Creating a False Memory in the Hippocampus

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Hypothesis

- Can artificially activating a previously formed contextual memory engram while simultaneously delivering foot shocks can result in the creation of a false fear memory for the context in which foot shocks were never delivered?

- Investigation whether a light-activated contextual memory in the DG or CA1 can serve as a functional conditioned stimulus in fear conditioning.

Requirements

- Capturing and marking the population of neurons active in a context

- Way to selectively re-activate them later

The Mice

- c-fos-tTA transgenic mice

- inject an AAV encoding TRE-ChR2-mCherry into their DG or CA1

- put an optical patch cord there

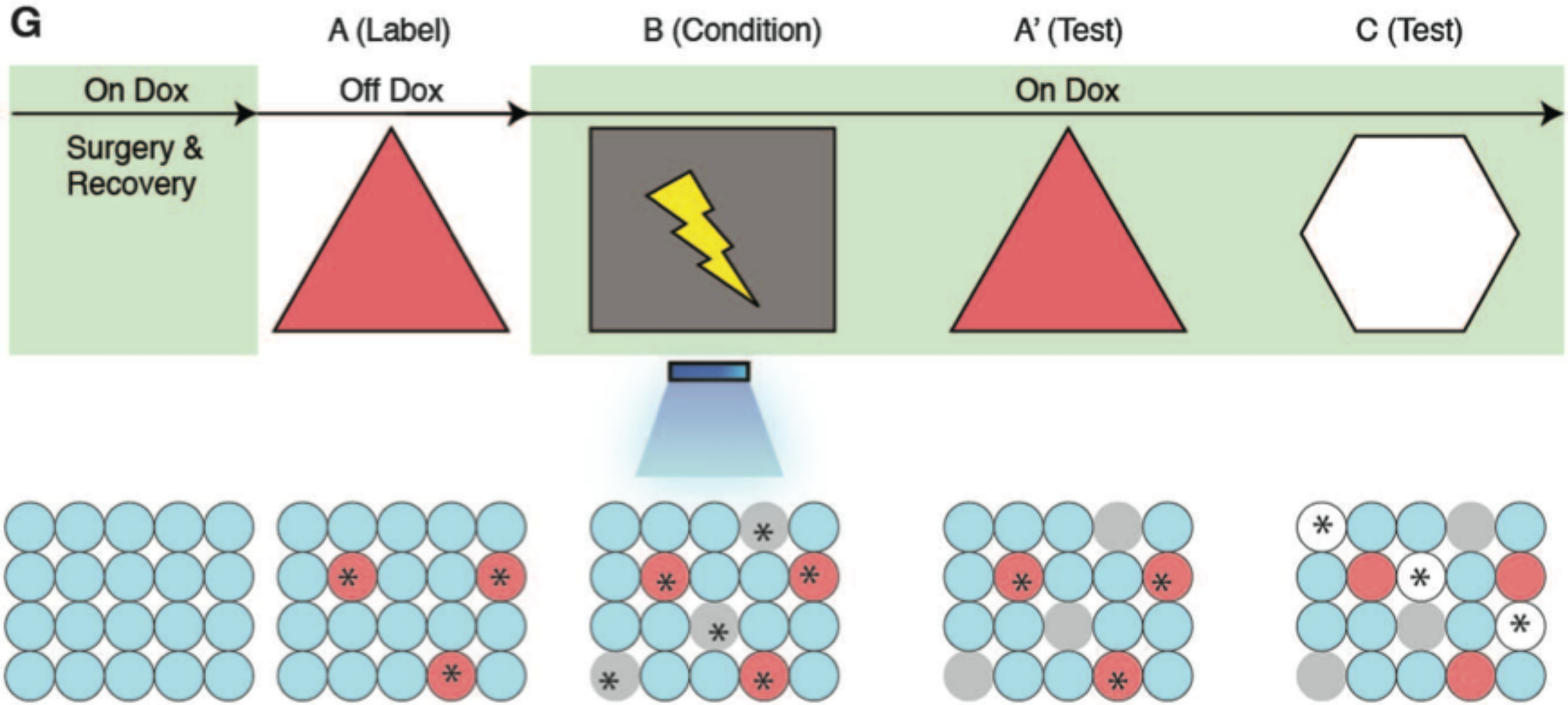
c-fos - an indirect marker of neuronal activity

tetracycline transactivator (tTA) - induce expression of a gene of interest downstream

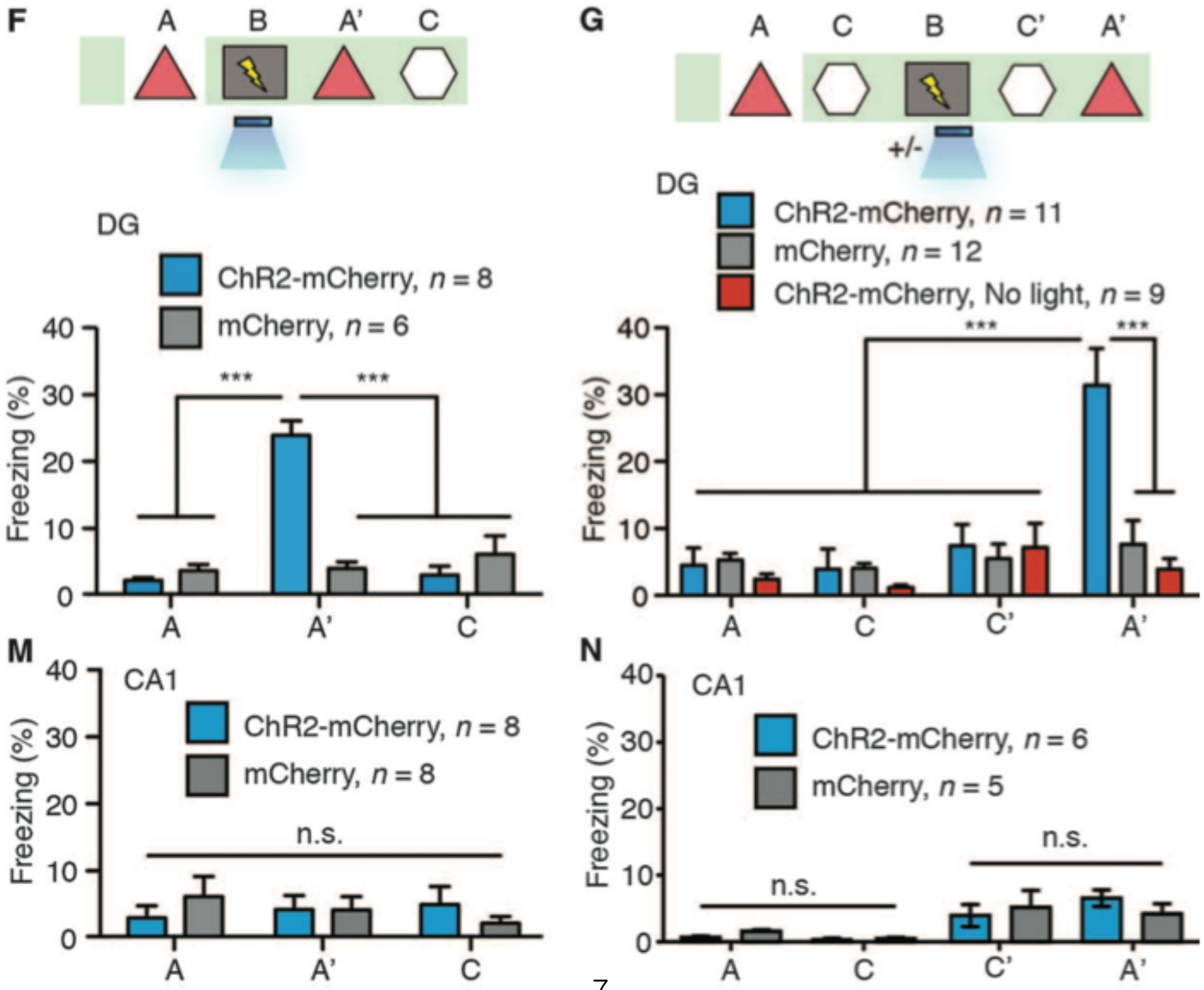
Channelrhodopsin-2 - protein functioning as light-gated ion channel

mCherry - fluorophore

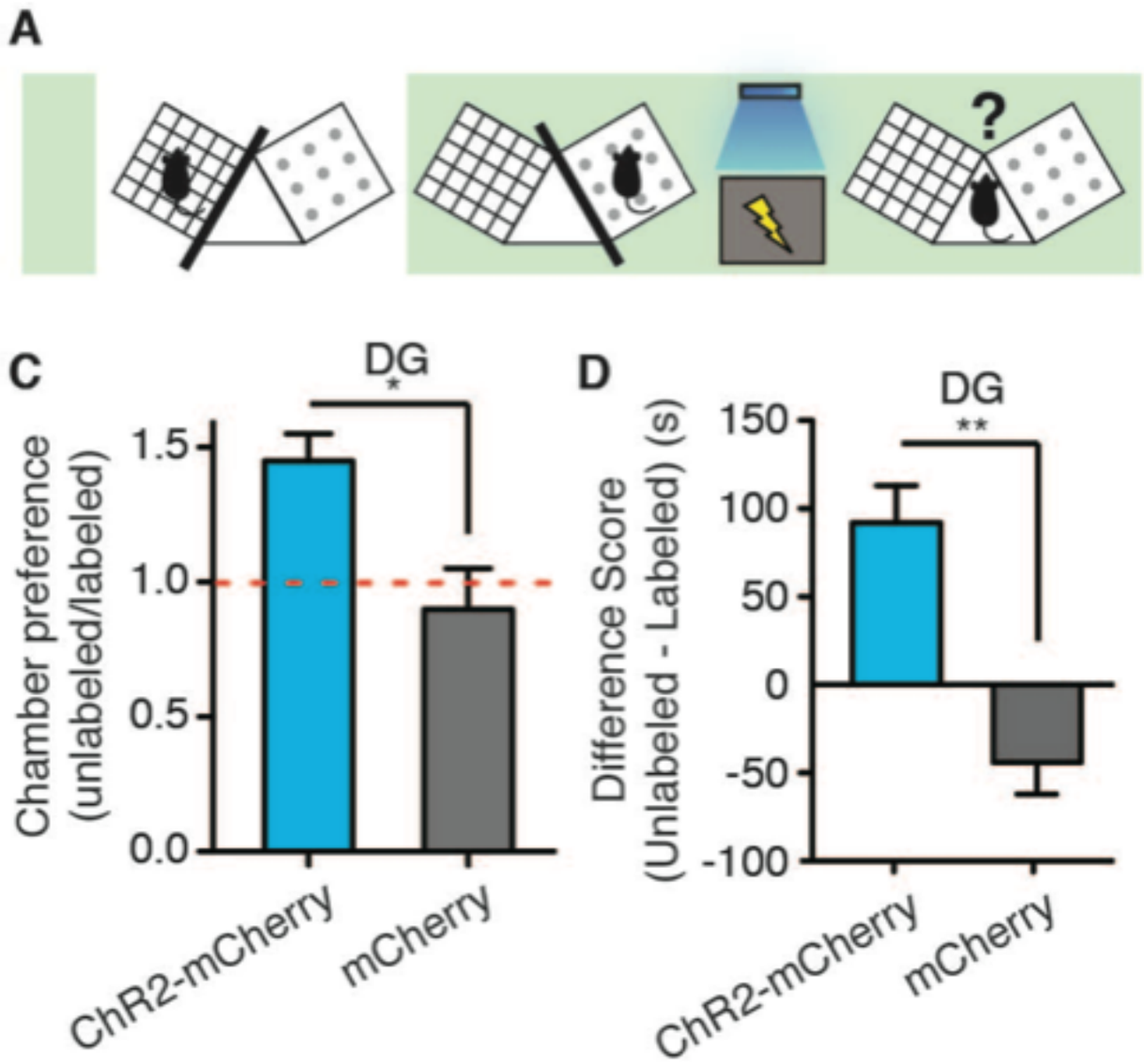
Basic experiment scheme



Results


F
A
B
A'
C
DG
ChR2-mCherry, n = 8
mCherry, n = 6
***
***
Freezing (%)
40
30
20
10
0
A
A'
C
G
A
C
B
C'
A'
+/-
DG
ChR2-mCherry, n = 11
mCherry, n = 12
ChR2-mCherry, No light, n = 9
***
***
Freezing (%)
40
30
20
10
0
A
C
C'
A'
M
CA1
ChR2-mCherry, n = 8
mCherry, n = 8
n.s.
Freezing (%)
40
30
20
10
0
A
A'
C
N
CA1
ChR2-mCherry, n = 6
mCherry, n = 5
n.s.
n.s.
Freezing (%)
40
30
20
10
0
A
C
C'
A'

Results


A
?
C
DG
*
Chamber preference
(unlabeled/labeled)
1.5
1.0
0.5
0.0
ChR2-mCherry
mCherry
D
DG
**
Difference Score
(Unlabeled - Labeled) (s)
150
100
50
0
-50
-100
ChR2-mCherry
mCherry

Discussion

- Scientific American: “The Era of Memory Engineering Has Arrived”

References

- Ramirez S, Liu X, Lin PA, Suh J, Pignatelli M, Redondo RL, Ryan TJ, Tonegawa S (July 2013). "Creating a false memory in the hippocampus". Science 341 (6144): 387-91.

- Nagel G, Szellas T, Huhn W, Kateriya S, Adeishvili N, Berthold P, Ollig D, Hegemann P, Bamberg E (November 2003). "Channelrhodopsin-2, a directly light-gated cation-selective membrane channel". Proc. Natl. Acad. Sci. U.S.A. 100 (24): 13940–5.