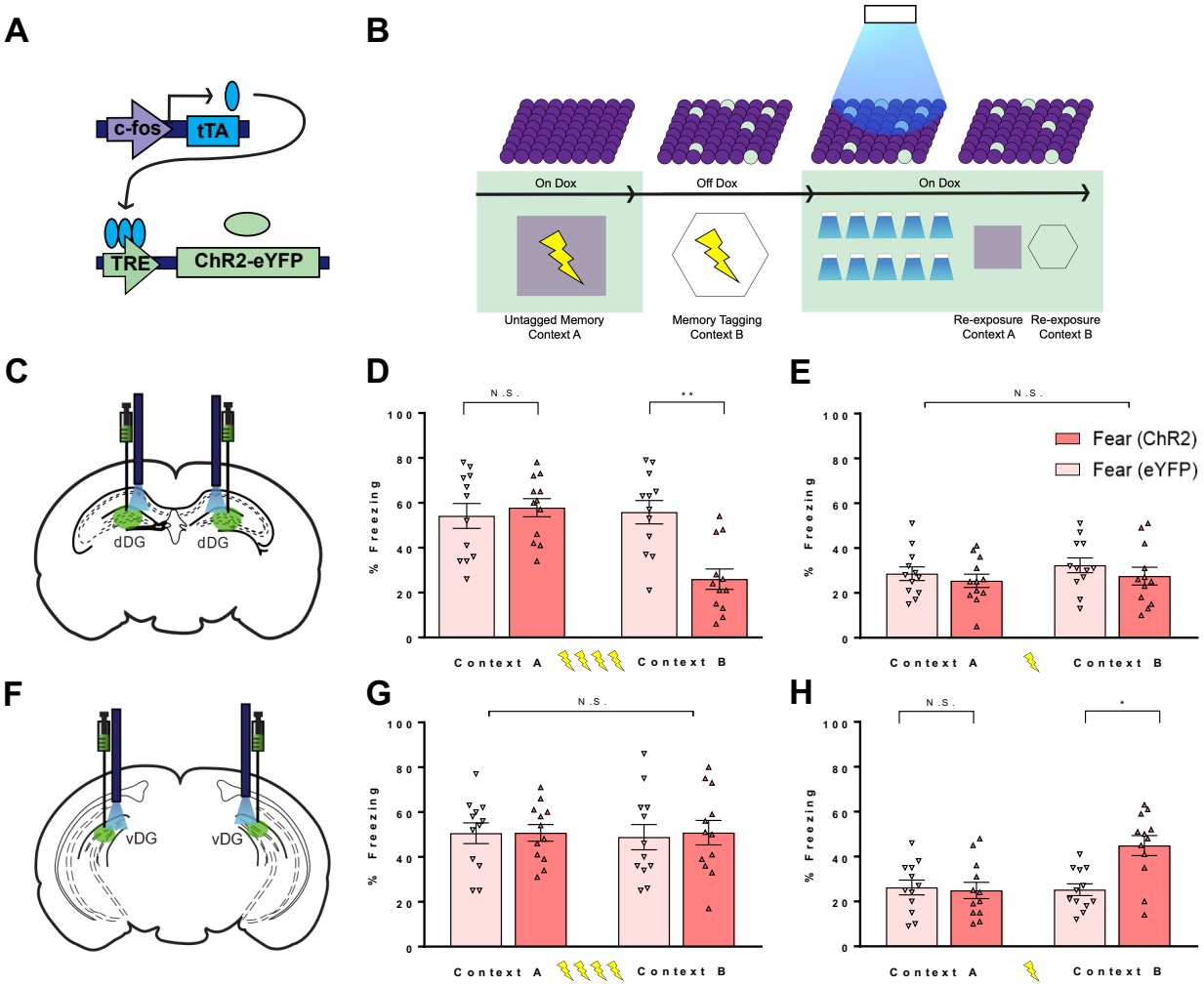
A
c-fos
tTA
TRE
ChR2-eYFP
B
On Dox
Off Dox
On Dox
Untagged Memory
Context A
Memory Tagging
Context B
Re-exposure
Context A
Re-exposure
Context B
C
dDG
dDG
D
N.S.
**
% Freezing
Context A
Context B
E
N.S.
Fear (ChR2)
Fear (eYFP)
% Freezing
Context A
Context B
F
vDG
vDG
G
N.S.
% Freezing
Context A
Context B
H
N.S.
*
% Freezing
Context A
Context B

Figure S1. **Chronic reactivation of a fear memory leads to enduring, context-specific, and bi-directional changes in fear memory expression. Related to Figure 3.** (A) A virus cocktail of AAV9-c-Fos-tTA and AAV9-TRE-ChR2-eYFP (ChR2) or AAV9-TRE-eYFP (eYFP) was infused into the dorsal and ventral DG. (B) Mice were fear conditioned in Context A while on Dox and in Context B while off Dox to label DG cells associated with Context B fear memory with ChR2 or eYFP. Mice were either conditioned to four shocks (high fear group) or one shock (low fear group). Following tagging, mice underwent 10 sessions over 5 days of optical stimulation while in a novel environment. Finally, mice were placed back into Context A and Context B and their levels of freezing were assessed. (C) Representative schematic of viral infusion and optogenetic stimulation in the dDG. (D) Chronic reactivation of a strong fear memory in the dDG led to a significant, context-dependent reduction in freezing behavior in mice infused with ChR2 relative to those infused with eYFP (n=12/group; Group X Context [$F(1,22)=10.78$, $p<0.003$]. (E) Chronic reactivation of a weak fear memory in the dDG did not alter freezing responses (ns). (F) Representative schematic of viral infusion and optogenetic stimulation in the vDG. (G) Chronic reactivation of a strong fear memory in the vDG did not alter freezing responses (ns). (H) Chronic reactivation of a fear memory in the vDG led to a significant, context-dependent increase in freezing behavior in mice infused with ChR2 relative to those infused with eYFP (n=12/group; Repeated-Measures ANOVA, Group X Context [$F(1,22)=5.33$, $p<0.03$].

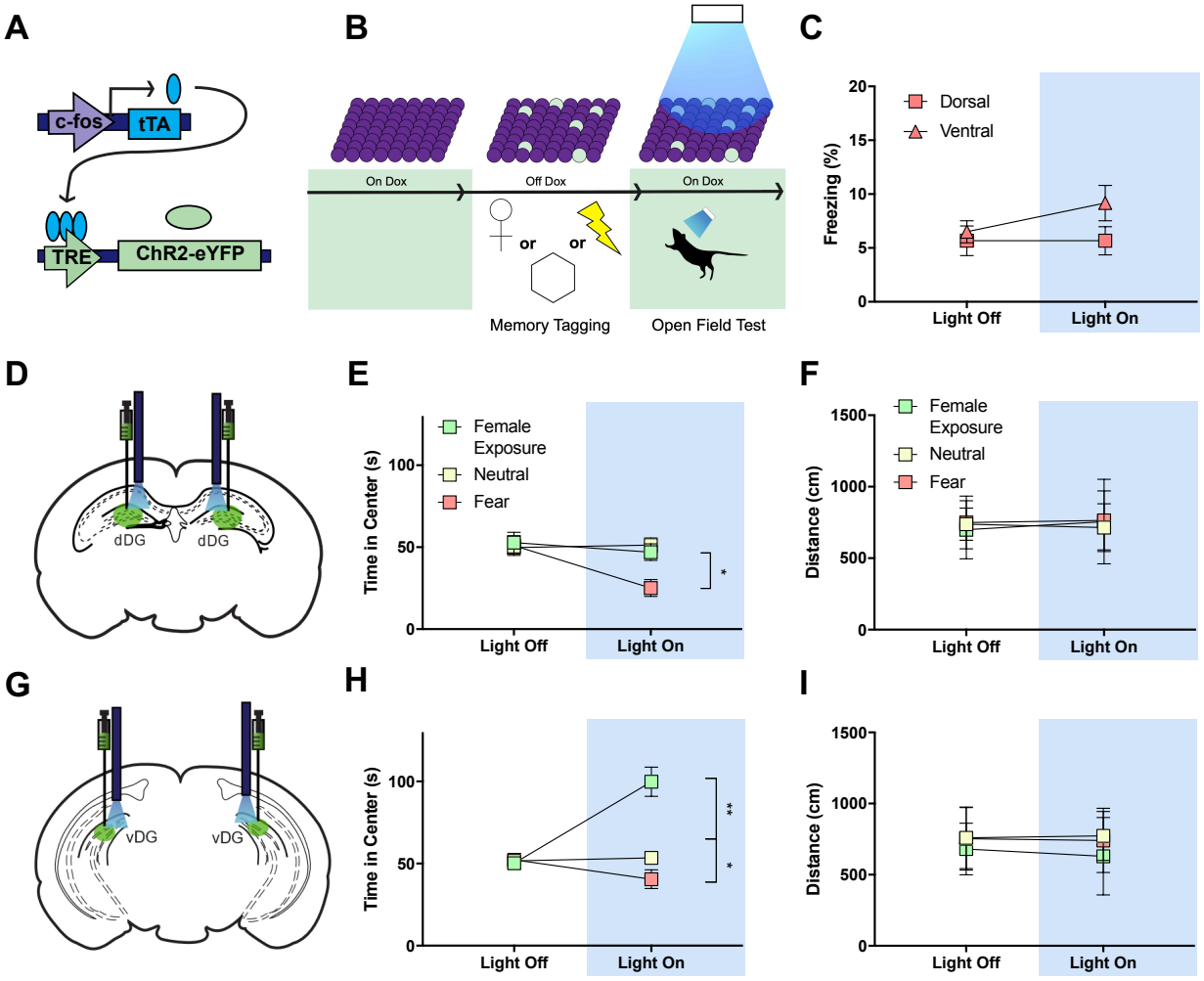
A
c-fos
tTA
TRE
ChR2-eYFP
B
On Dox
Off Dox
On Dox
or
or
Memory Tagging
Open Field Test
C
Dorsal
Ventral
Freezing (%)
20
15
10
5
0
Light Off
Light On
D
dDG
dDG
E
Female Exposure
Neutral
Fear
Time in Center (s)
100
50
0
*
Light Off
Light On
F
Female Exposure
Neutral
Fear
Distance (cm)
1500
1000
500
0
Light Off
Light On
G
vDG
vDG
H
Time in Center (s)
100
50
0
**
*
Light Off
Light On
I
Distance (cm)
1500
1000
500
0
Light Off
Light On

Figure S2. Acute activation of hippocampus memories drives differential anxiety behavior across the longitudinal axis of the hippocampus. Related to Figure 3. (A) A virus cocktail of AAV9-c-Fos-tTA and AAV9-TRE-ChR2-eYFP was infused into the dorsal or ventral DG. (B) While off Dox, mice were exposed to a female, neutral, or fear experience to label active cells with ChR2, returned to Dox, and administered light stimulation during behavior. (C) Acute reactivation of a fear memory led to comparable freezing behavior between dorsal and ventral DG groups during Light On and Light Off epochs. (D) Representative schematic of viral injection and optogenetic stimulation in the dDG. (E-F) Acute reactivation of cells in the dDG processing a fear memory decreased time spent in the center relative to reactivation of cells processing female and neutral memories but did not affect total distance travelled during Light On and Light Off epochs (n=12/group; Repeated-Measures ANOVA, Trial x Group [$F(2,33)=3.98$, $p<0.03$]. Posthoc demonstrated only the fear group spent significantly less time in the center during Light On relative to Light Off epochs and compared to all other groups ($p<0.05$). (G) Representative schematic of viral injection and optogenetic stimulation in the vDG. (H-I) Acute reactivation of cells in vDG processing a fear memory decreased whereas cells processing a female exposure memory increased time spent in the center relative to cells processing fear and neutral memories; total distance travelled was comparable across all groups during both Light On and Light Off epochs (n=12/group; Repeated-Measures ANOVA, Trial x Group [$F(2,33)=3.98$, $p<0.03$]. Posthoc demonstrated that only fear group showed significant difference between Light Off and Light On epoch and Light On was lower than all other groups ($p<0.05$) whereas only female exposure group showed a significant increase in the time spent in the center between the Light Off and Light On epochs ($p<0.001$).