FIG. 1

a

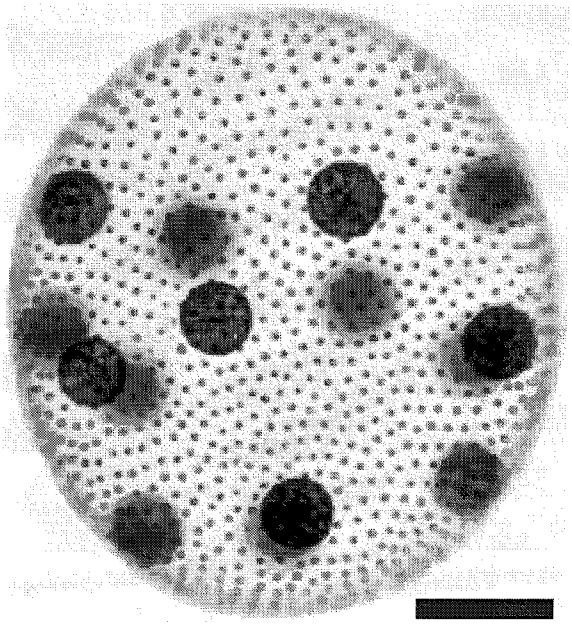
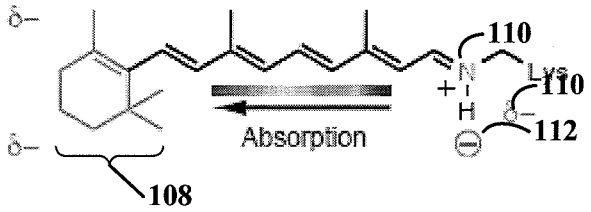


FIG. 1B




```
ChR2   M......... ......DYGG ALSAVG.... .......... .......REL  14
ChR1   MSRRPWLLAL ALAVALAAGS AGASTGSDAT VPVATQDGPD YVFHRAHERM  50
VChR1  M......... ......DY.. .......... .......... .....PVARS  8

ChR2   LFVTNPVVVN .GSVLVP..E DQCYCAGWIE SRGTNGAQTA SNVLQWLAAG  61
ChR1   LFQTSYTLEN NGSVICIPNN GQCFCLAWLK SNGTNAEKLA ANILQWITFA  100
VChR1  LIVRYPTDLG NGTVCMP..R GQCYCEGWLR SRGTSIEKTI AITLQWVVFA  56
                                                  TM1

ChR2   FSILLLMFYA YQTWKSTCGW EEIYVCAIEM VKVILEFFFE FKNPSMLYLA  111
ChR1   LSALCLMFYG YQTWKSTCGW EEIYVATIEM IKFIIEYFHE FDEPAVIYSS  150
VChR1  LSVACLGWYA YQAWRATCGW EEVYVALIEM MKSIIEAFHE FDSPATLWLS  106
          TM2
          102  104 104
ChR2   TGHRVQWLRY AEWLLTCPVI LIHLSNLTGL SNDYSRRTMG LLVSDIGTIV  161
ChR1   NGNKTVWLRY AEWLLTCRVI LIHLSNLTGL ANDYNKRTMG LLVSDIGTIV  200
VChR1  SGNGVVWMRY GEWLLTCPVL LIHLSNLTGL KDDYSKRTMG LLVSDVGCIV  156
          TM3                                  TM4
                  106
ChR2   WGATSAMATG YVKVIFFCLG LCYGANTFFH AAKAYIEGYH TVPKGRCRQV  211
ChR1   WGTTAALSKG YVRVIFFLMG LCYGIYTFFN AAKVYIEAYH TVPKGICRDL  250
VChR1  WGATSAMCTG WTKILFFLIS LSYGMYTYFH AAKVYIEAFH TVPKGICREL  206
                  TM5
          102          102      104 106
ChR2   VTGMAWLFFV SWGMFPILFI LGPEGFGVLS VYGSTVGHTI IDLMSKNCWG  261
ChR1   VRYLAWLYFC SWAMFPVLFL LGPEGFGHIN QFNSAIAHAI LDLASKNAWS  300
VChR1  VRVMAWTFFV AWGMFPVLFL LGTEGFGHIS PYGSAIGHSI LDLIAKNMWG  256
          TM6                                  TM7

ChR2   LLGHYLRVLI HEHILIHGDI RKTTKLNIGG TEIEVETLVE DEAE        311
ChR1   MMGHFLRVKI HEHILLYGDI RKKQKVNVAG QEMEVETMVH EEDD        350
VChR1  VLGNYLRVKI HEHILLYGDI RKKQKITIAG QEMEVETLVA EEED        306
```

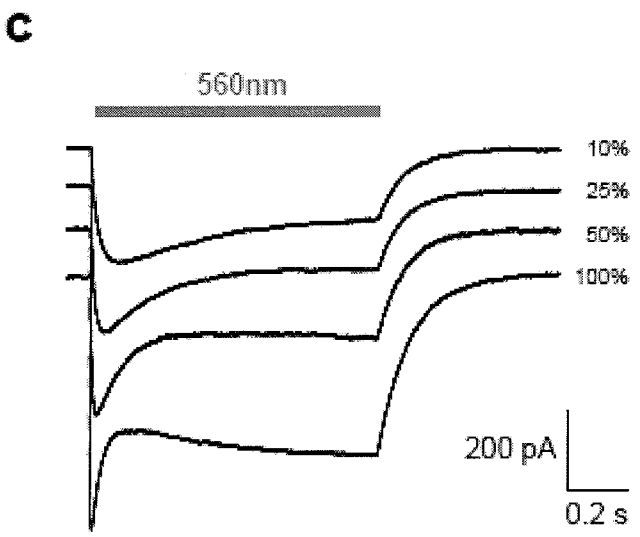
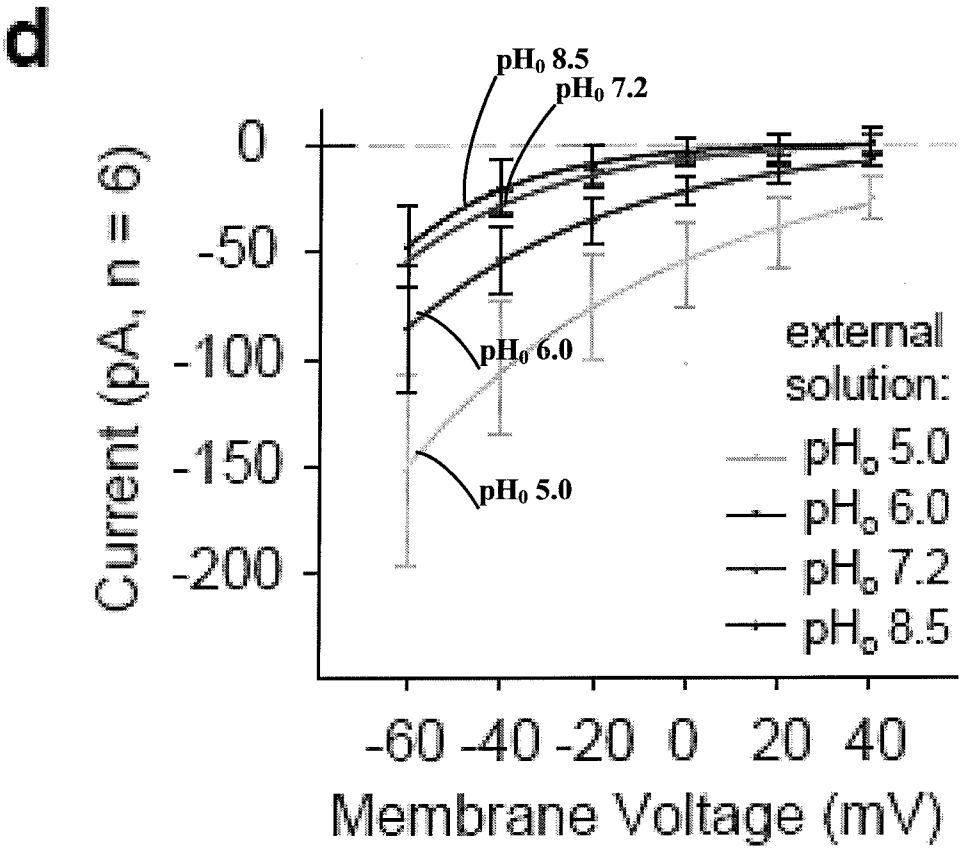

c
560nm
10%
25%
50%
100%
200 pA
0.2 s

FIG. 1


d
pH0 8.5
pH0 7.2
pH0 6.0
pH0 5.0
0
-50
-100
-150
-200
Current (pA, n = 6)
external solution:
pHo 5.0
pHo 6.0
pHo 7.2
pHo 8.5
-60 -40 -20 0 20 40
Membrane Voltage (mV)

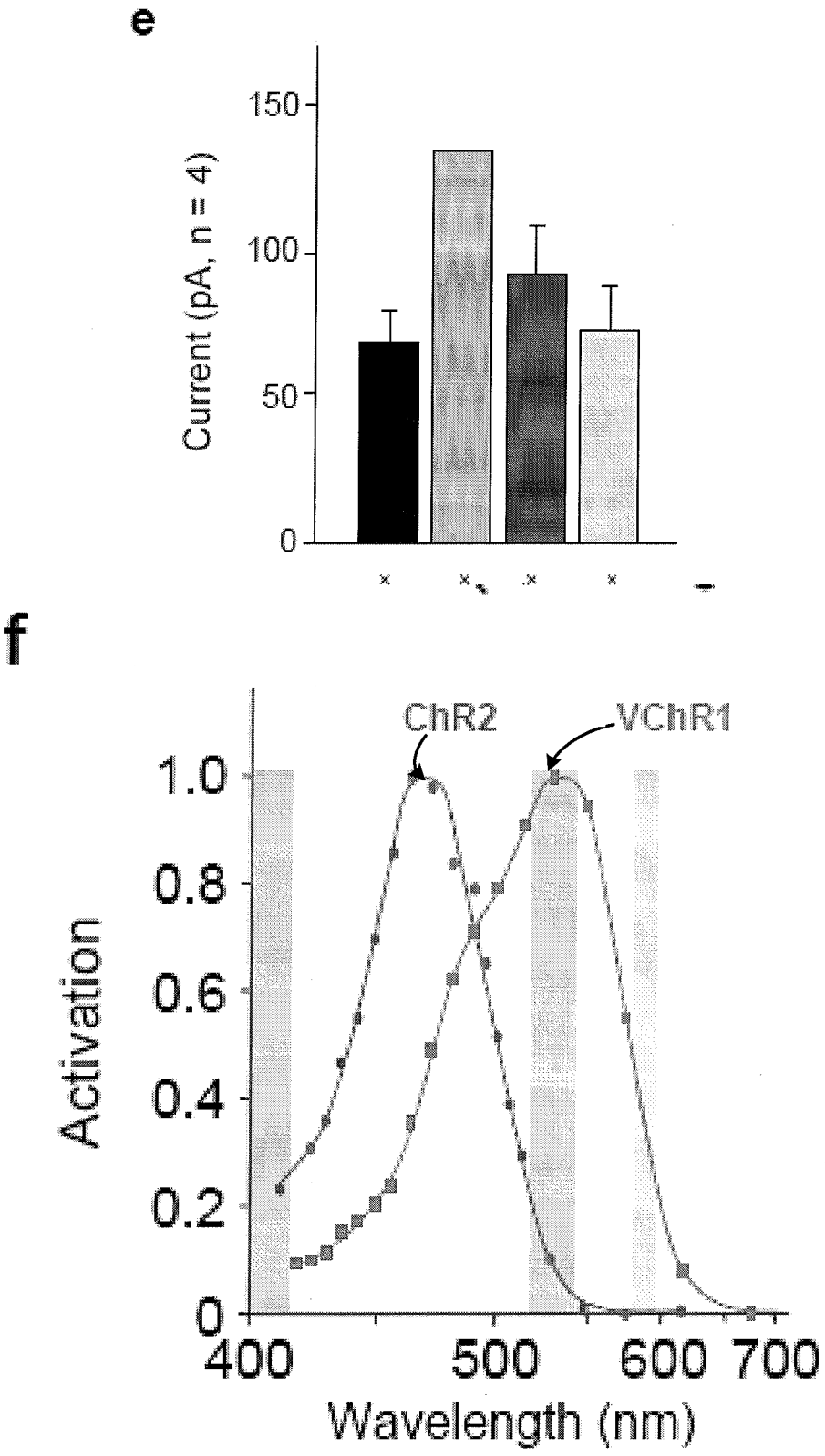

e
150
100
50
0
Current (pA, n = 4)
f
ChR2
VChR1
1.0
0.8
0.6
0.4
0.2
0
Activation
400
500
600
700
Wavelength (nm)

FIG. 1

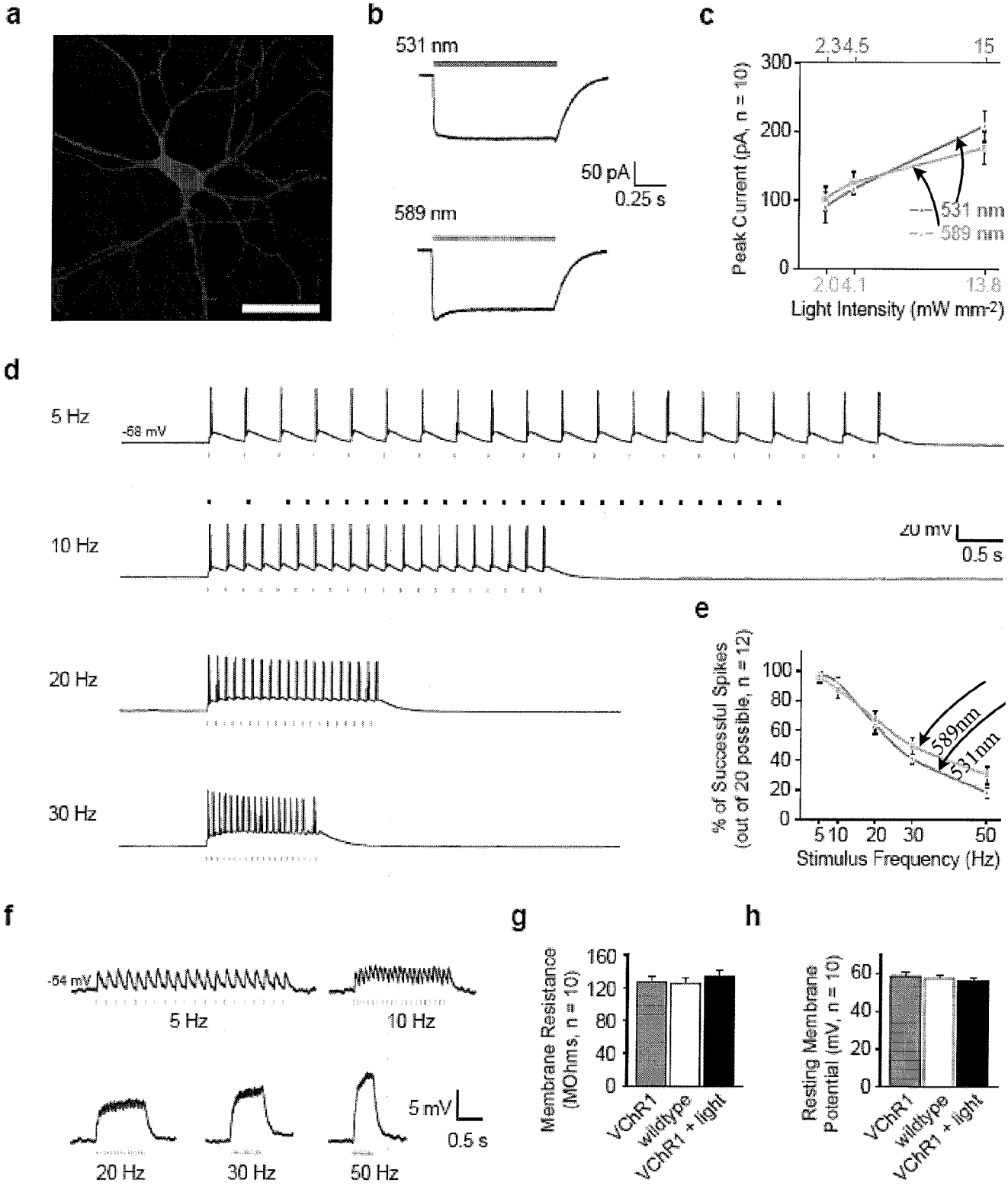

a
b
531 nm
50 pA
0.25 s
589 nm
c
2.3 4.5
15
300
200
100
0
Peak Current (pA, n = 10)
531 nm
589 nm
2.0 4.1
13.8
Light Intensity (mW mm-2)
d
5 Hz
-68 mV
10 Hz
20 mV
0.5 s
20 Hz
30 Hz
e
% of Successful Spikes
(out of 20 possible, n = 12)
100
80
60
40
20
0
589nm
531nm
5 10 20 30 50
Stimulus Frequency (Hz)
f
-64 mV
5 Hz
10 Hz
5 mV
0.5 s
20 Hz
30 Hz
50 Hz
g
Membrane Resistance
(MOhms, n = 10)
160
120
80
40
0
VChR1
wildtype
VChR1 + light
h
Resting Membrane
Potential (mV, n = 10)
60
40
20
0
VChR1
wildtype
VChR1 + light

FIG. 2

FIG. 3

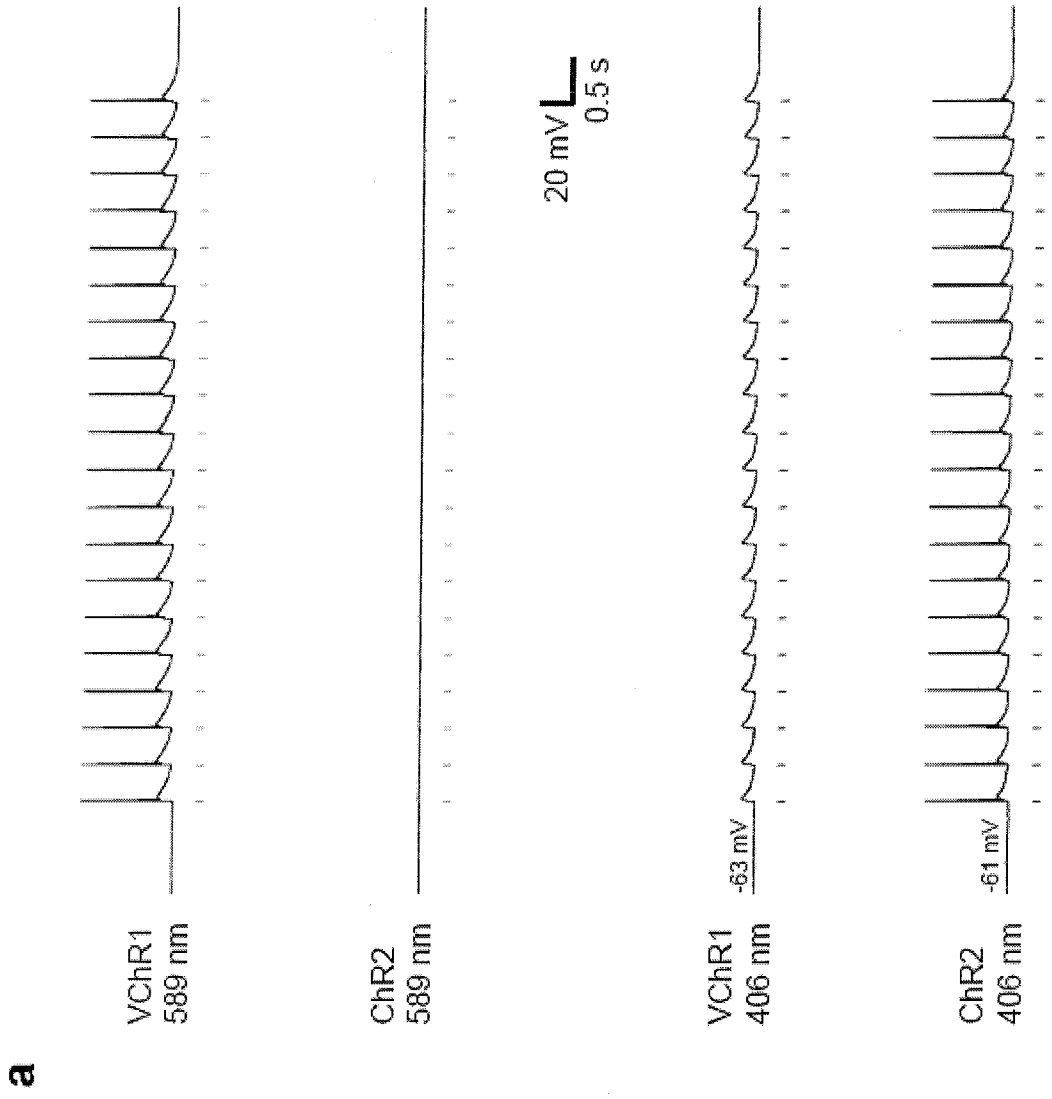

a
VChR1
589 nm
ChR2
589 nm
20 mV
0.5 s
VChR1
406 nm
-63 mV
ChR2
406 nm
-61 mV
b
% of Successful ChR2 Spikes
(out of 20 possible, n = 7)
406 nm
589 nm
1.2 2.3
7.8
2.0 4.1
13.8
Light Intensity (mW mm-2)
c
% of Successful VChR1 Spikes
(out of 20 possible, n = 10)
589 nm
406 nm
1.2 2.3
7.8
2.0 4.1
13.8
Light Intensity (mW mm-2)

Figure 4

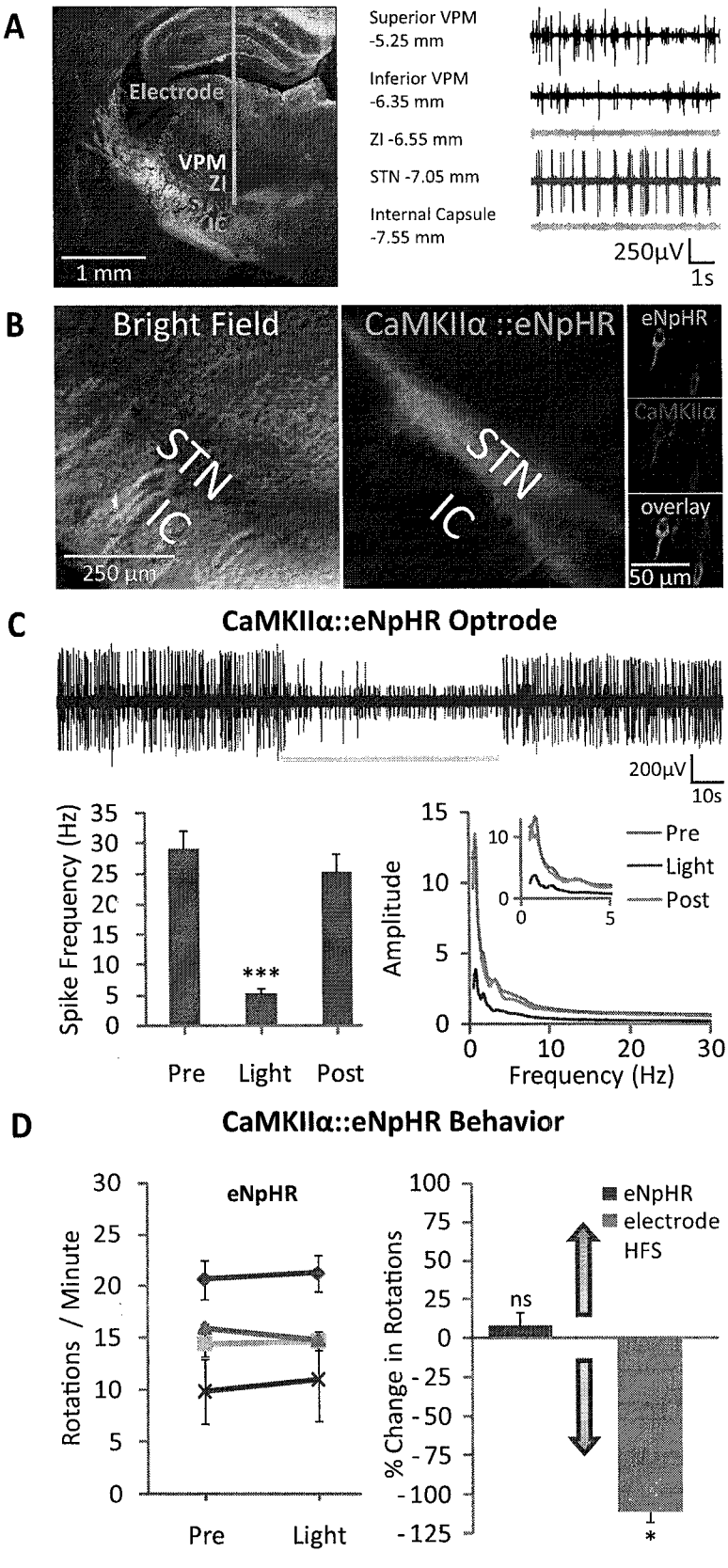

A
Electrode
VPM
ZI
STN
IC
1 mm
Superior VPM
-5.25 mm
Inferior VPM
-6.35 mm
ZI -6.55 mm
STN -7.05 mm
Internal Capsule
-7.55 mm
250µV
1s
B
Bright Field
STN
IC
250 µm
CaMKIIα ::eNpHR
STN
IC
eNpHR
CaMKIIα
overlay
50 µm
C
CaMKIIα::eNpHR Optrode
200µV
10s
Spike Frequency (Hz)
35
30
25
20
15
10
5
0
***
Pre
Light
Post
Amplitude
15
10
5
0
10
0
0
5
Pre
Light
Post
0
10
20
30
Frequency (Hz)
D
CaMKIIα::eNpHR Behavior
eNpHR
Rotations / Minute
30
25
20
15
10
5
0
Pre
Light
% Change in Rotations
100
75
50
25
0
-25
-50
-75
-100
-125
ns
*
eNpHR
electrode
HFS

Figure 5

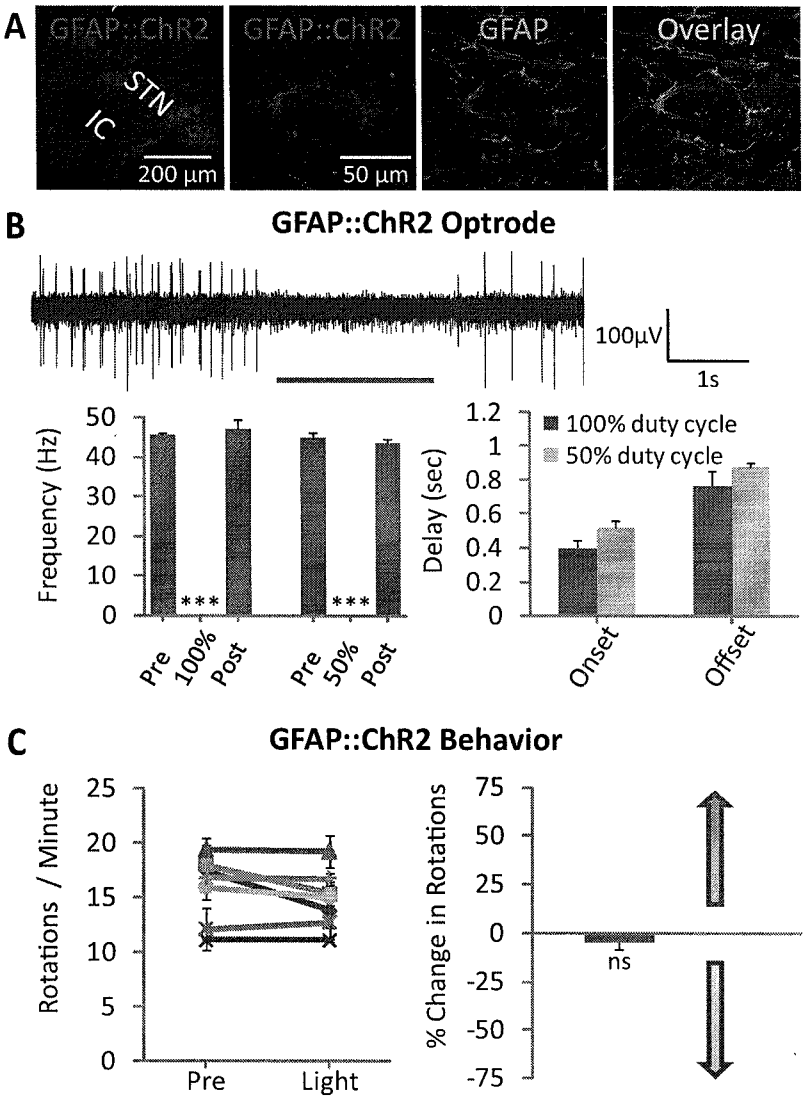

A
GFAP::ChR2
GFAP::ChR2
GFAP
Overlay
STN
IC
200 µm
50 µm
B
GFAP::ChR2 Optrode
100µV
1s
Frequency (Hz)
50
40
30
20
10
0
***
***
Pre
100%
Post
Pre
50%
Post
Delay (sec)
1.2
1
0.8
0.6
0.4
0.2
0
100% duty cycle
50% duty cycle
Onset
Offset
C
GFAP::ChR2 Behavior
Rotations / Minute
25
20
15
10
5
0
Pre
Light
% Change in Rotations
75
50
25
0
-25
-50
-75
ns

Figure 6

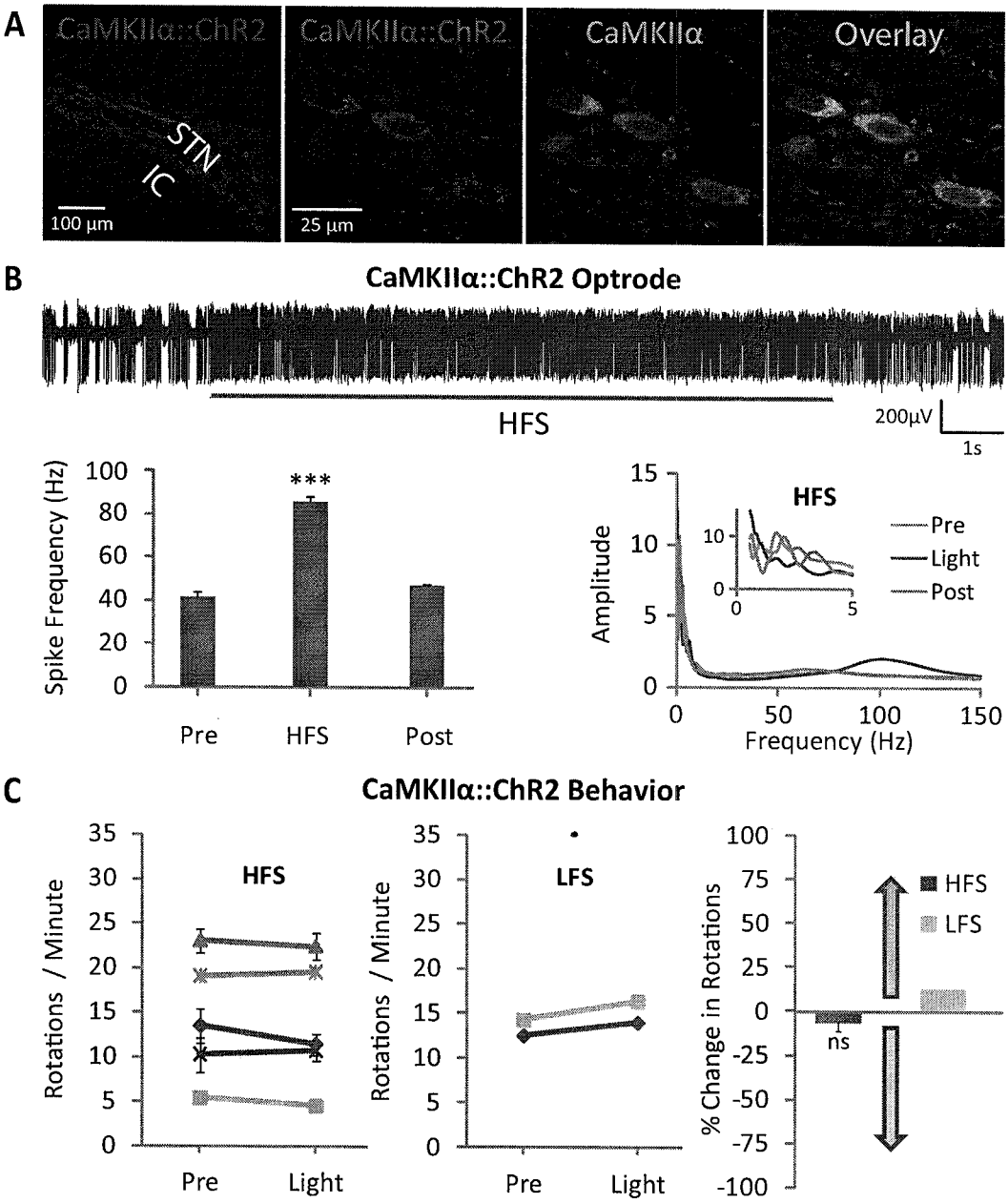

A
CaMKIIα::ChR2
CaMKIIα::ChR2
CaMKIIα
Overlay
STN
IC
100 µm
25 µm
B
CaMKIIα::ChR2 Optrode
HFS
200µV
1s
Spike Frequency (Hz)
***
Pre
HFS
Post
Amplitude
HFS
Pre
Light
Post
Frequency (Hz)
C
CaMKIIα::ChR2 Behavior
Rotations / Minute
HFS
LFS
% Change in Rotations
ns
HFS
LFS

Figure 7

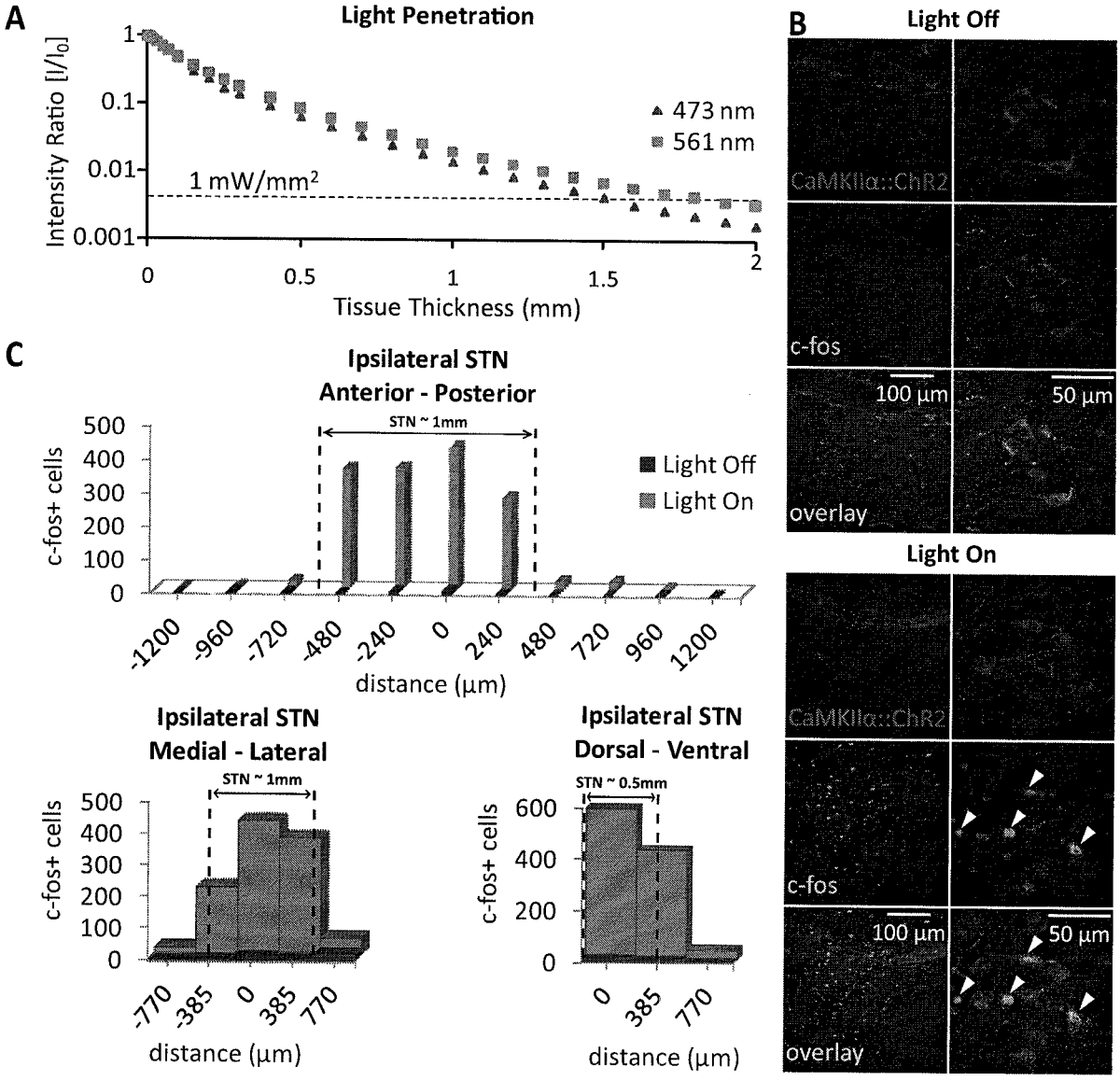

A
Light Penetration
Intensity Ratio [I/I0]
1
0.1
0.01
0.001
473 nm
561 nm
1 mW/mm2
0
0.5
1
1.5
2
Tissue Thickness (mm)
B
Light Off
CaMKIIα::ChR2
c-fos
100 µm
50 µm
overlay
Light On
CaMKIIα::ChR2
c-fos
100 µm
50 µm
overlay
C
Ipsilateral STN
Anterior - Posterior
STN ~ 1mm
Light Off
Light On
c-fos+ cells
500
400
300
200
100
0
-1200
-960
-720
-480
-240
0
240
480
720
960
1200
distance (µm)
Ipsilateral STN
Medial - Lateral
STN ~ 1mm
c-fos+ cells
500
400
300
200
100
0
-770
-385
0
385
770
distance (µm)
Ipsilateral STN
Dorsal - Ventral
STN ~ 0.5mm
c-fos+ cells
600
400
200
0
0
385
770
distance (µm)

Figure 8

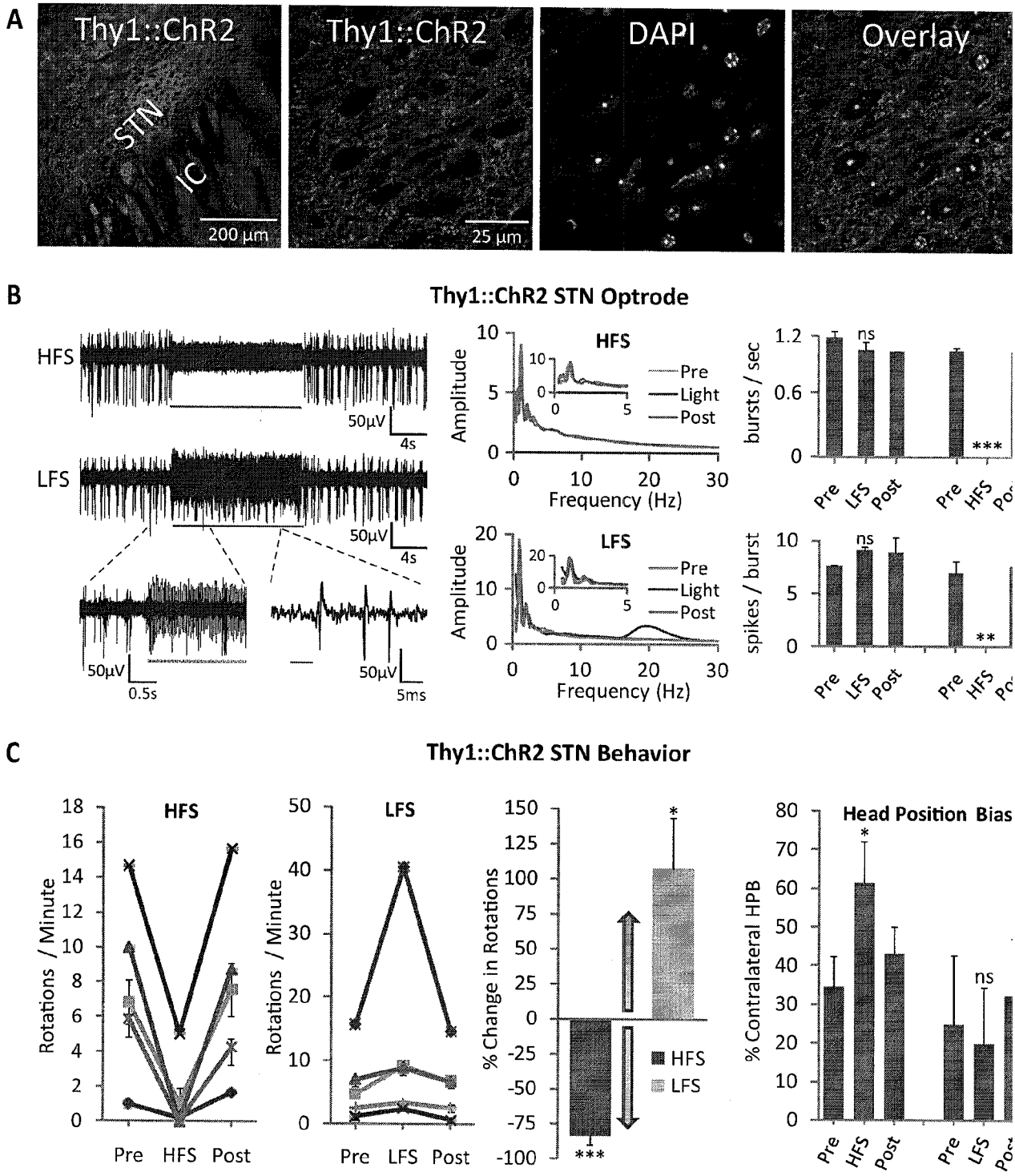

A
Thy1::ChR2
STN
IC
200 µm
Thy1::ChR2
25 µm
DAPI
Overlay
B
Thy1::ChR2 STN Optrode
HFS
50µV
4s
LFS
50µV
4s
50µV
0.5s
50µV
5ms
HFS
Amplitude
Frequency (Hz)
Pre
Light
Post
LFS
Amplitude
Frequency (Hz)
Pre
Light
Post
bursts / sec
ns
***
Pre LFS Post Pre HFS Post
spikes / burst
ns
**
Pre LFS Post Pre HFS Post
C
Thy1::ChR2 STN Behavior
HFS
Rotations / Minute
Pre HFS Post
LFS
Rotations / Minute
Pre LFS Post
% Change in Rotations
***
*
HFS
LFS
Head Position Bias
% Contralateral HPB
*
ns
Pre HFS Post Pre LFS Post

Figure 9

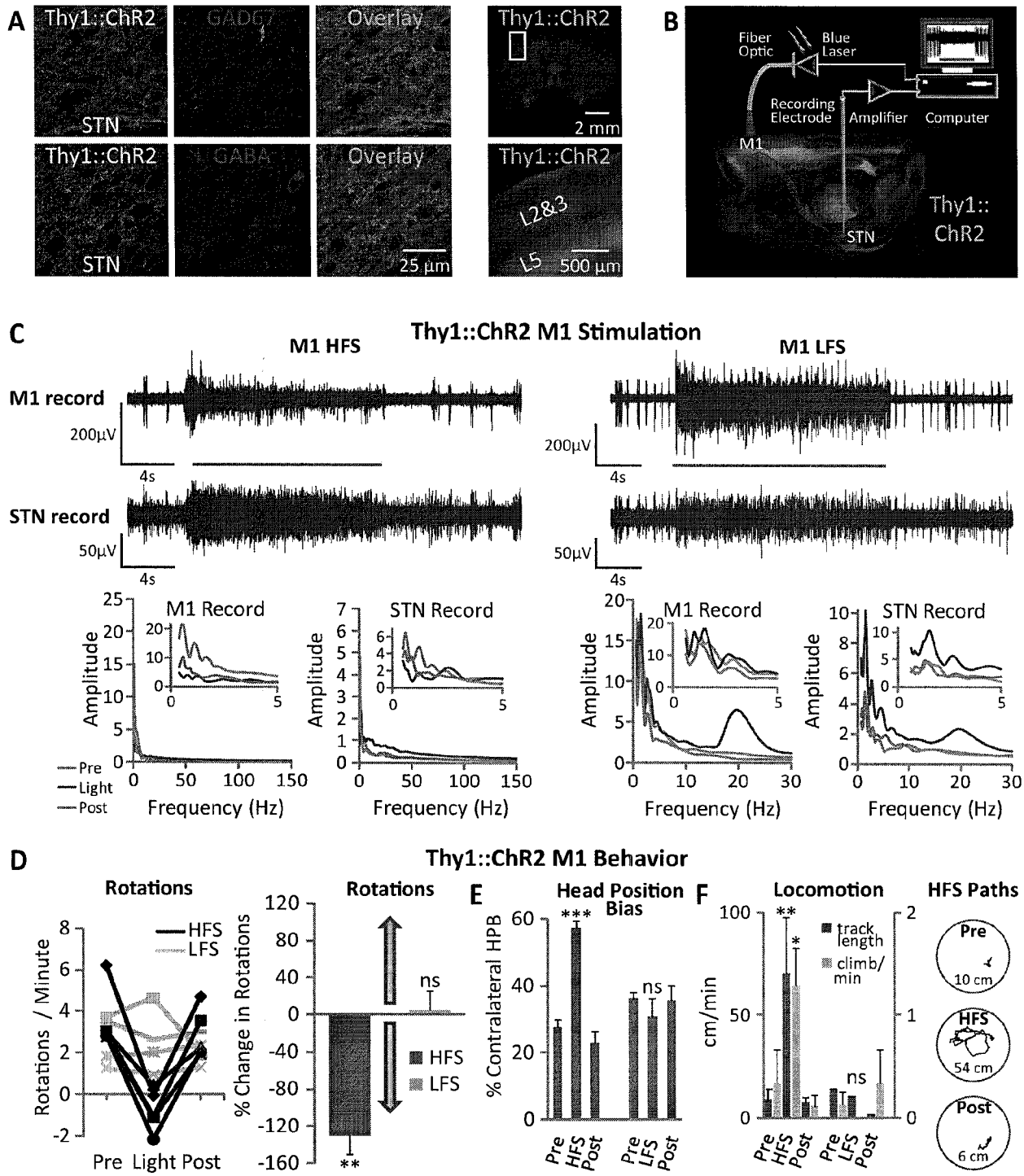

A
Thy1::ChR2
GAD67
Overlay
STN
Thy1::ChR2
GABA
Overlay
STN
25 µm
Thy1::ChR2
2 mm
Thy1::ChR2
L2&3
L5
500 µm
B
Fiber Optic
Blue Laser
Recording Electrode
Amplifier
Computer
M1
STN
Thy1::ChR2
C
Thy1::ChR2 M1 Stimulation
M1 HFS
M1 LFS
M1 record
200µV
4s
STN record
50µV
4s
M1 Record
STN Record
Amplitude
Pre
Light
Post
Frequency (Hz)
D
Thy1::ChR2 M1 Behavior
Rotations
HFS
LFS
Rotations / Minute
Pre Light Post
Rotations
% Change in Rotations
ns
HFS
LFS
**
E
Head Position Bias
% Contralateral HPB
***
ns
Pre HFS Post
Pre LFS Post
F
Locomotion
track length
climb/ min
cm/min
**
*
ns
Pre HFS Post
Pre LFS Post
HFS Paths
Pre
10 cm
HFS
54 cm
Post
6 cm

Figure 10

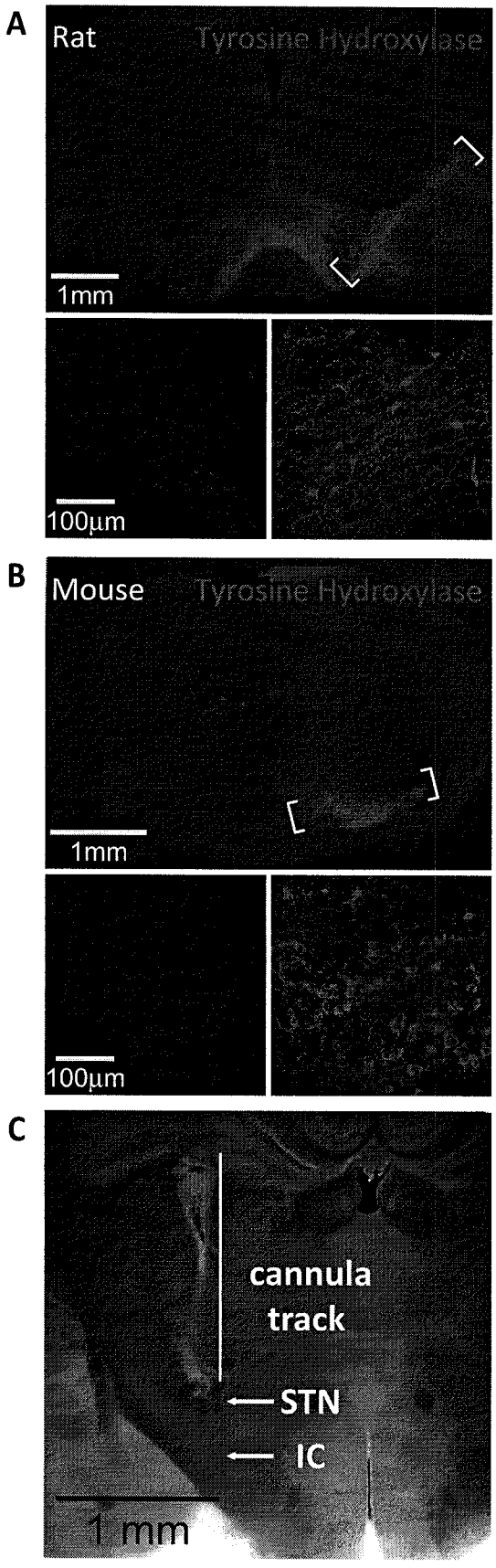

A
Rat
Tyrosine Hydroxylase
1mm
100µm
B
Mouse
Tyrosine Hydroxylase
1mm
100µm
C
cannula
track
STN
IC
1 mm

Figure 11

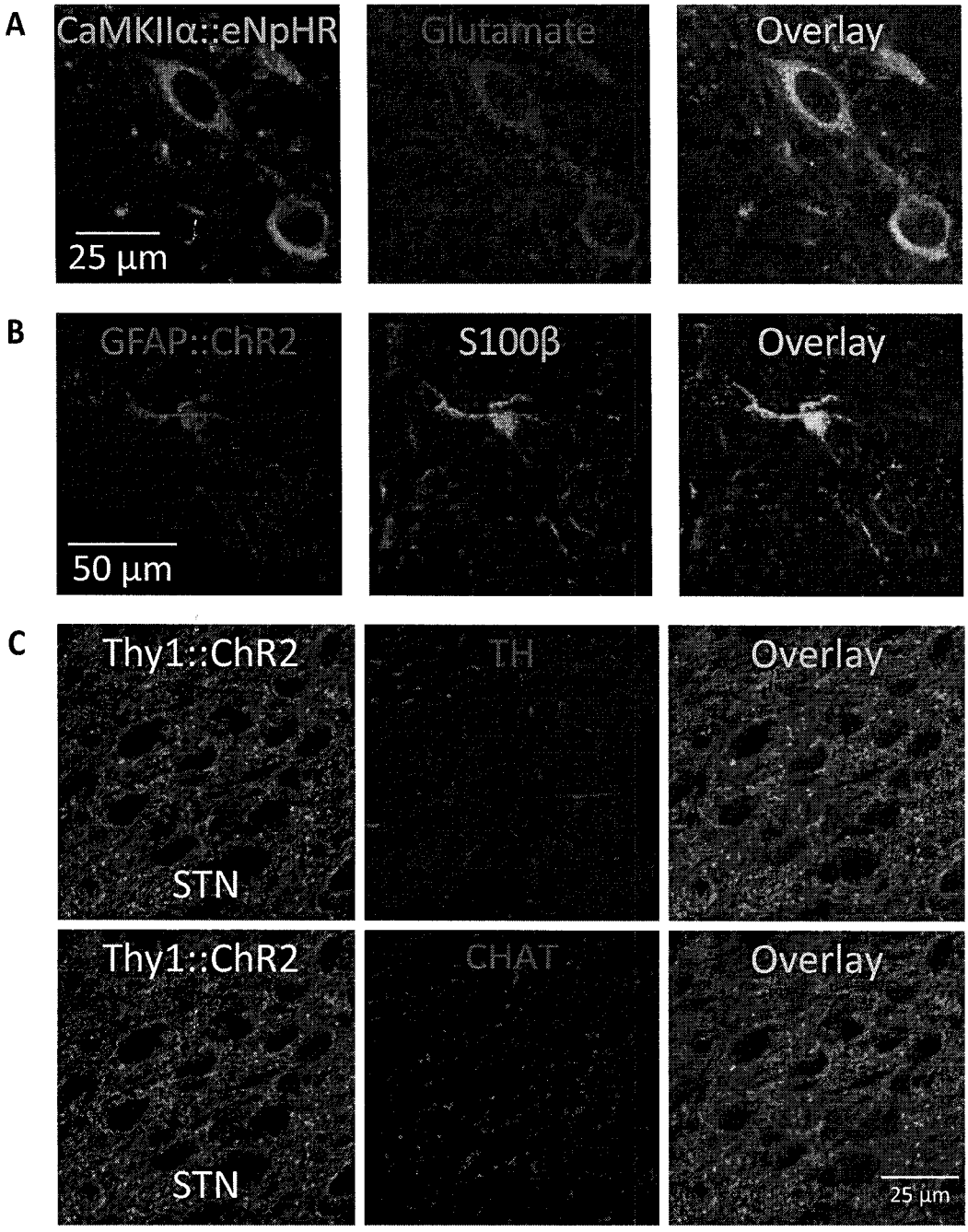

A
CaMKIIα::eNpHR
Glutamate
Overlay
25 µm
B
GFAP::ChR2
S100β
Overlay
50 µm
C
Thy1::ChR2
TH
Overlay
STN
Thy1::ChR2
CHAT
Overlay
STN
25 µm

Figure 12

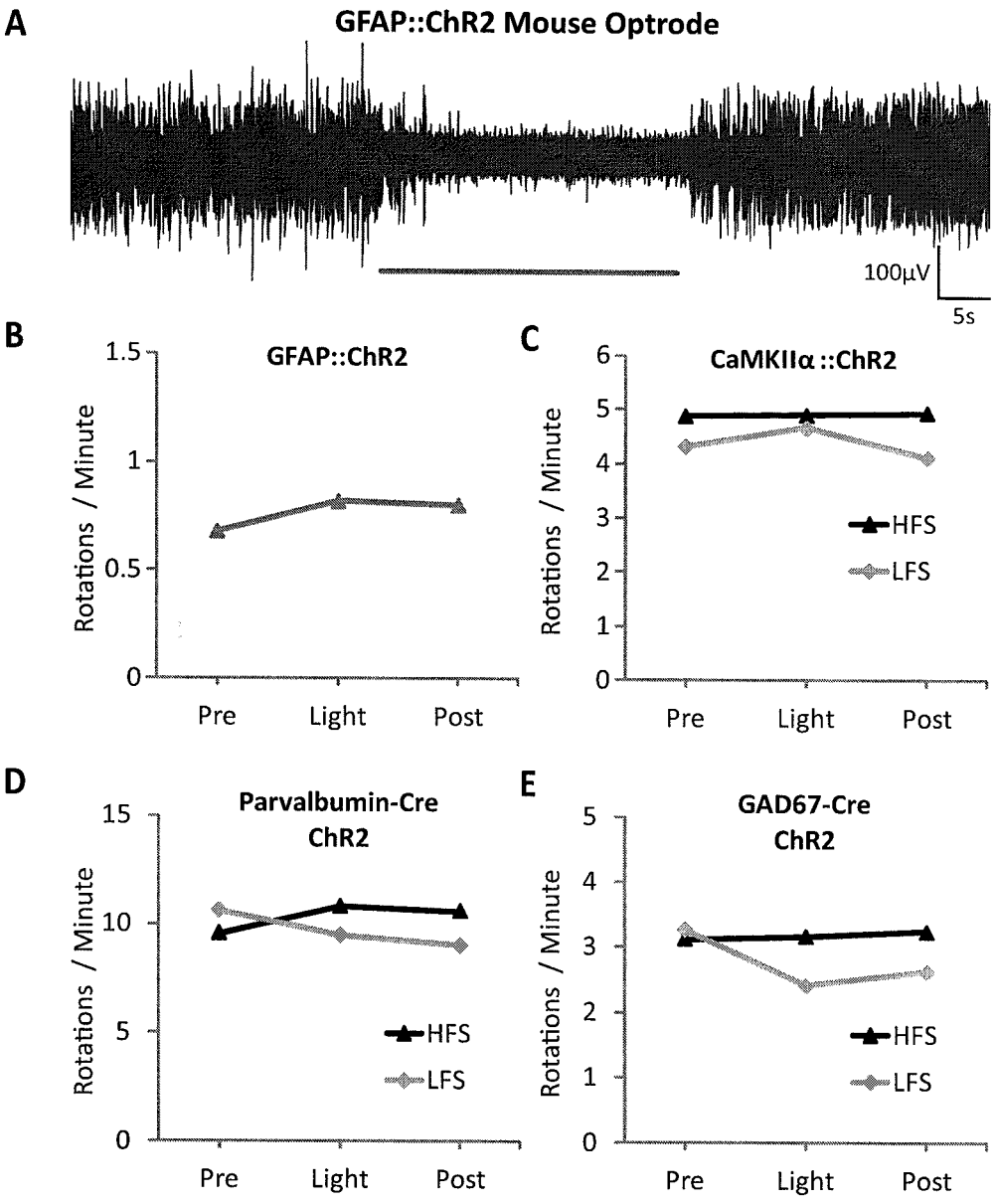

A
GFAP::ChR2 Mouse Optrode
100µV
5s
B
GFAP::ChR2
Rotations / Minute
1.5
1
0.5
0
Pre
Light
Post
C
CaMKIIα ::ChR2
Rotations / Minute
6
5
4
3
2
1
0
HFS
LFS
Pre
Light
Post
D
Parvalbumin-Cre
ChR2
Rotations / Minute
15
10
5
0
HFS
LFS
Pre
Light
Post
E
GAD67-Cre
ChR2
Rotations / Minute
5
4
3
2
1
0
HFS
LFS
Pre
Light
Post

Figure 13

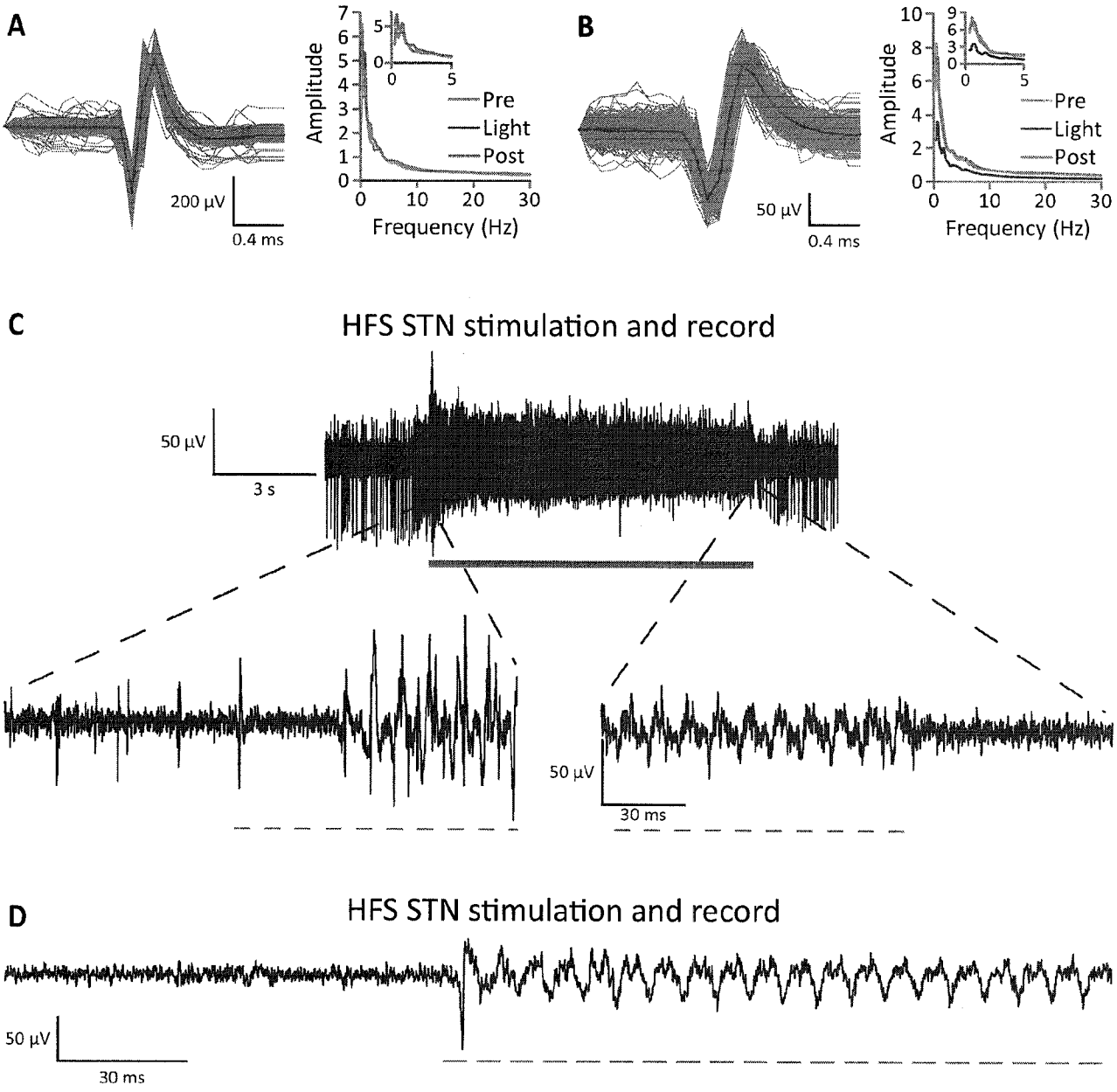

A
200 µV
0.4 ms
Amplitude
Frequency (Hz)
Pre
Light
Post
B
50 µV
0.4 ms
Amplitude
Frequency (Hz)
Pre
Light
Post
C
HFS STN stimulation and record
50 µV
3 s
50 µV
30 ms
D
HFS STN stimulation and record
50 µV
30 ms

Figure 14

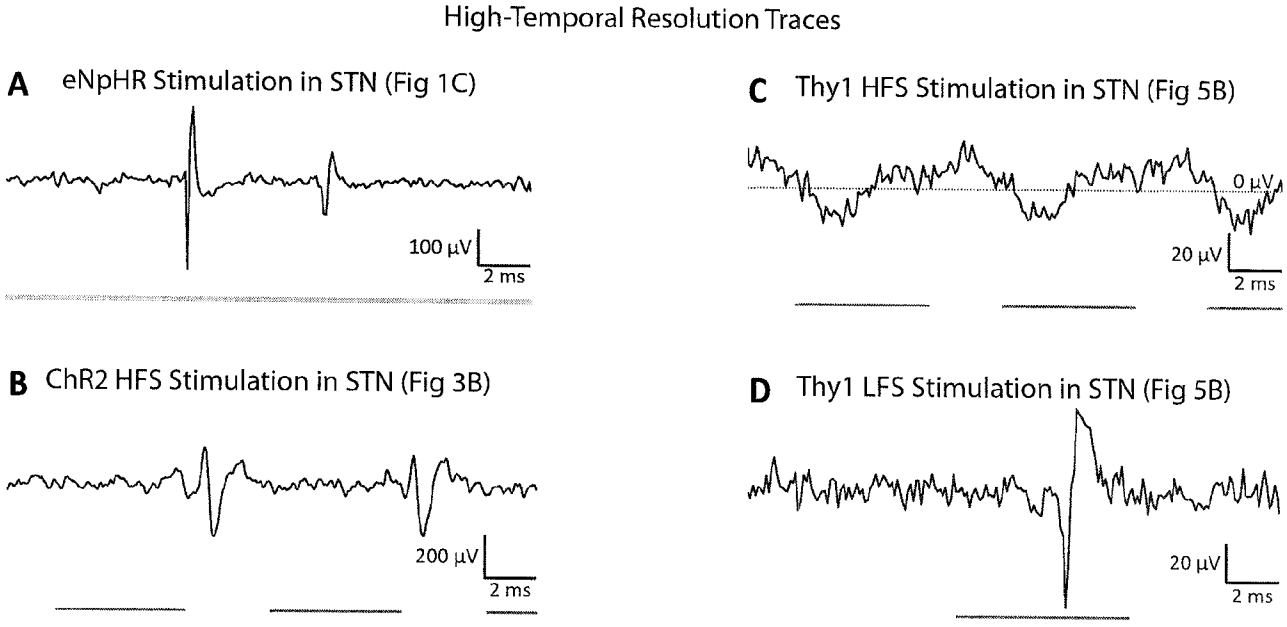

High-Temporal Resolution Traces
A eNpHR Stimulation in STN (Fig 1C)
100 µV
2 ms
B ChR2 HFS Stimulation in STN (Fig 3B)
200 µV
2 ms
C Thy1 HFS Stimulation in STN (Fig 5B)
0 µV
20 µV
2 ms
D Thy1 LFS Stimulation in STN (Fig 5B)
20 µV
2 ms

Figure 15

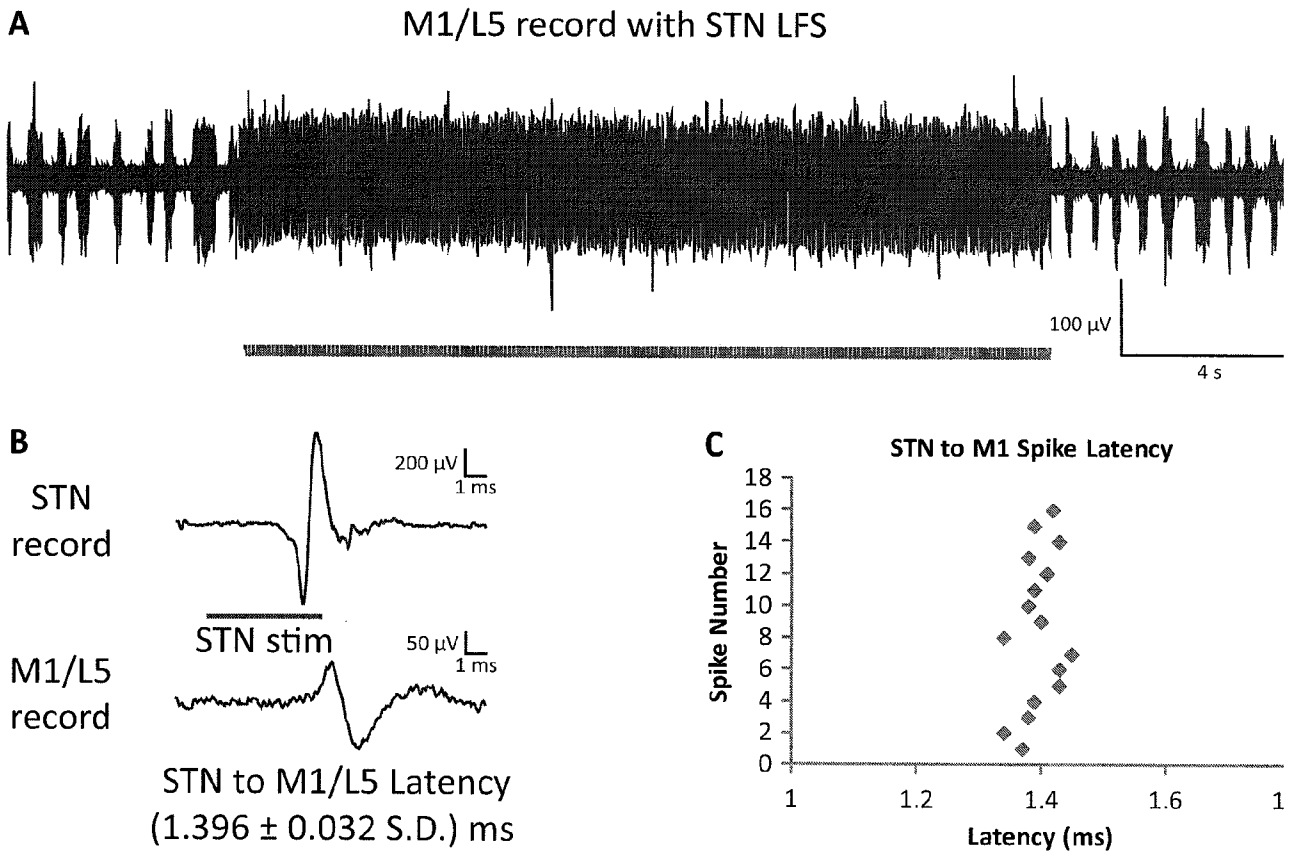
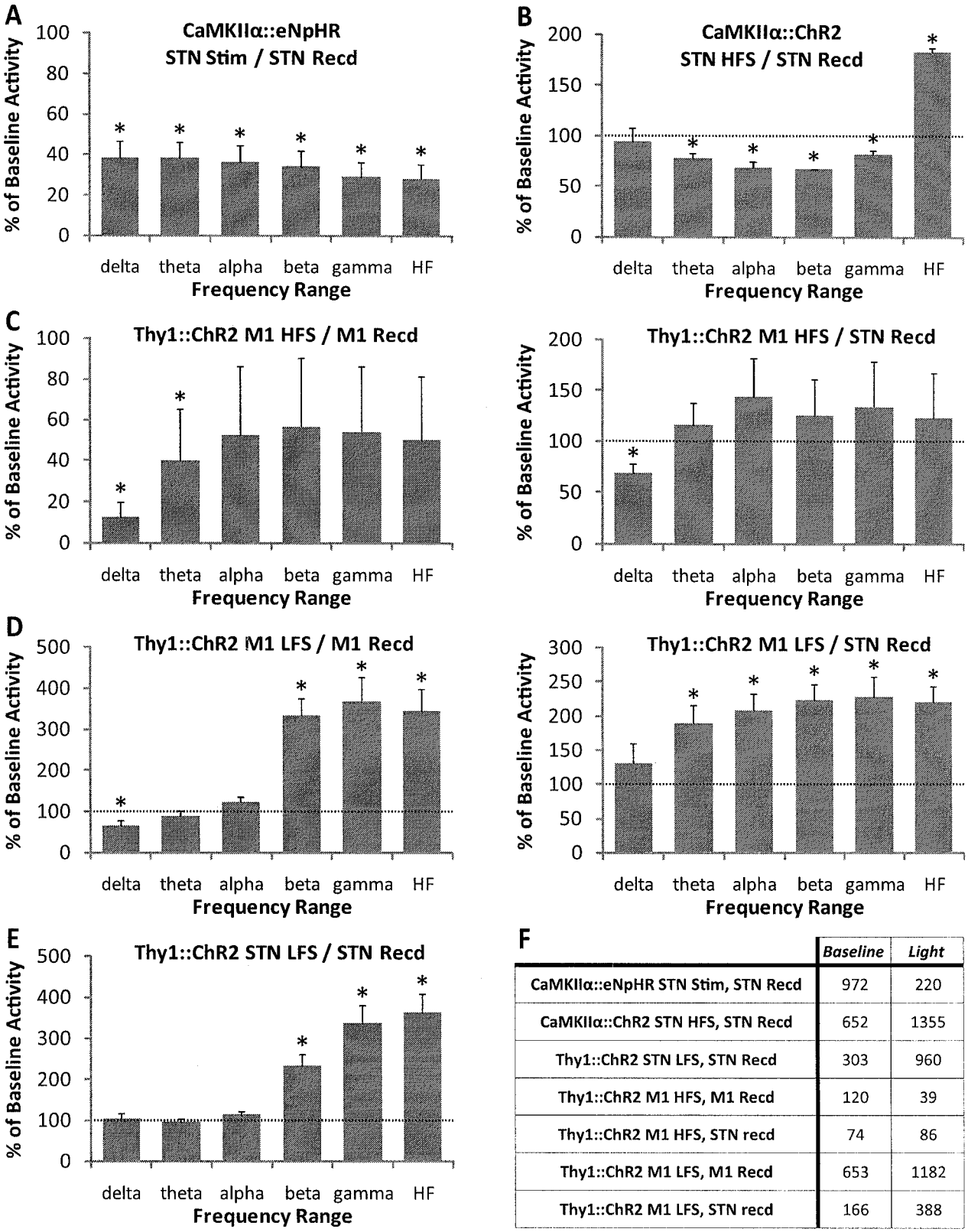

A
M1/L5 record with STN LFS
100 µV
4 s
B
STN record
200 µV
1 ms
STN stim
M1/L5 record
50 µV
1 ms
STN to M1/L5 Latency
(1.396 ± 0.032 S.D.) ms
C
STN to M1 Spike Latency
Spike Number
18
16
14
12
10
8
6
4
2
0
1
1.2
1.4
1.6
1
Latency (ms)

Figure 16



F

	Baseline	*Light*
CaMKIIα::eNpHR STN Stim, STN Recd	972	220
CaMKIIα::ChR2 STN HFS, STN Recd	652	1355
Thy1::ChR2 STN LFS, STN Recd	303	960
Thy1::ChR2 M1 HFS, M1 Recd	120	39
Thy1::ChR2 M1 HFS, STN recd	74	86
Thy1::ChR2 M1 LFS, M1 Recd	653	1182
Thy1::ChR2 M1 LFS, STN recd	166	388