levels.

Supplementary Table 3 Extinction experiments freezing data

| Group | N | Pre-US (mean±SEM) | Post-US (mean±SEM) | Ext Start (mean±SEM) | Ext End (mean±SEM) | Recall 1 (mean±SEM) | Recall 2 (mean±SEM) |
|---|---|----------------------|-----------------------|-------------------------|-----------------------|------------------------|------------------------|
| The effect of 25 mg/kg pre-training ketamine on the extinction of contextual fear memory | | | | | | | |
| S-S-S-S | 6 | 2.78±1.76 | 83.33±4.30 | 59.72±3.98 | 18.06±5.86 | 22.22±5.56 | 15.28±4.52 |
| S-K-S-K | 6 | 4.17±1.86 | 77.78±5.56 | 61.11±3.51 | 29.17±4.69 | 66.67±8.87 | 36.11±5.12 |
| K-K-K-S | 6 | 6.94±2.56 | 63.89±6.69 | 45.8±4.69 | 18.06±5.01 | 40.28±8.45 | 8.33±6.80 |
| The effect of 8 mg/kg pre-training ketamine on the extinction of contextual fear memory | | | | | | | |
| S-S | 6 | 1.39±1.39 | 80.56±7.95 | 61.11±11.92 | 20.83±8.54 | 25.00±8.87 | 26.39±9.96 |
| S-K | 6 | 1.39±1.39 | 63.89±5.12 | 52.78±7.66 | 12.50±2.85 | 12.50±4.17 | 6.94±4.52 |
| K-S | 6 | 1.39±1.39 | 63.89±6.69 | 59.72±10.85 | 16.67±6.80 | 33.33±9.86 | 22.22±4.12 |
| K-K | 6 | 4.17±2.85 | 58.33±5.69 | 61.11±12.67 | 20.83±8.81 | 38.89±10.47 | 41.67±10.76 |
| The effect of 25 mg/kg post-training ketamine on the extinction of contextual fear memory | | | | | | | |
| S-S-S | 6 | 2.78±1.76 | 75.00±3.73 | 58.33±7.45 | 20.83±5.16 | 27.78±6.33 | 41.67±8.05 |
| S-K-S | 6 | 1.39±1.39 | 75.00±5.69 | 58.33±6.45 | 30.56±3.51 | 29.17±8.54 | 26.39±6.60 |
| K-K-S | 6 | 2.78±1.76 | 66.67±7.45 | 68.06±11.67 | 16.67±8.61 | 26.39±7.27 | 37.5±5.59 |

Mean ± SEM percent freezing without normalisation to post-US levels. US, unconditioned stimulus; Ext, extinction trial; S, saline; K, ketamine.