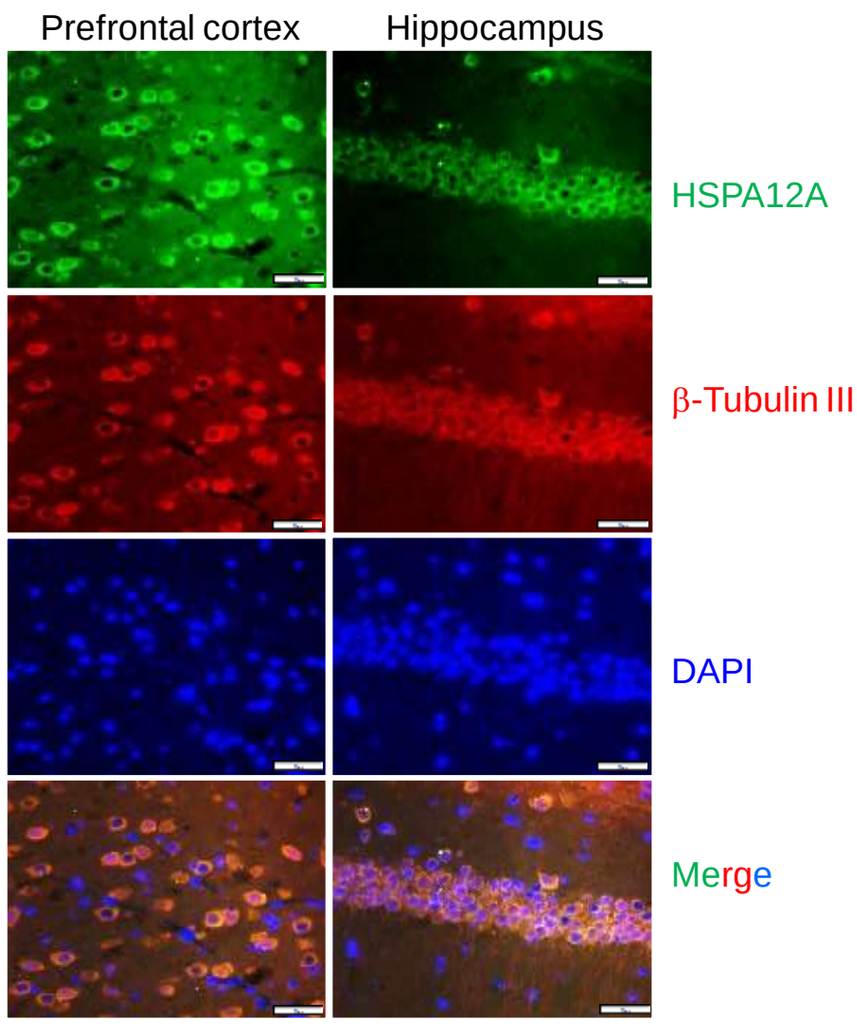
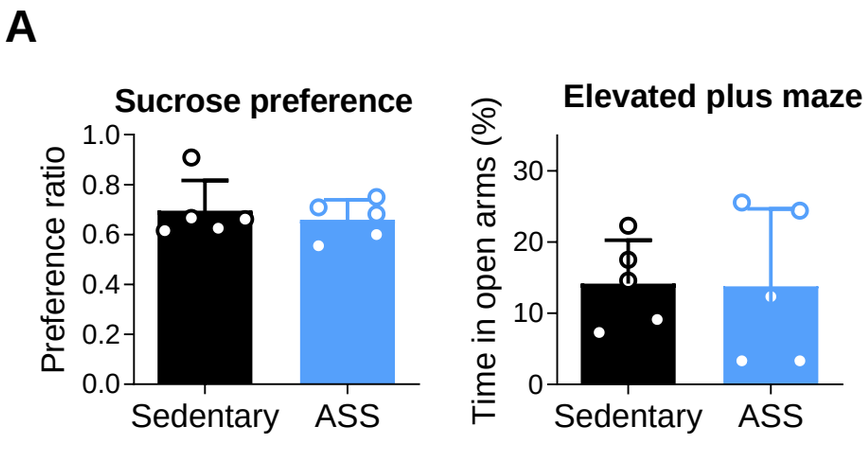
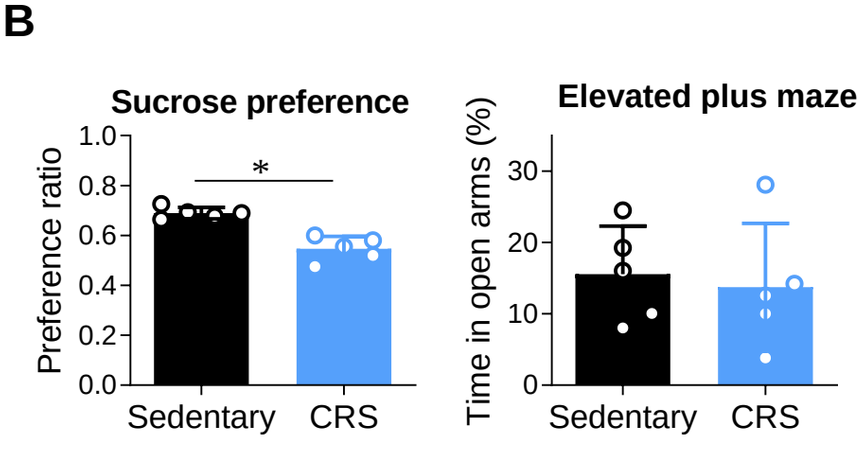
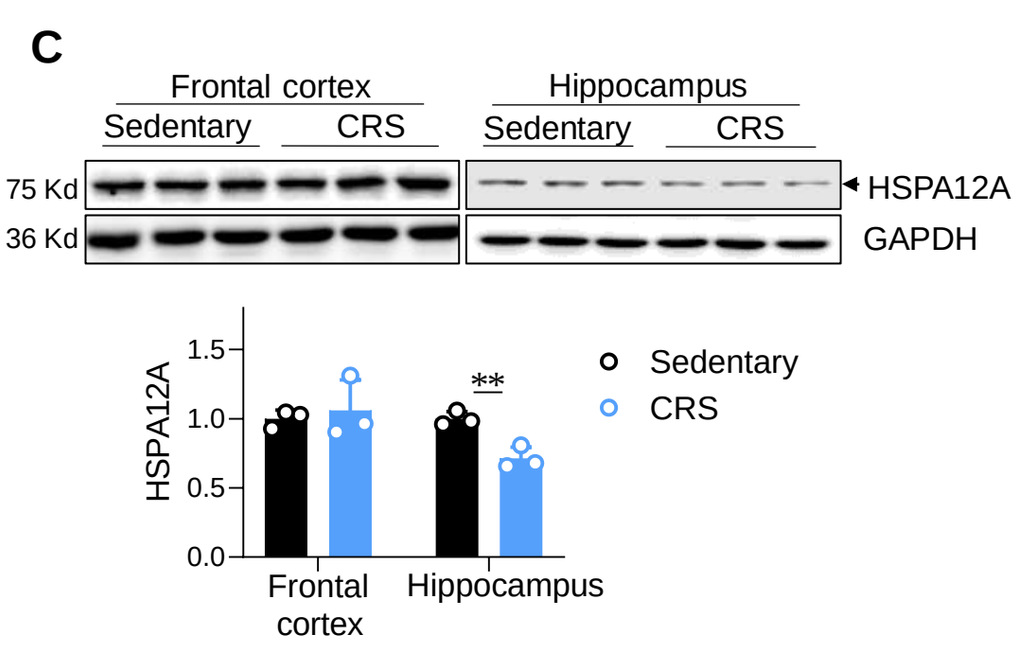
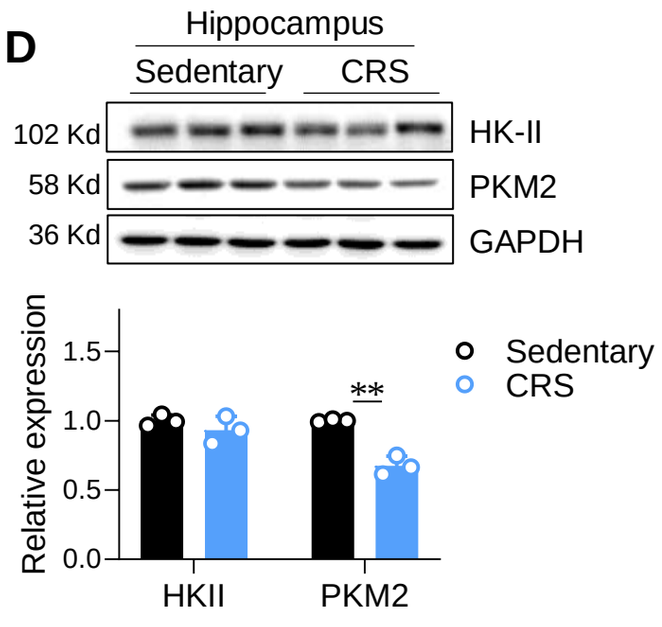

Prefrontal cortex
Hippocampus
HSPA12A
β-Tubulin III
DAPI
Merge

Figure S1


A
Sucrose preference
Preference ratio
1.0
0.8
0.6
0.4
0.2
0.0
Sedentary
ASS
Elevated plus maze
Time in open arms (%)
30
20
10
0
Sedentary
ASS


B
Sucrose preference
Preference ratio
1.0
0.8
0.6
0.4
0.2
0.0
*
Sedentary
CRS
Elevated plus maze
Time in open arms (%)
30
20
10
0
Sedentary
CRS


C
Frontal cortex
Hippocampus
Sedentary
CRS
Sedentary
CRS
75 Kd
36 Kd
HSPA12A
GAPDH
HSPA12A
1.5
1.0
0.5
0.0
**
Sedentary
CRS
Frontal cortex
Hippocampus


D
Hippocampus
Sedentary
CRS
102 Kd
58 Kd
36 Kd
HK-II
PKM2
GAPDH
Relative expression
1.5
1.0
0.5
0.0
**
Sedentary
CRS
HKII
PKM2

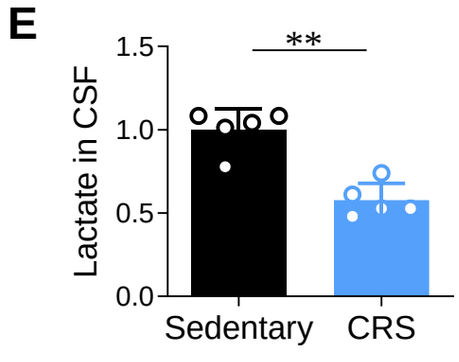

E
Lactate in CSF
1.5
1.0
0.5
0.0
**
Sedentary
CRS

Figure S2

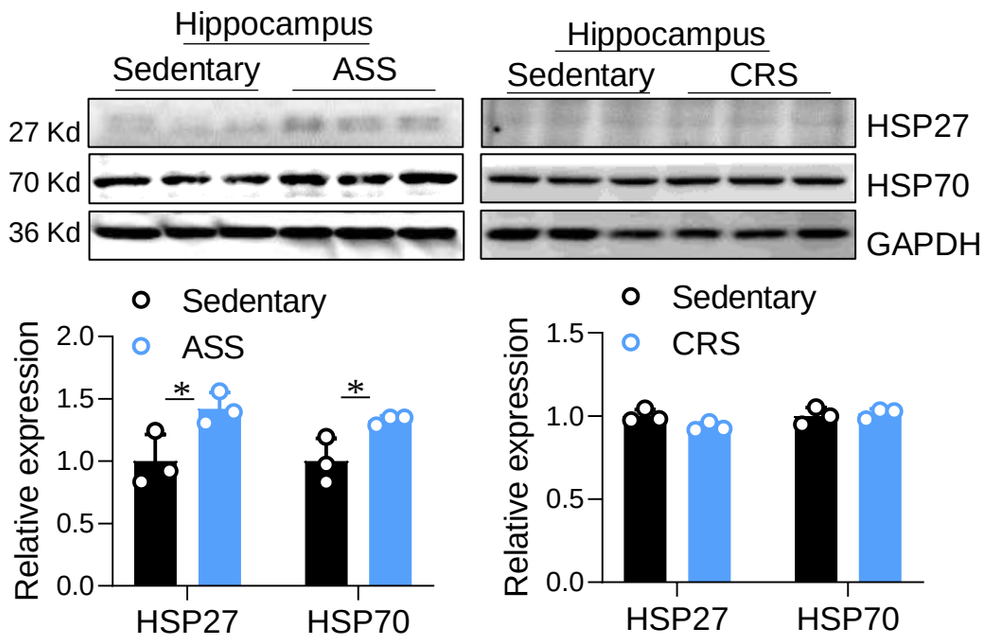

Hippocampus
Sedentary
ASS
Hippocampus
Sedentary
CRS
27 Kd
70 Kd
36 Kd
HSP27
HSP70
GAPDH
Sedentary
ASS
Relative expression
2.0
1.5
1.0
0.5
0.0
*
*
HSP27
HSP70
Sedentary
CRS
Relative expression
1.5
1.0
0.5
0.0
HSP27
HSP70

Figure S3

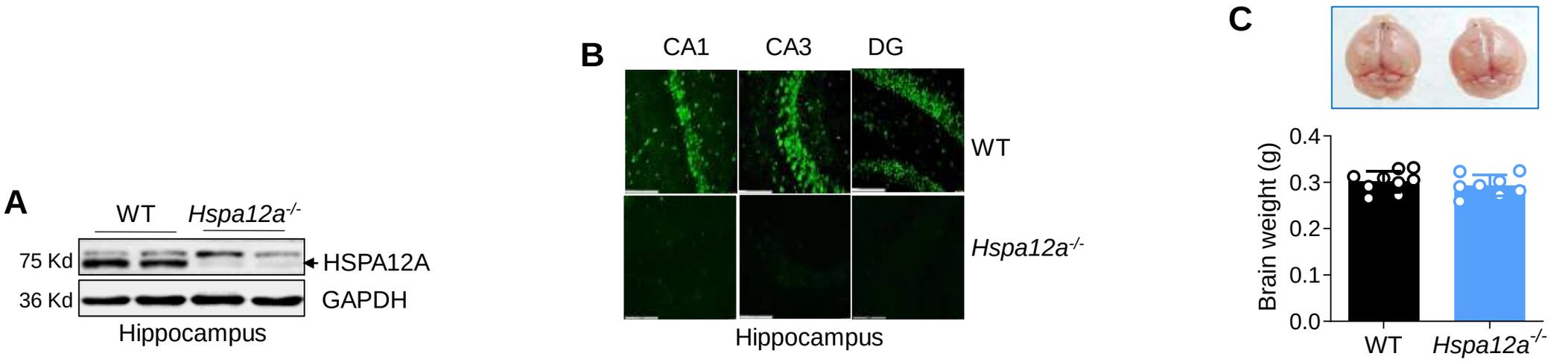

A
WT
Hspa12a-/-
75 Kd
HSPA12A
36 Kd
GAPDH
Hippocampus
B
CA1
CA3
DG
WT
Hspa12a-/-
Hippocampus
C
Brain weight (g)
0.4
0.3
0.2
0.1
0.0
WT
Hspa12a-/-

Figure S4

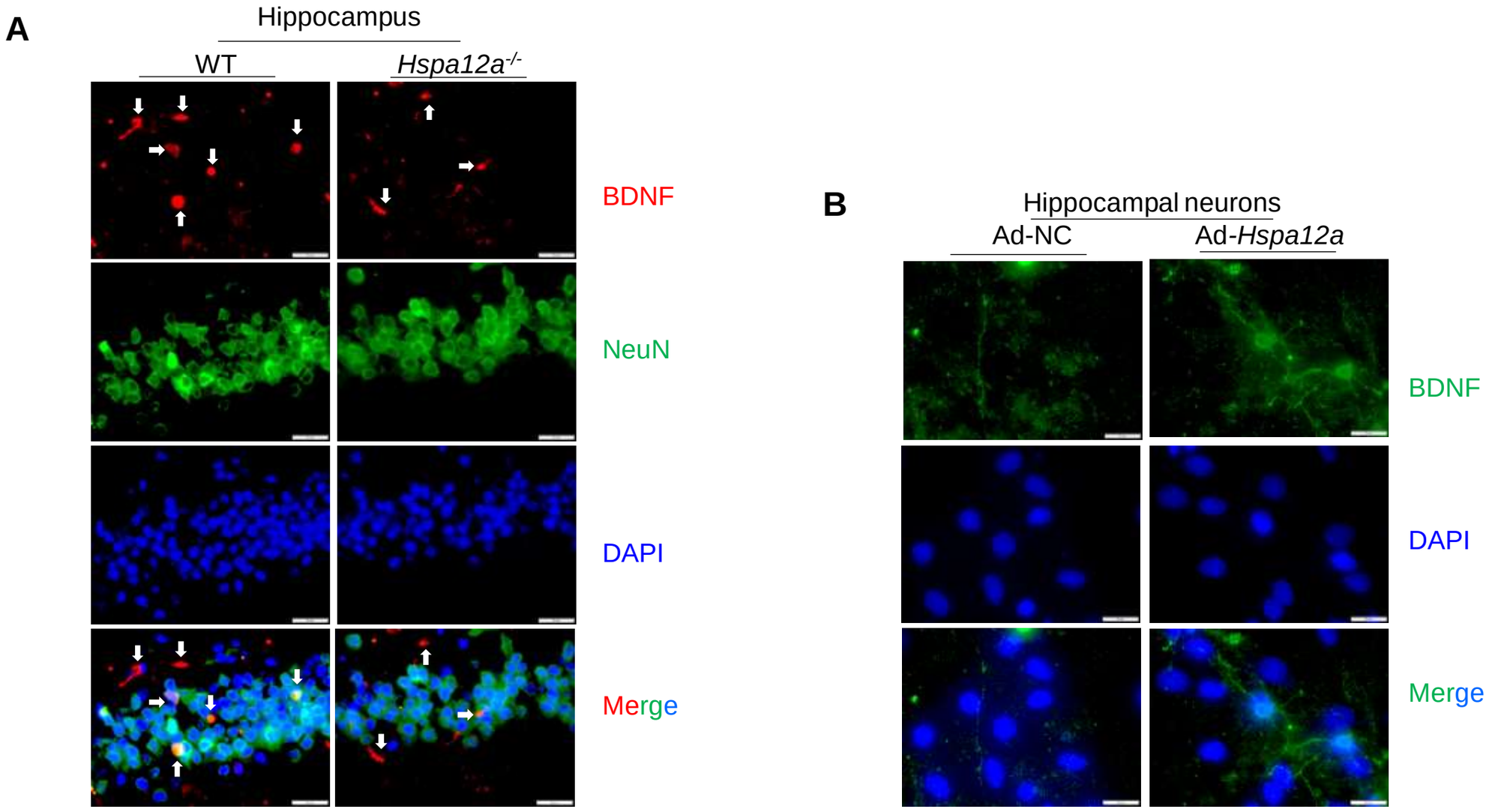
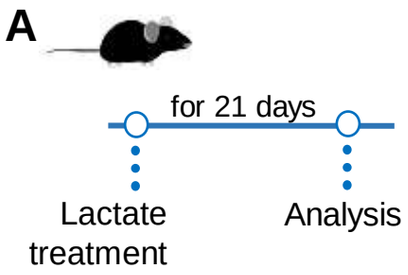

A
Hippocampus
WT
Hspa12a-/-
BDNF
NeuN
DAPI
Merge
B
Hippocampal neurons
Ad-NC
Ad-Hspa12a
BDNF
DAPI
Merge

Figure S5


A
for 21 days
Lactate treatment
Analysis

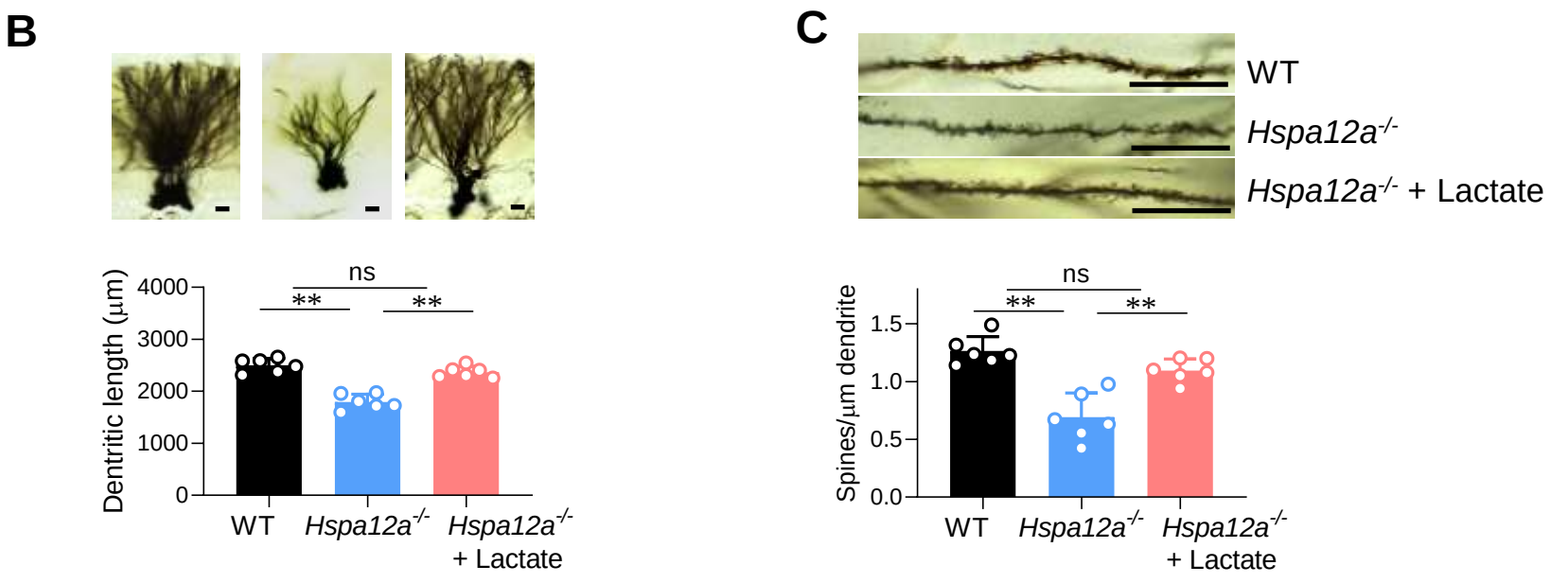

B
Dentritic length (μm)
4000
3000
2000
1000
0
ns
**
**
WT
Hspa12a-/-
Hspa12a-/- + Lactate
C
WT
Hspa12a-/-
Hspa12a-/- + Lactate
Spines/μm dendrite
1.5
1.0
0.5
0.0
ns
**
**
WT
Hspa12a-/-
Hspa12a-/- + Lactate

Figure S6

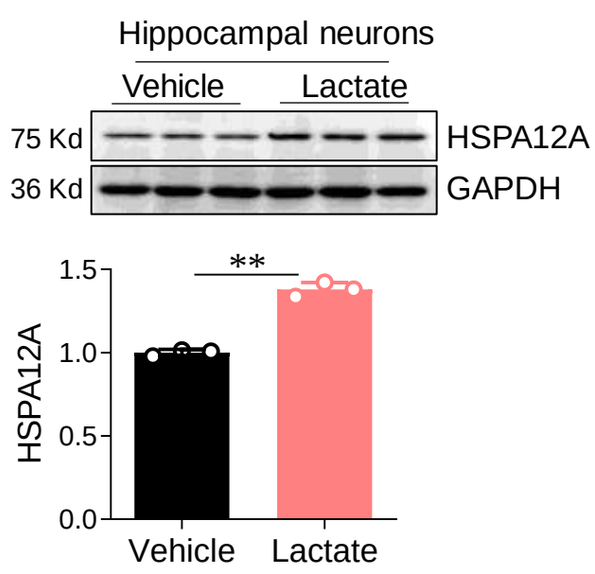

Hippocampal neurons
Vehicle
Lactate
75 Kd
HSPA12A
36 Kd
GAPDH
HSPA12A
1.5
1.0
0.5
0.0
**
Vehicle
Lactate

Figure S7

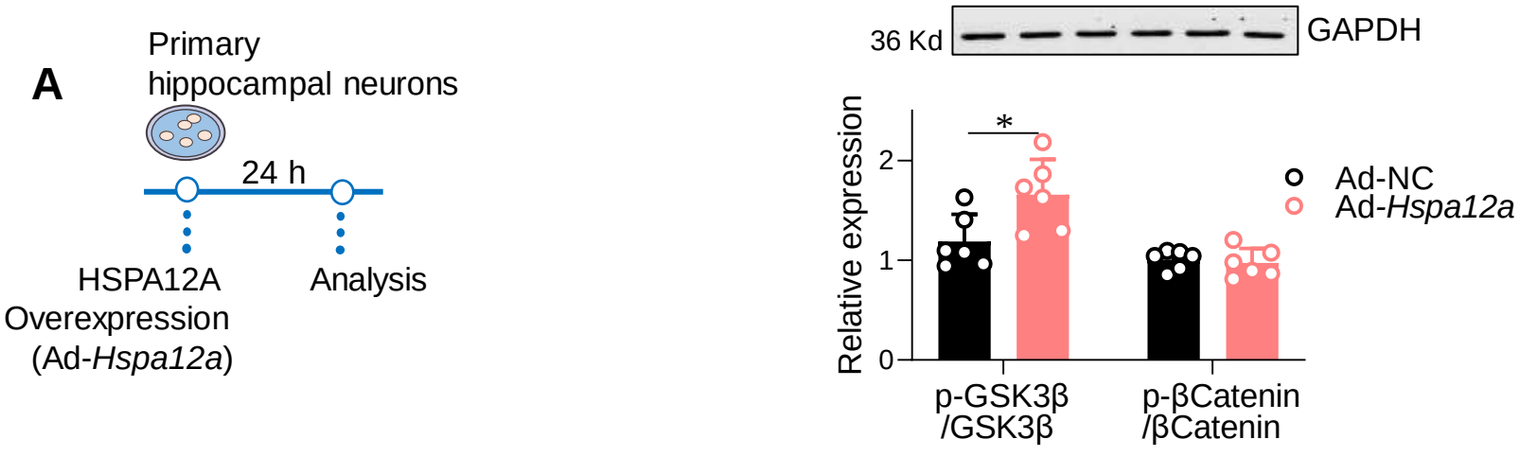
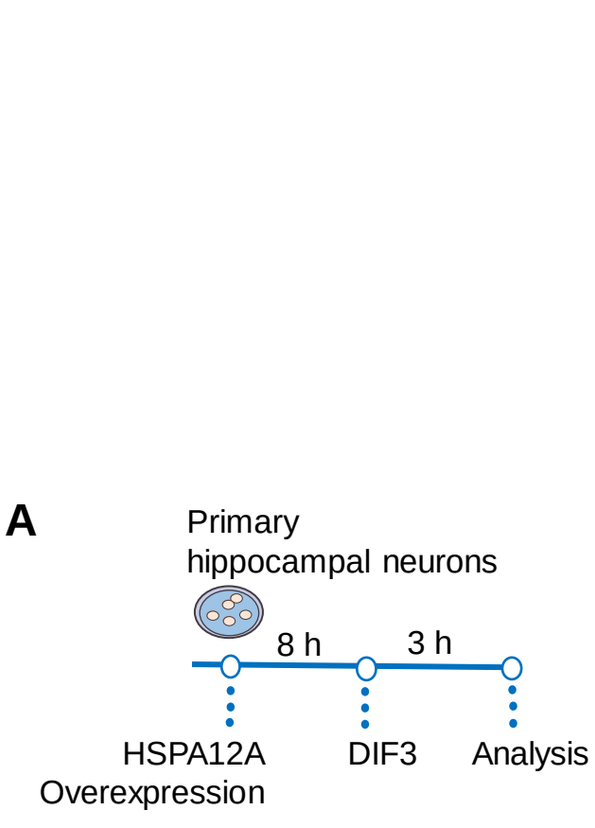
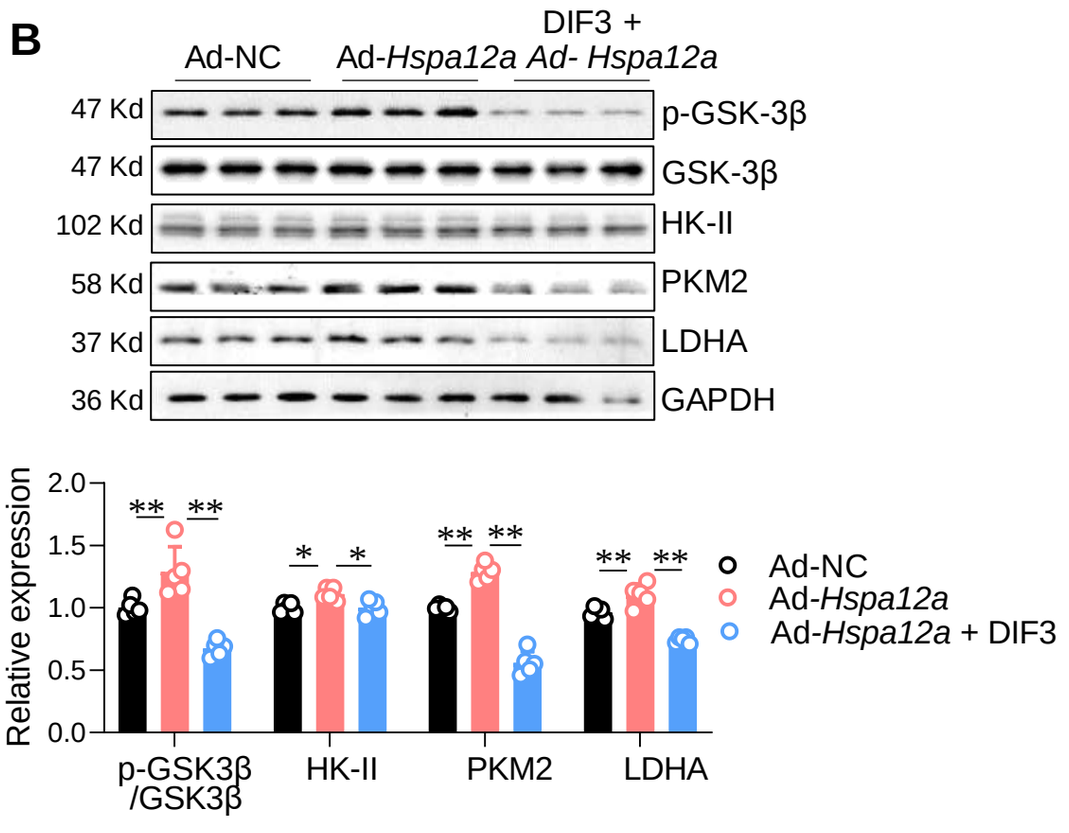
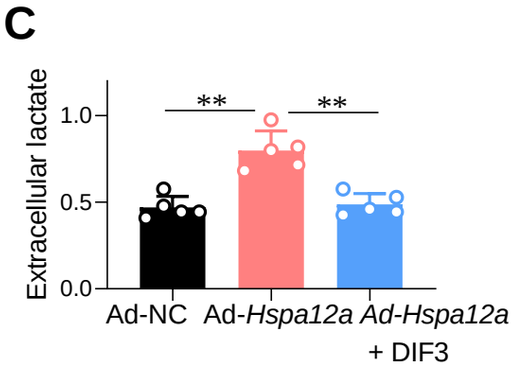
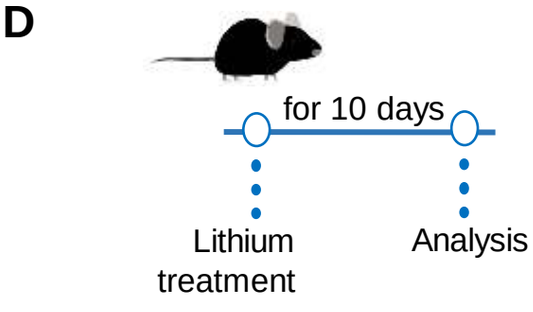

A
Primary
hippocampal neurons
24 h
HSPA12A
Overexpression
(Ad-Hspa12a)
Analysis
B
Hippocampal neurons
Ad-NC
Ad-Hspa12a
75 Kd
HSPA12A
47 Kd
p-GSK3β
47 Kd
GSK3β
92 Kd
p-βCatenin
92 Kd
βCatenin
36 Kd
GAPDH
Relative expression
2
1
0
*
Ad-NC
Ad-Hspa12a
p-GSK3β
/GSK3β
p-βCatenin
/βCatenin

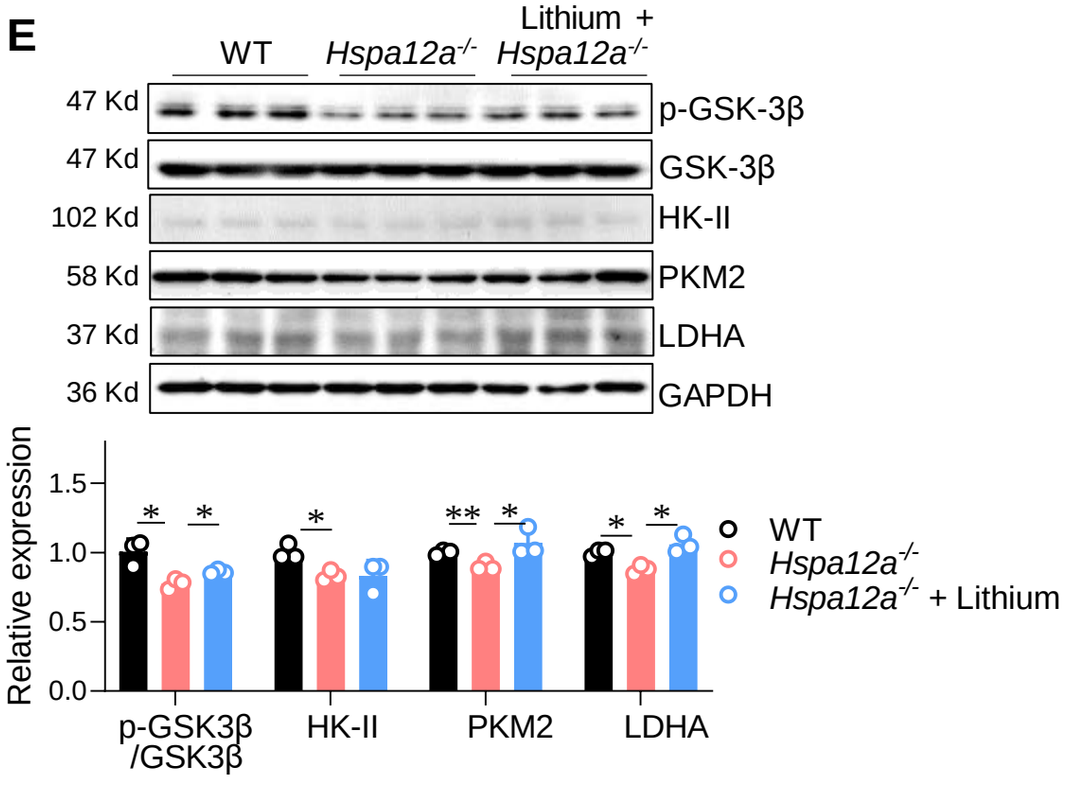
Figure S8


A
Primary
hippocampal neurons
8 h
3 h
HSPA12A
Overexpression
DIF3
Analysis


B
Ad-NC
Ad-Hspa12a
DIF3 +
Ad- Hspa12a
47 Kd
p-GSK-3β
47 Kd
GSK-3β
102 Kd
HK-II
58 Kd
PKM2
37 Kd
LDHA
36 Kd
GAPDH
Relative expression
2.0
1.5
1.0
0.5
0.0
p-GSK3β
/GSK3β
HK-II
PKM2
LDHA
Ad-NC
Ad-Hspa12a
Ad-Hspa12a + DIF3


C
Extracellular lactate
1.0
0.5
0.0
Ad-NC
Ad-Hspa12a
Ad-Hspa12a
+ DIF3


D
for 10 days
Lithium
treatment
Analysis


E
WT
Hspa12a-/-
Lithium +
Hspa12a-/-
47 Kd
p-GSK-3β
47 Kd
GSK-3β
102 Kd
HK-II
58 Kd
PKM2
37 Kd
LDHA
36 Kd
GAPDH
Relative expression
1.5
1.0
0.5
0.0
p-GSK3β
/GSK3β
HK-II
PKM2
LDHA
WT
Hspa12a-/-
Hspa12a-/- + Lithium

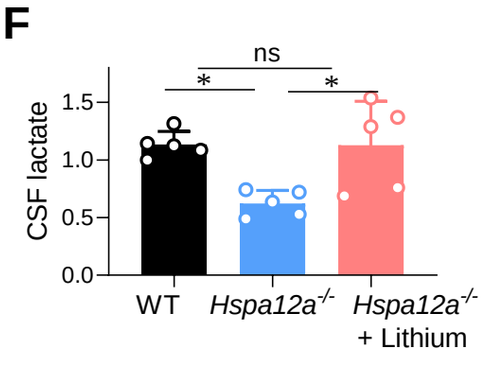

F
ns
CSF lactate
1.5
1.0
0.5
0.0
WT
Hspa12a-/-
Hspa12a-/-
+ Lithium

Figure S9

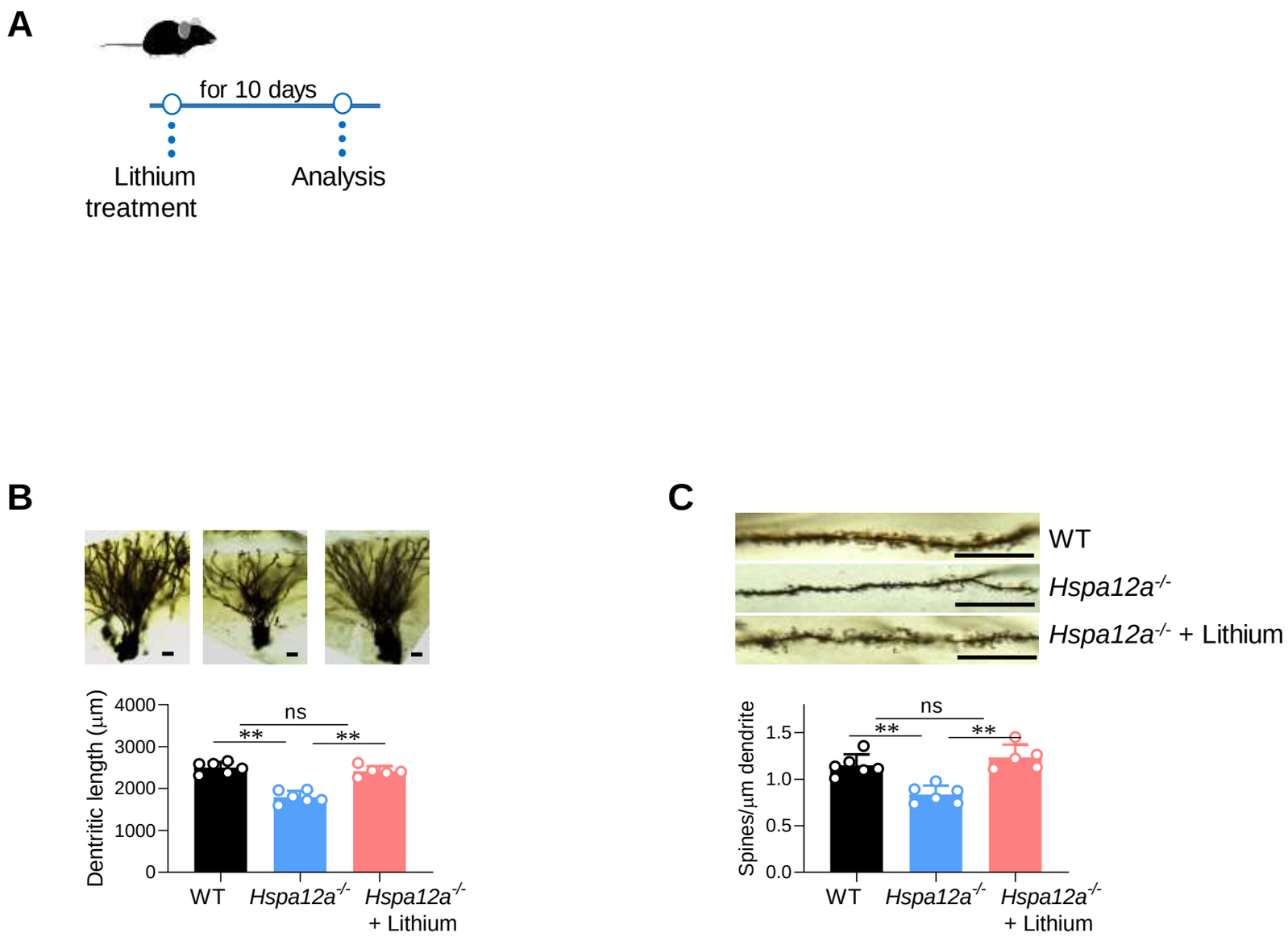
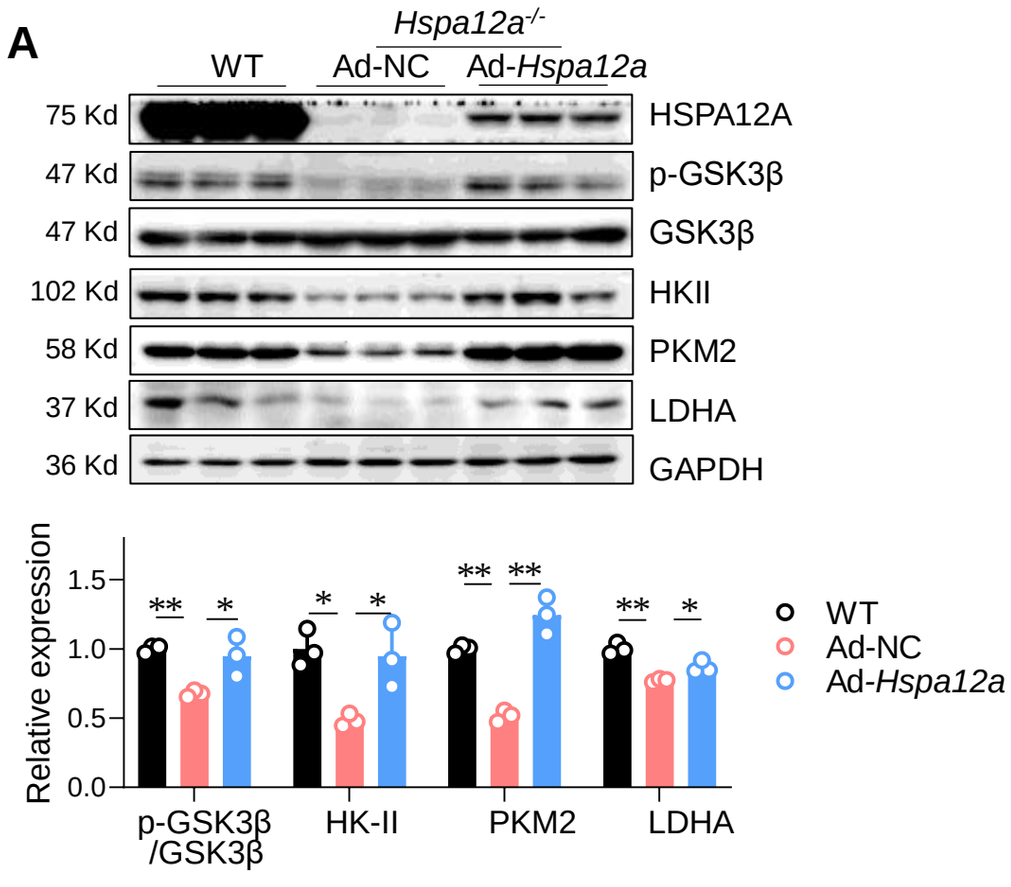
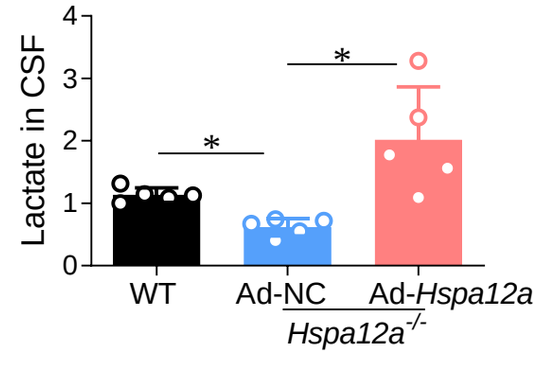

A
for 10 days
Lithium treatment
Analysis
B
C
WT
Hspa12a-/-
Hspa12a-/- + Lithium
Dentritic length (μm)
4000
3000
2000
1000
0
ns
**
**
WT
Hspa12a-/-
Hspa12a-/- + Lithium
Spines/μm dendrite
1.5
1.0
0.5
0.0
ns
**
**
WT
Hspa12a-/-
Hspa12a-/- + Lithium

Figure S10


A
Hspa12a-/-
WT
Ad-NC
Ad-Hspa12a
75 Kd
HSPA12A
47 Kd
p-GSK3β
47 Kd
GSK3β
102 Kd
HKII
58 Kd
PKM2
37 Kd
LDHA
36 Kd
GAPDH
Relative expression
1.5
1.0
0.5
0.0
p-GSK3β /GSK3β
HK-II
PKM2
LDHA
WT
Ad-NC
Ad-Hspa12a


B
Lactate in CSF
4
3
2
1
0
WT
Ad-NC
Ad-Hspa12a
Hspa12a-/-

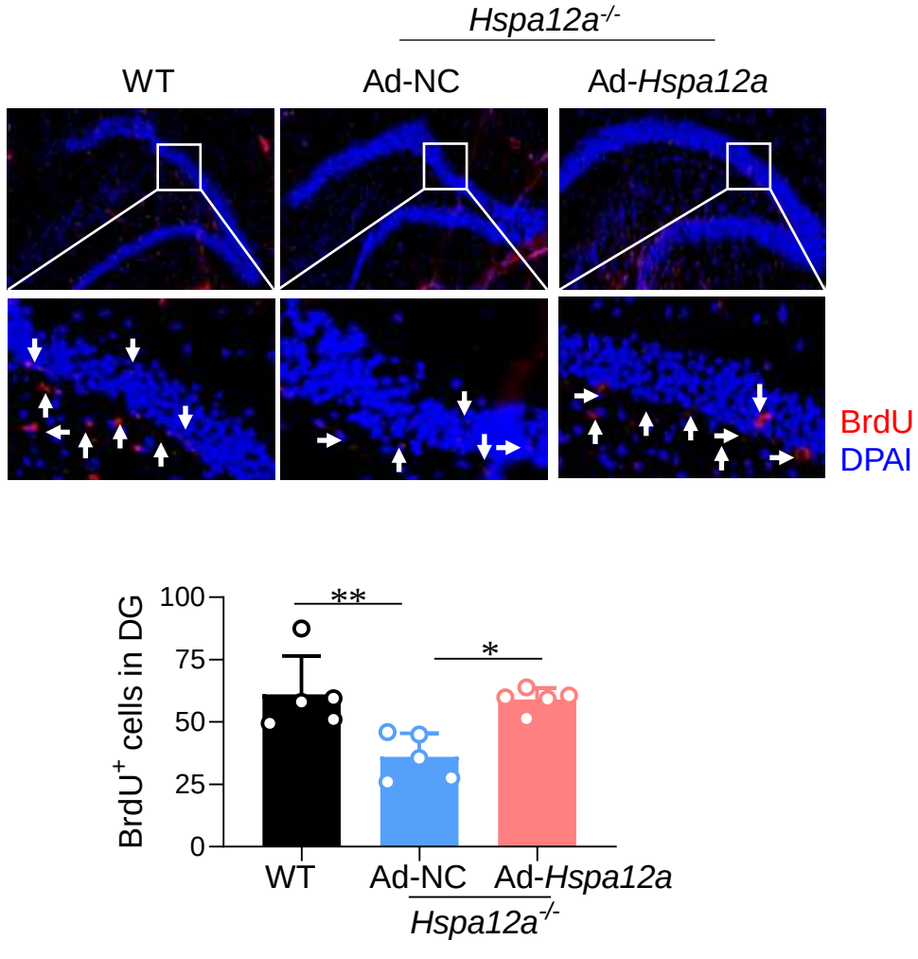

C
Hspa12a-/-
WT
Ad-NC
Ad-Hspa12a
BrdU
DPAI
BrdU+ cells in DG
100
75
50
25
0
WT
Ad-NC
Ad-Hspa12a
Hspa12a-/-

Figure S11

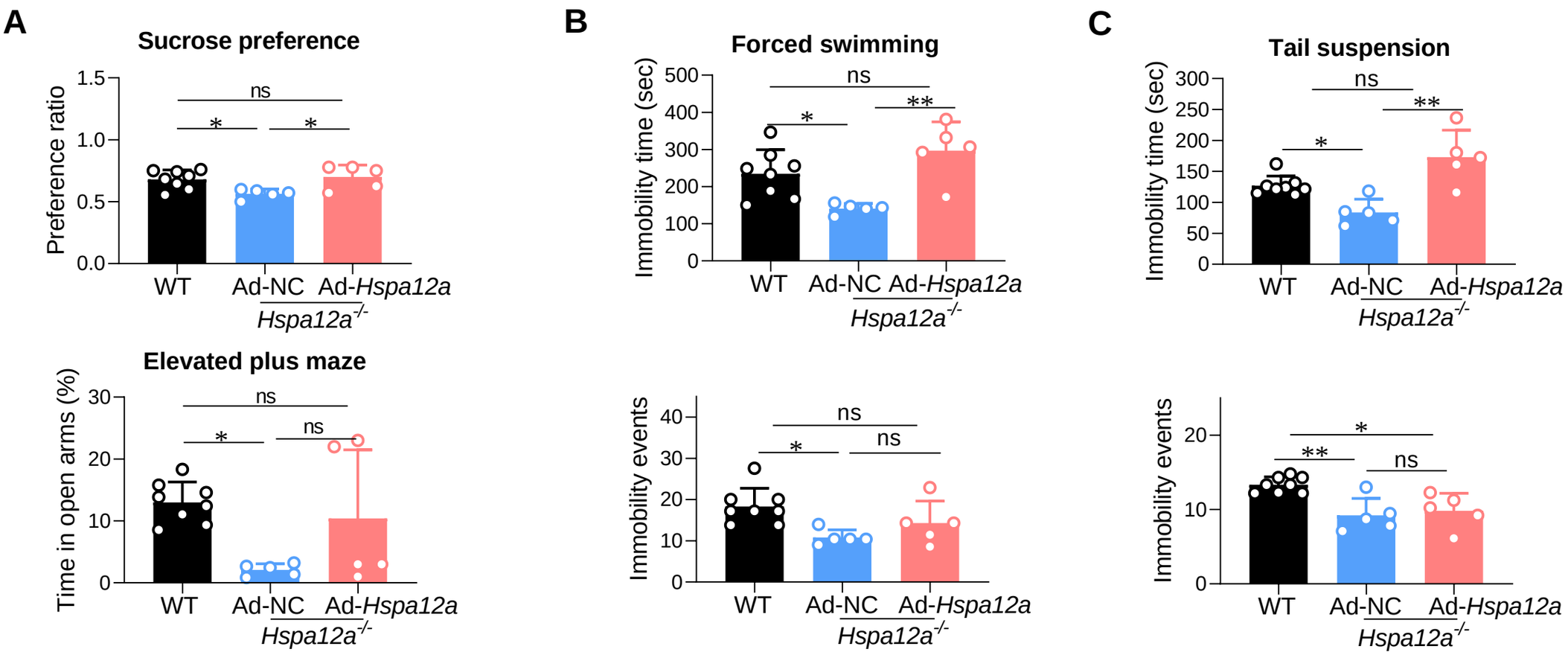

A
Sucrose preference
Preference ratio
1.5
1.0
0.5
0.0
ns
*
*
WT
Ad-NC
Ad-Hspa12a
Hspa12a-/-
B
Forced swimming
Immobility time (sec)
500
400
300
200
100
0
ns
*
**
WT
Ad-NC
Ad-Hspa12a
Hspa12a-/-
C
Tail suspension
Immobility time (sec)
300
250
200
150
100
50
0
ns
**
*
WT
Ad-NC
Ad-Hspa12a
Hspa12a-/-
Elevated plus maze
Time in open arms (%)
30
20
10
0
ns
*
ns
WT
Ad-NC
Ad-Hspa12a
Hspa12a-/-
Immobility events
40
30
20
10
0
ns
*
ns
WT
Ad-NC
Ad-Hspa12a
Hspa12a-/-
Immobility events
20
10
0
*
**
ns
WT
Ad-NC
Ad-Hspa12a
Hspa12a-/-

Figure S12