Fig. 1

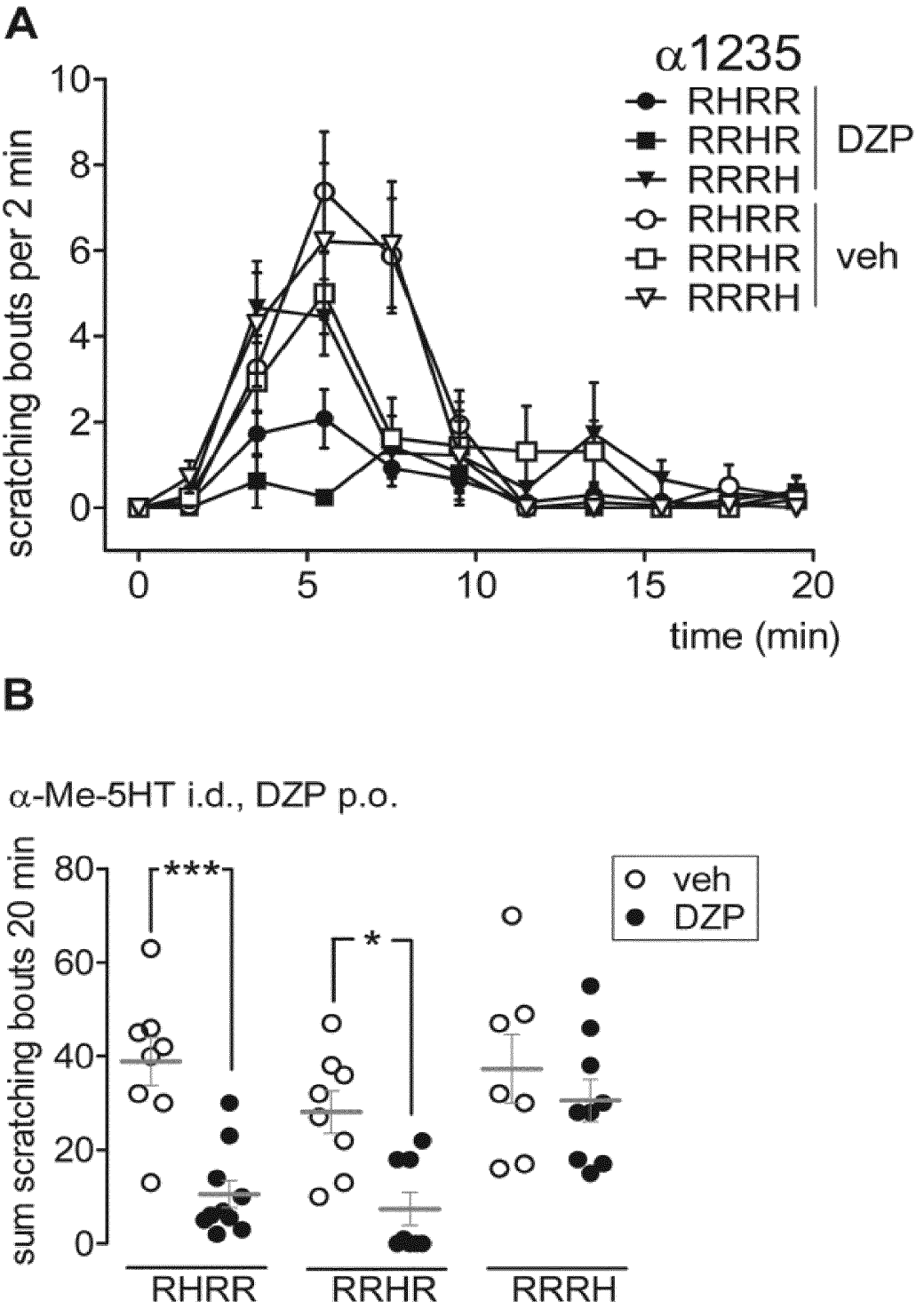
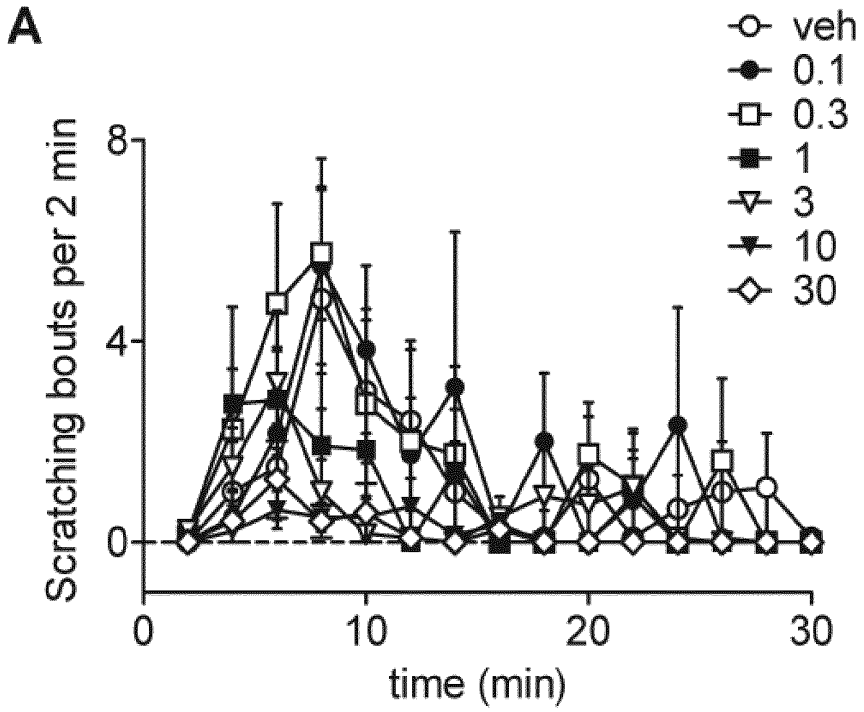

A
α1235
RHRR
RRHR
RRRH
DZP
RHRR
RRHR
RRRH
veh
scratching bouts per 2 min
time (min)
B
α-Me-5HT i.d., DZP p.o.
sum scratching bouts 20 min
***
*
veh
DZP
RHRR
RRHR
RRRH

Fig. 2a, b


A
veh
0.1
0.3
1
3
10
30
Scratching bouts per 2 min
8
4
0
0
10
20
30
time (min)

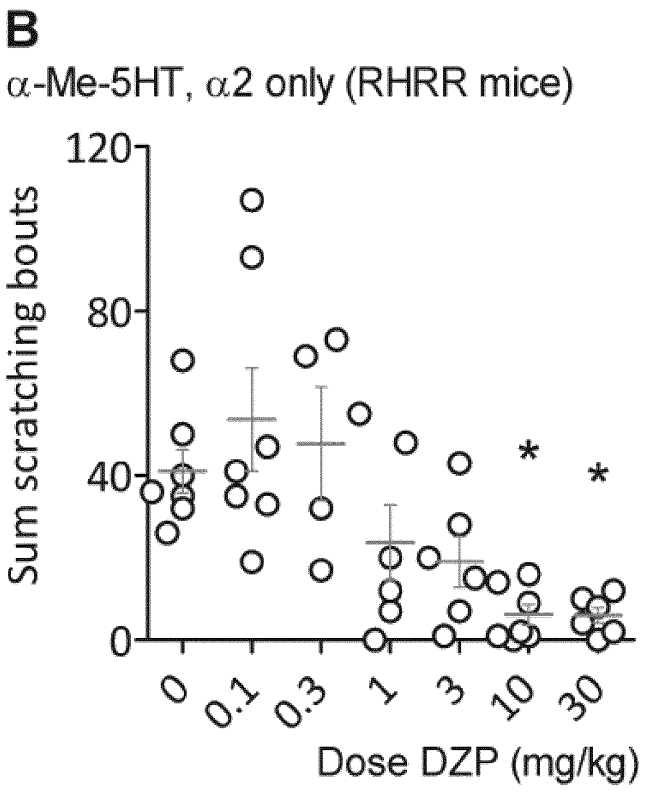

B
α-Me-5HT, α2 only (RHRR mice)
Sum scratching bouts
120
80
40
0
0
0.1
0.3
1
3
10
30
Dose DZP (mg/kg)

Fig. 2c

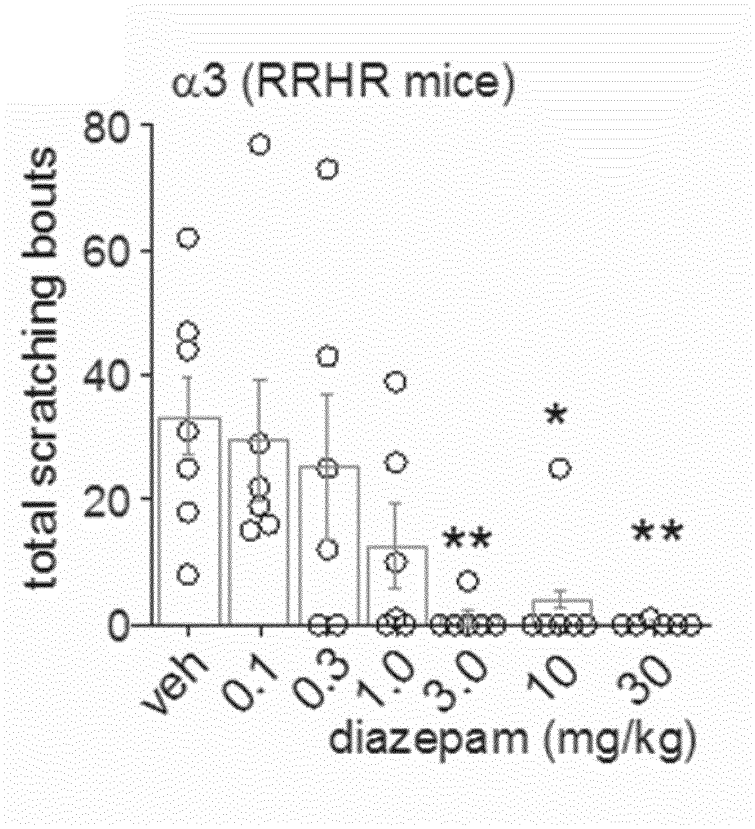

α3 (RRHR mice)
total scratching bouts
80
60
40
20
0
*
**
**
veh
0.1
0.3
1.0
3.0
10
30
diazepam (mg/kg)

Fig. 3a, b

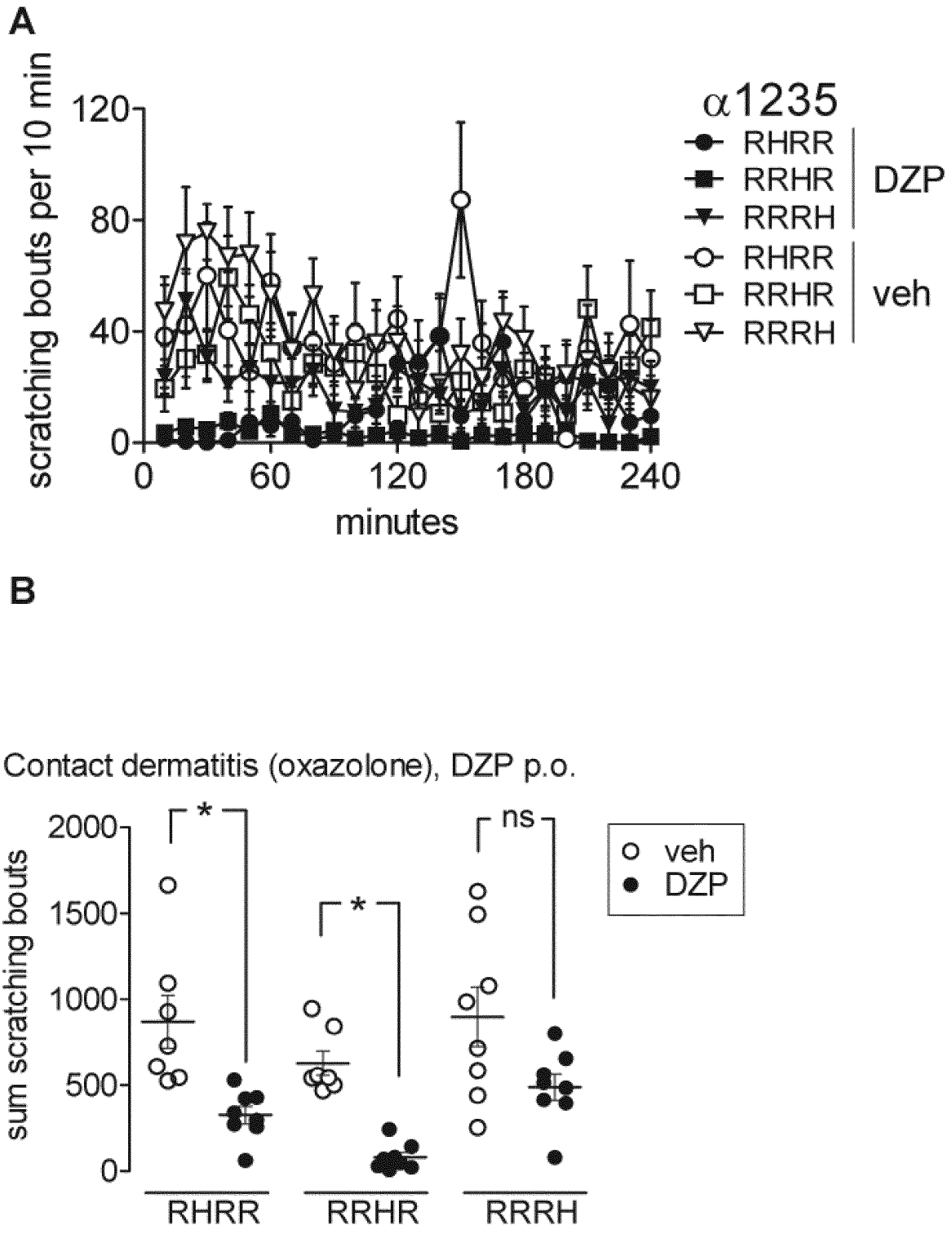

A
scratching bouts per 10 min
120
80
40
0
0
60
120
180
240
minutes
α1235
RHRR
RRHR
RRRH
DZP
RHRR
RRHR
RRRH
veh
B
Contact dermatitis (oxazolone), DZP p.o.
sum scratching bouts
2000
1500
1000
500
0
*
*
ns
RHRR
RRHR
RRRH
veh
DZP

Fig. 3 c, d

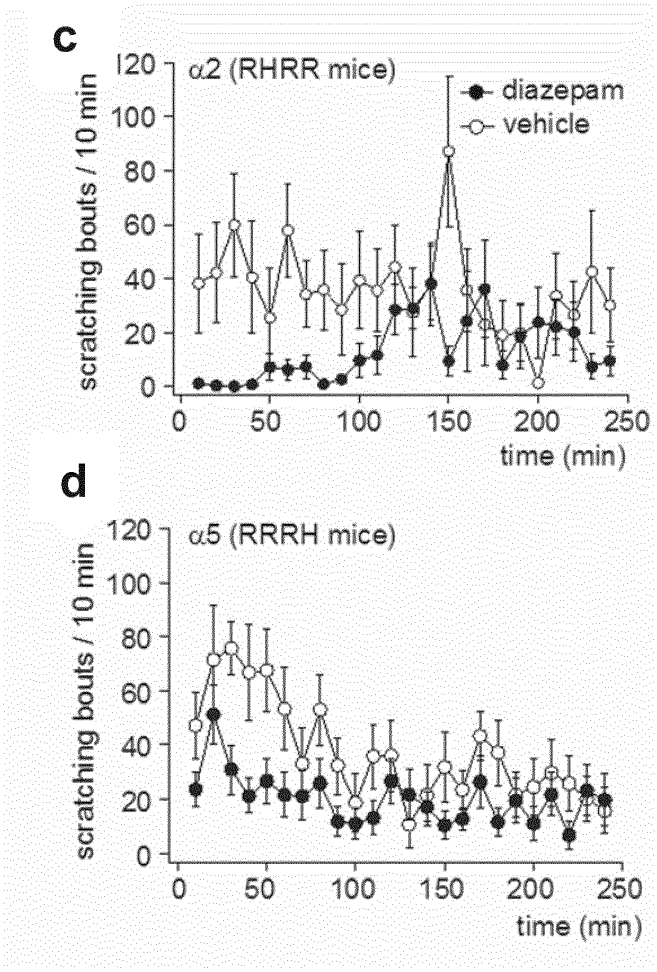


Fig. 3e

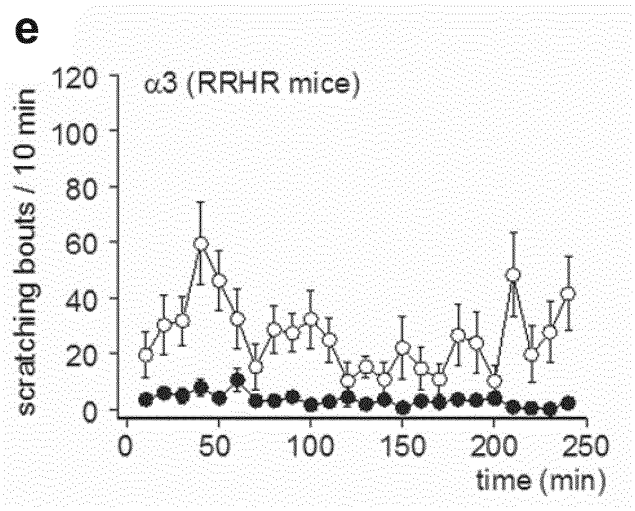


Fig. 4

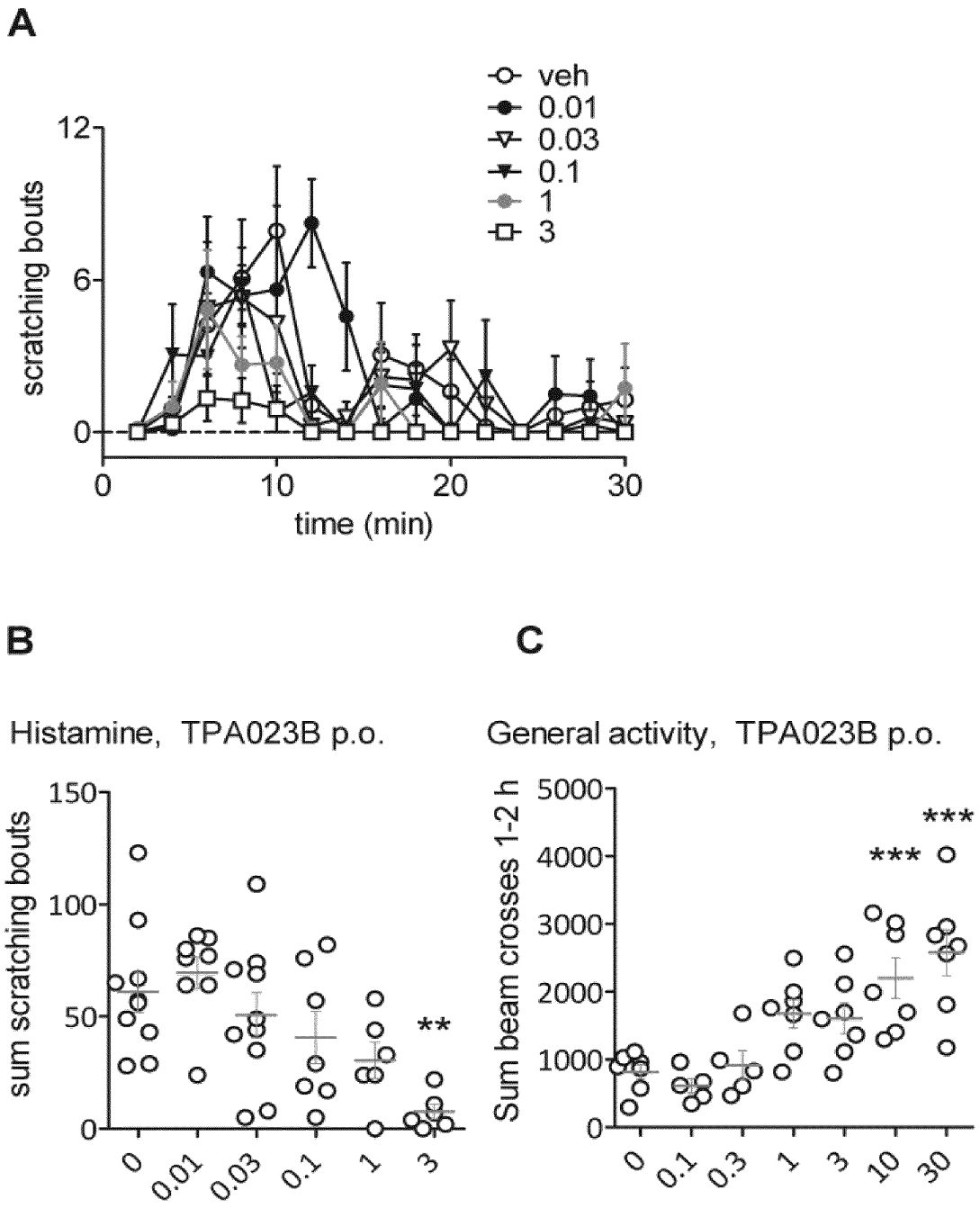
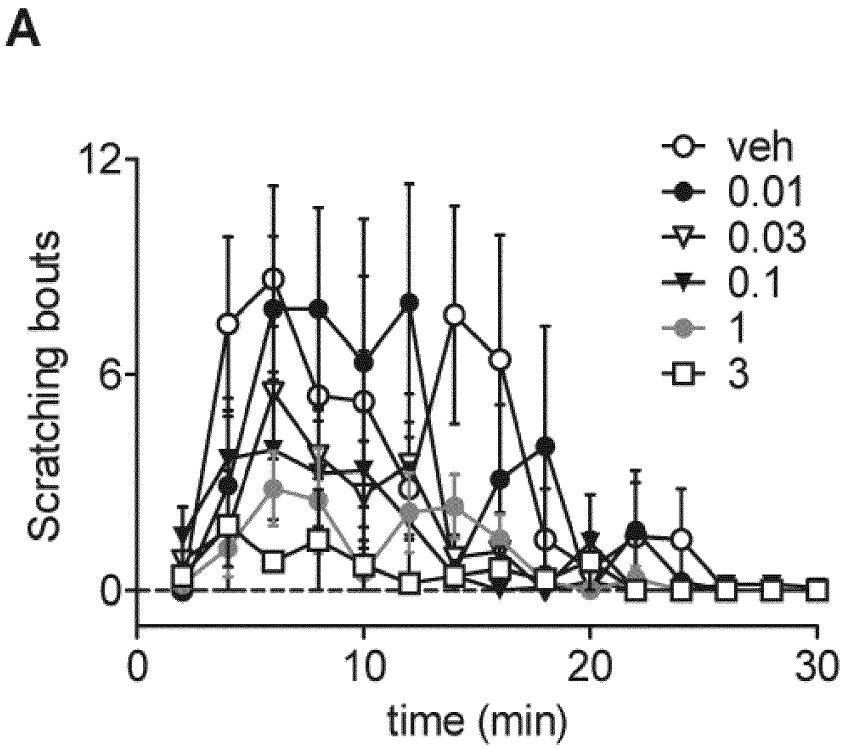

A
veh
0.01
0.03
0.1
1
3
scratching bouts
12
6
0
0
10
20
30
time (min)
B
Histamine, TPA023B p.o.
sum scratching bouts
150
100
50
0
**
0
0.01
0.03
0.1
1
3
C
General activity, TPA023B p.o.
Sum beam crosses 1-2 h
5000
4000
3000
2000
1000
0
***
***
0
0.1
0.3
1
3
10
30

Fig. 5


A
Scratching bouts
12
6
0
0
10
20
30
time (min)
veh
0.01
0.03
0.1
1
3

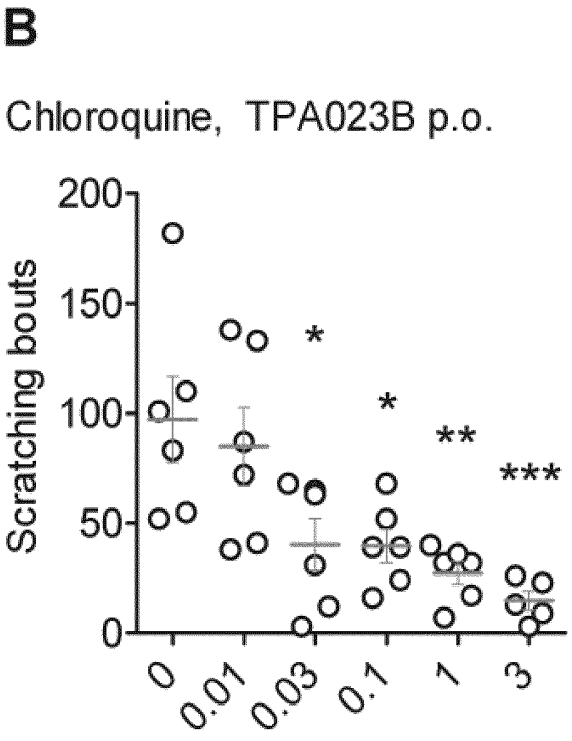
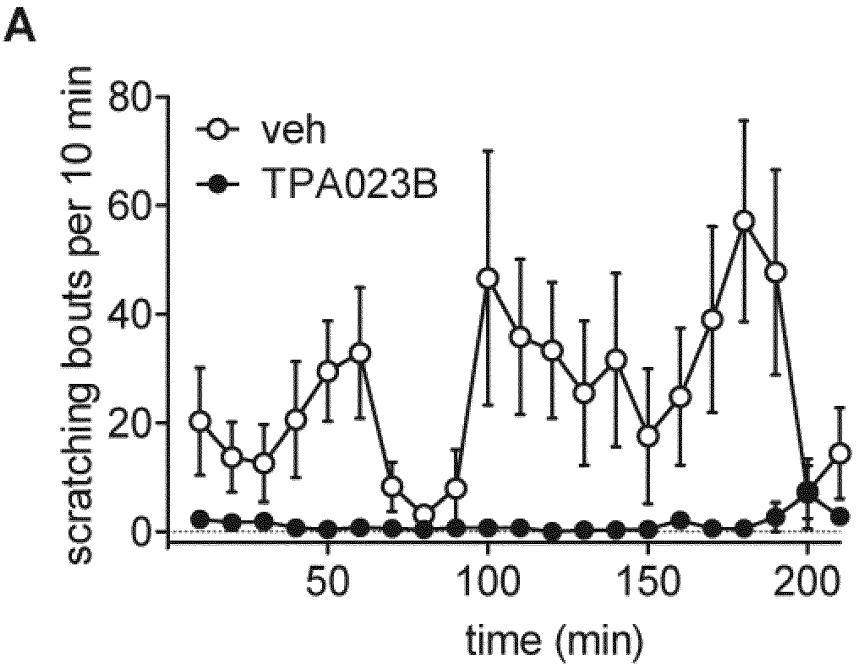

B
Chloroquine, TPA023B p.o.
Scratching bouts
200
150
100
50
0
*
*
**
***
0
0.01
0.03
0.1
1
3

Fig. 6


A
scratching bouts per 10 min
80
60
40
20
0
veh
TPA023B
50
100
150
200
time (min)

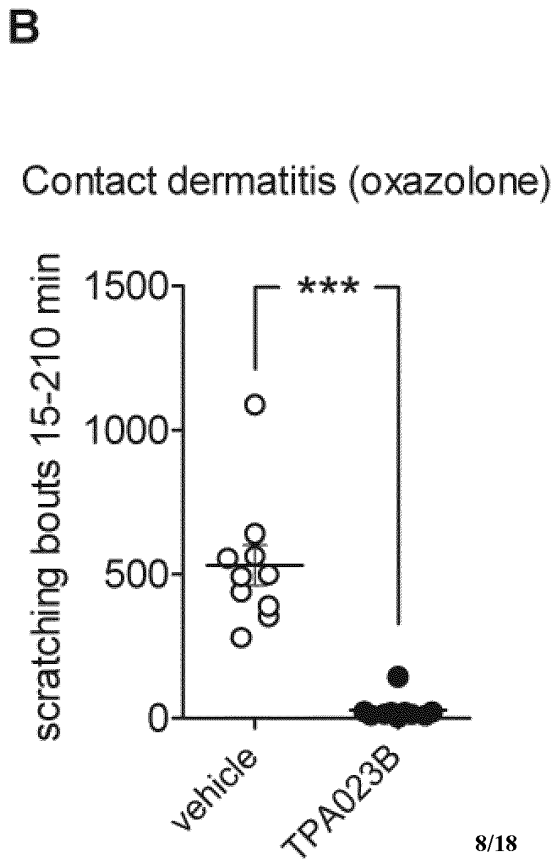
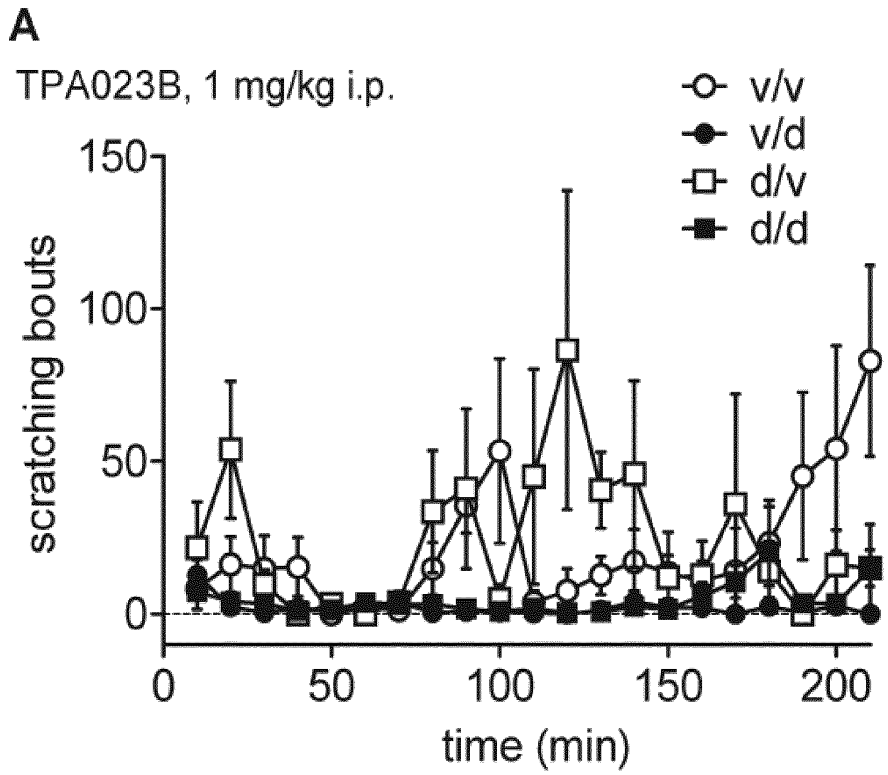

B
Contact dermatitis (oxazolone)
scratching bouts 15-210 min
1500
1000
500
0
***
vehicle
TPA023B

Fig. 7


A
TPA023B, 1 mg/kg i.p.
v/v
v/d
d/v
d/d
scratching bouts
150
100
50
0
0
50
100
150
200
time (min)

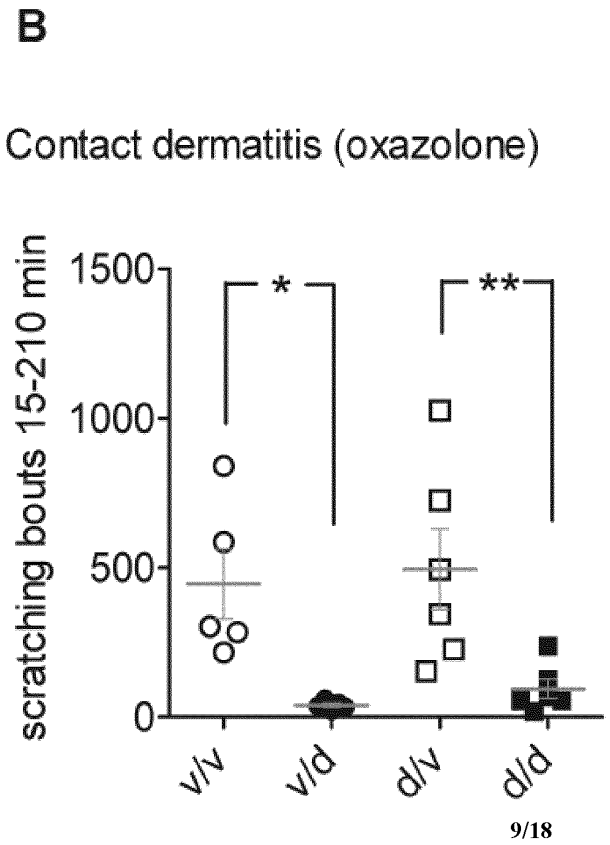
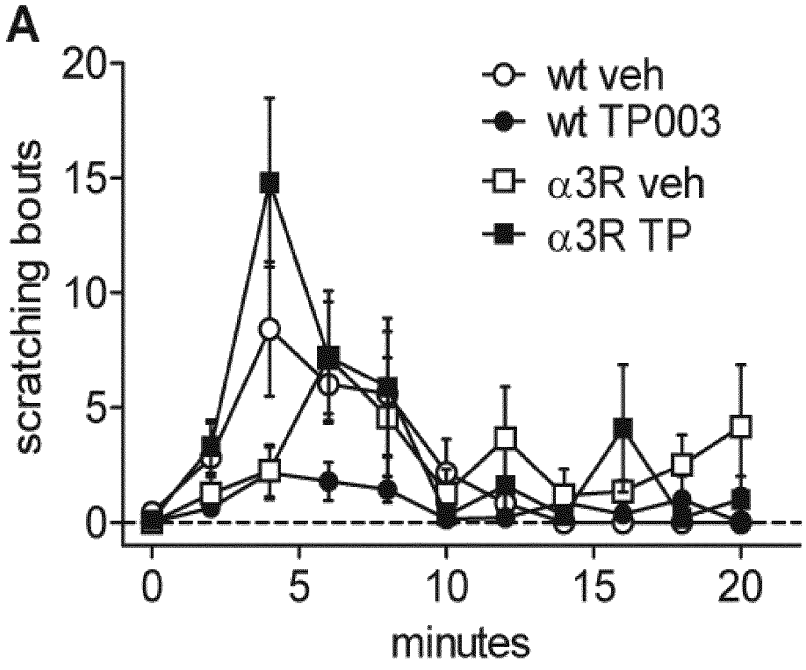

B
Contact dermatitis (oxazolone)
scratching bouts 15-210 min
1500
1000
500
0
*
**
v/v
v/d
d/v
d/d

Fig. 8


A
scratching bouts
20
15
10
5
0
0
5
10
15
20
minutes
wt veh
wt TP003
α3R veh
α3R TP

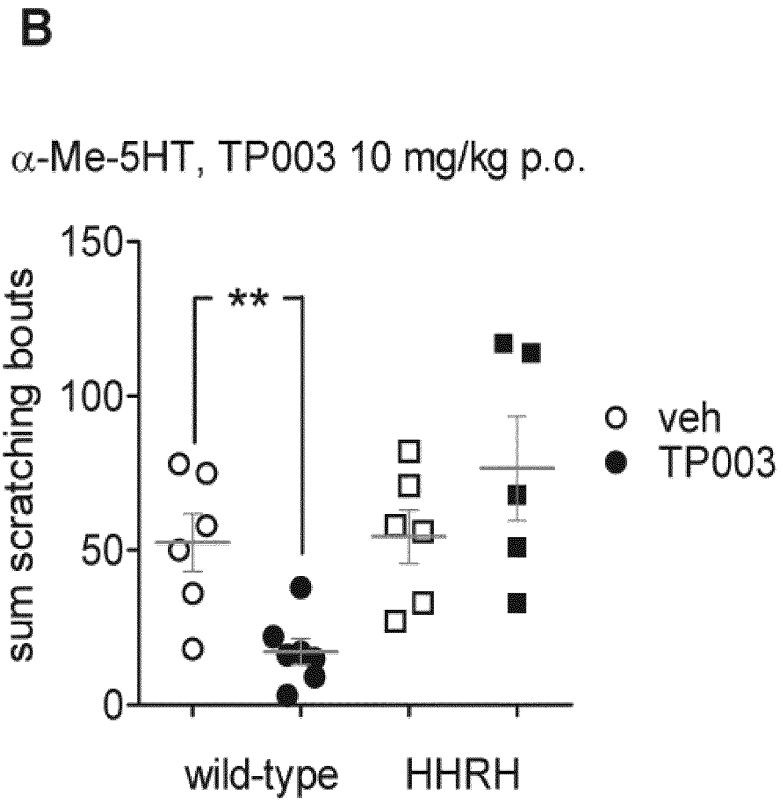
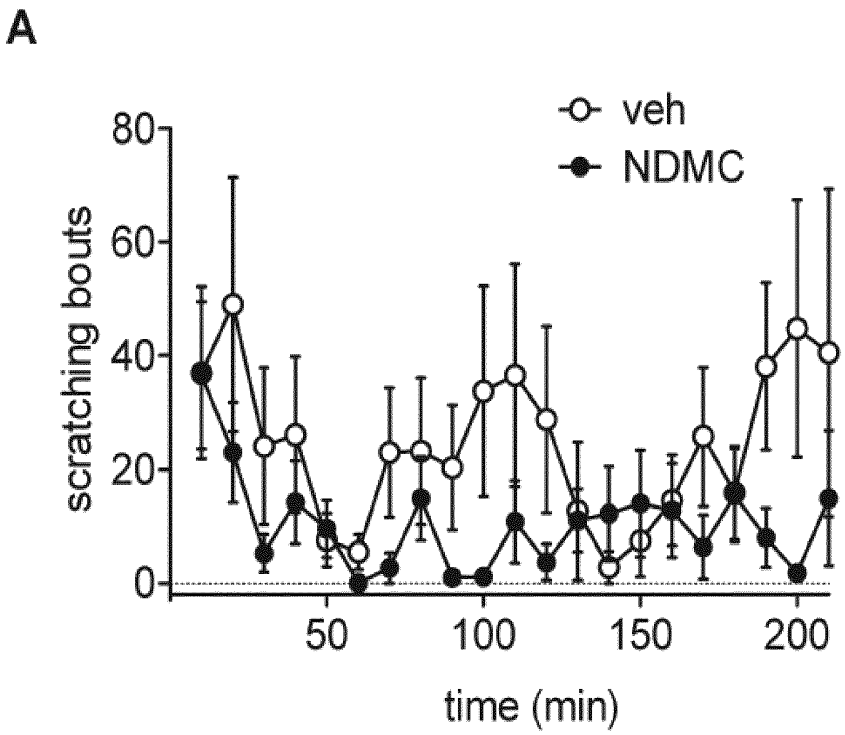

B
α-Me-5HT, TP003 10 mg/kg p.o.
sum scratching bouts
150
100
50
0
**
wild-type
HHRH
veh
TP003

Fig. 9


A
veh
NDMC
scratching bouts
80
60
40
20
0
50
100
150
200
time (min)

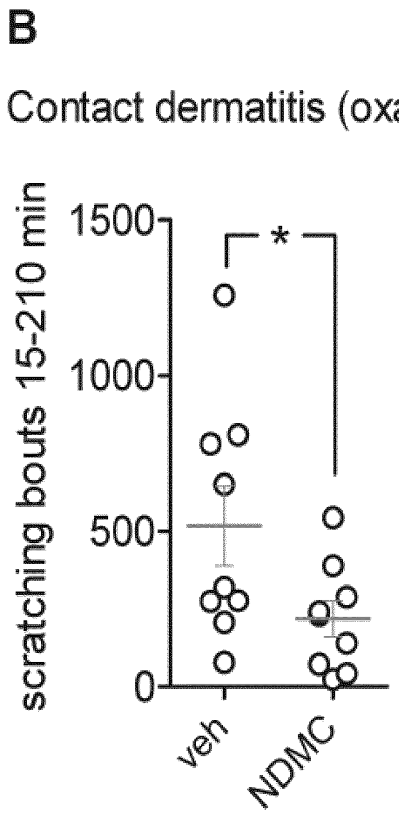
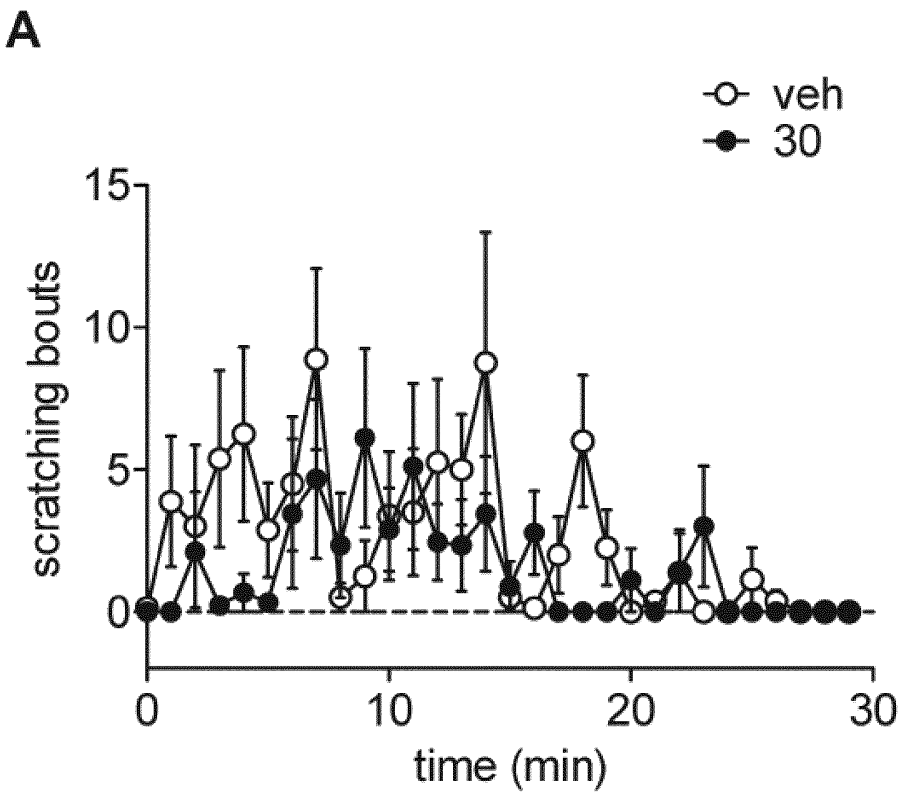

B
Contact dermatitis (oxazolone)
scratching bouts 15-210 min
1500
1000
500
0
*
veh
NDMC

Fig. 10


A
veh
30
scratching bouts
15
10
5
0
0
10
20
30
time (min)

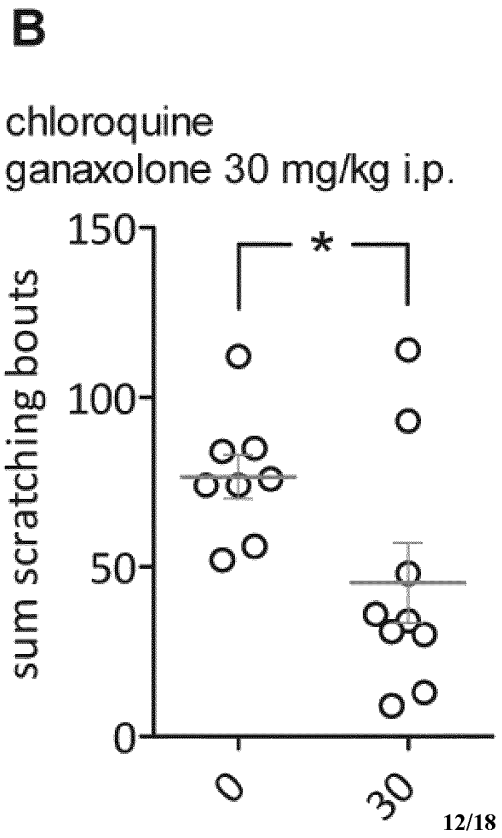

B
chloroquine
ganaxolone 30 mg/kg i.p.
sum scratching bouts
150
100
50
0
*
0
30

Fig. 11

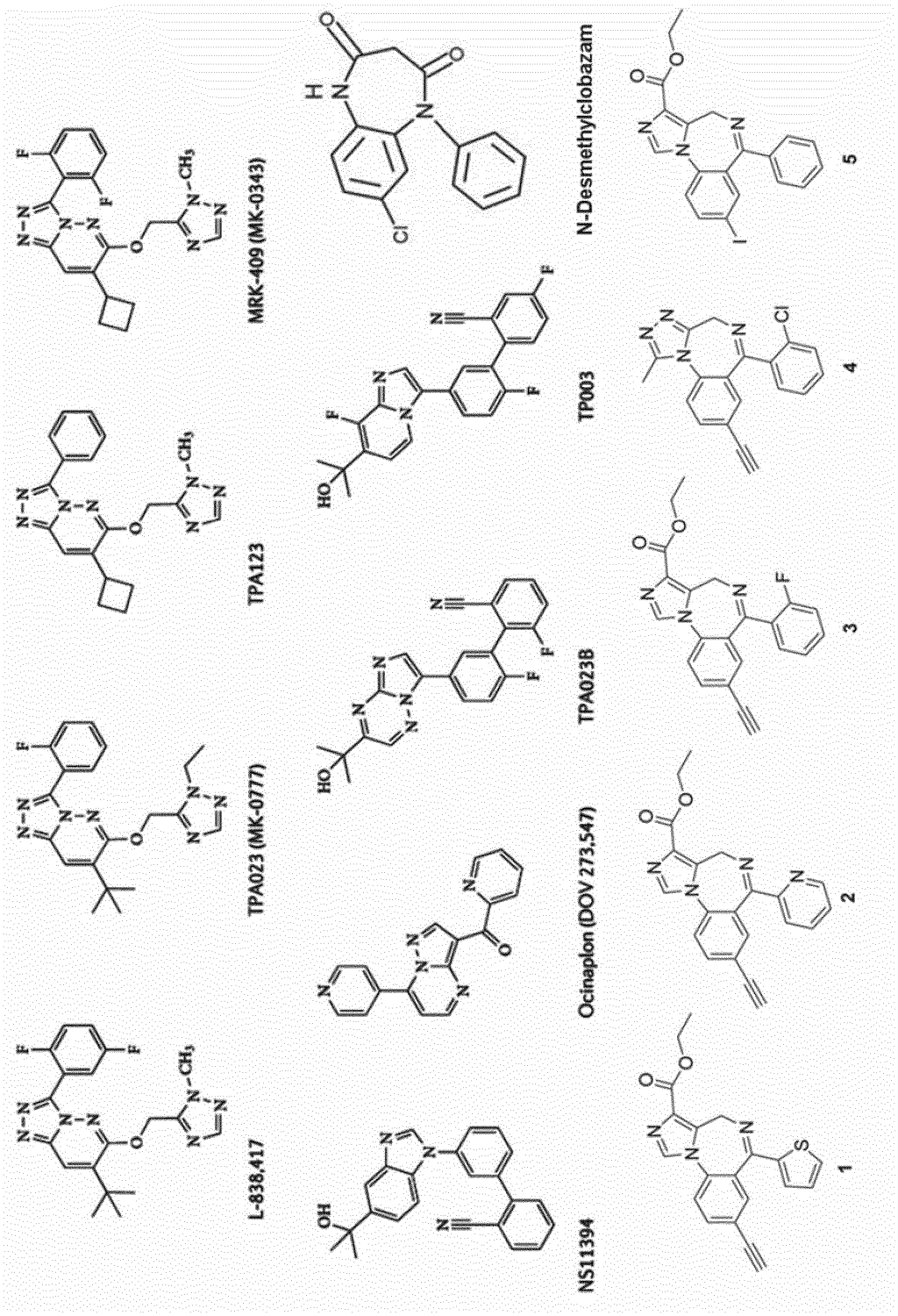
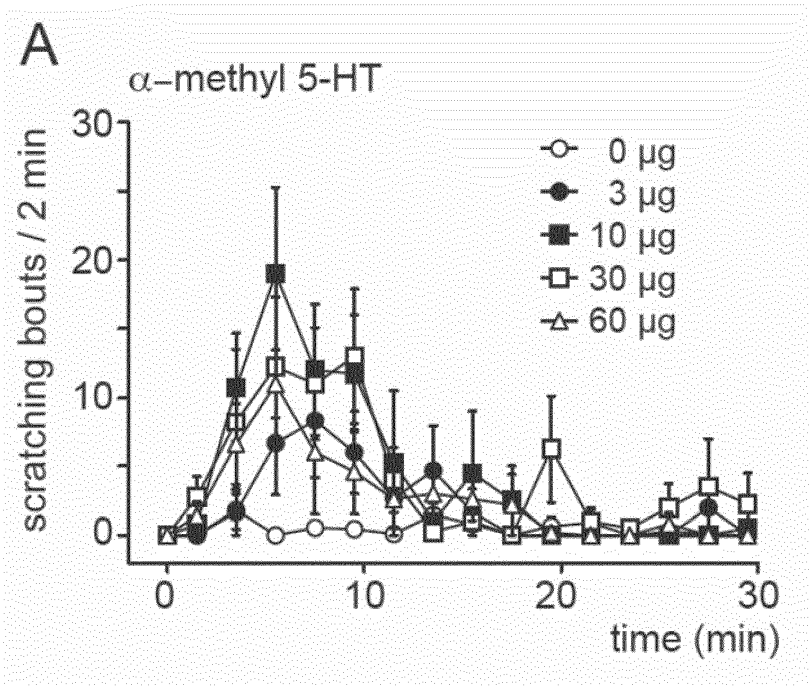

L-838,417
TPA023 (MK-0777)
TPA123
MRK-409 (MK-0343)
NS11394
Ocinaplon (DOV 273,547)
TPA023B
TP003
N-Desmethylclobazam
1
2
3
4
5

Fig. 12


A
α–methyl 5-HT
scratching bouts / 2 min
30
20
10
0
0 µg
3 µg
10 µg
30 µg
60 µg
0
10
20
30
time (min)

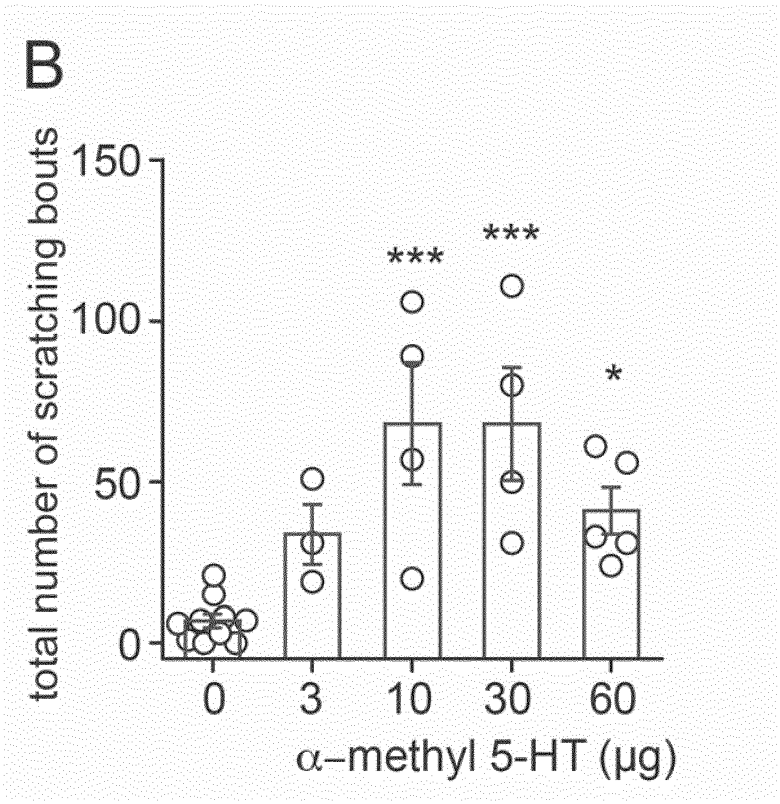

B
total number of scratching bouts
150
100
50
0
***
***
*
0
3
10
30
60
α–methyl 5-HT (µg)

Fig. 13

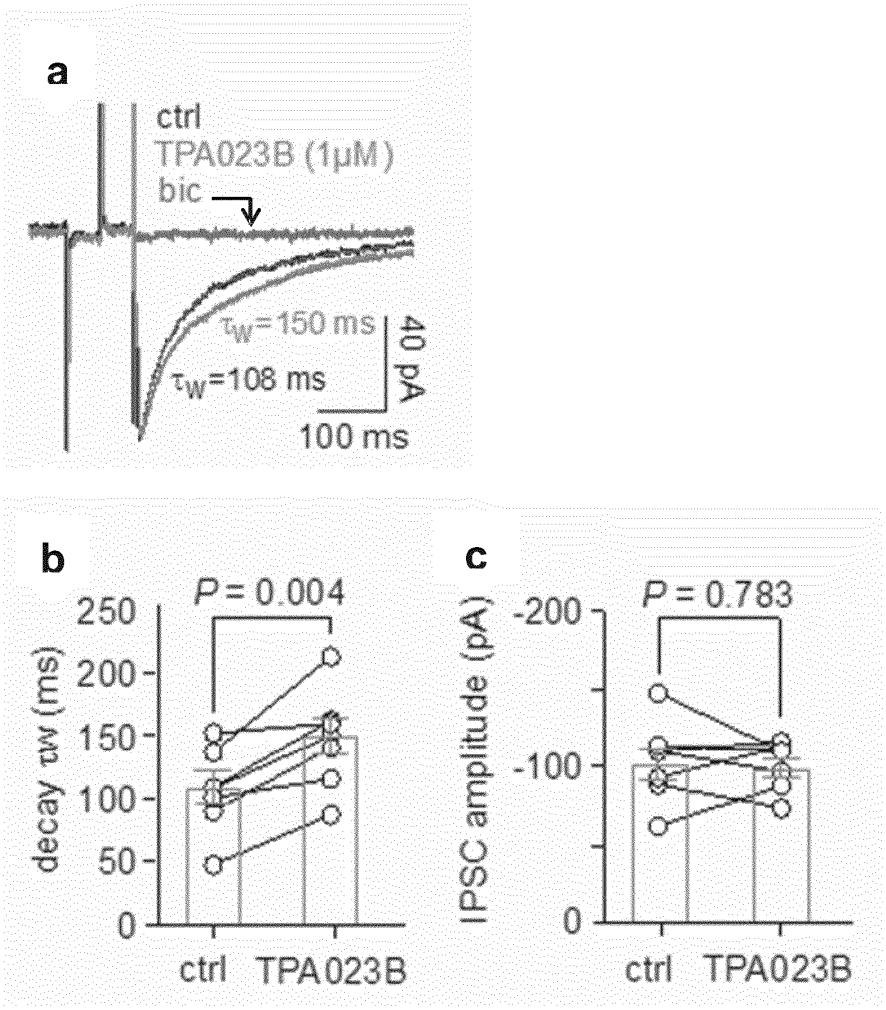

a
ctrl
TPA023B (1µM)
bic
τW=150 ms
τW=108 ms
40 pA
100 ms
b
P = 0.004
decay τw (ms)
250
200
150
100
50
0
ctrl
TPA023B
c
P = 0.783
IPSC amplitude (pA)
-200
-100
0
ctrl
TPA023B

Fig. 14

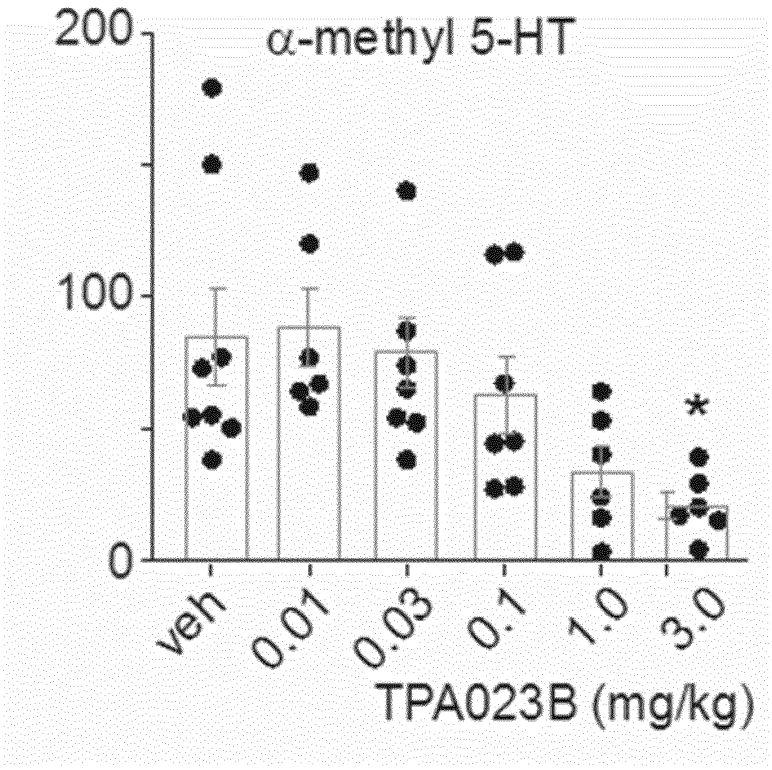

200
100
0
α-methyl 5-HT
*
veh
0.01
0.03
0.1
1.0
3.0
TPA023B (mg/kg)

Fig. 15

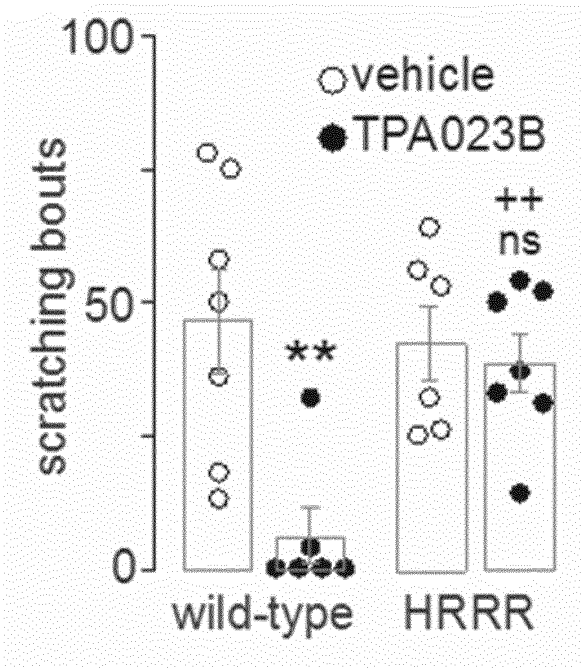
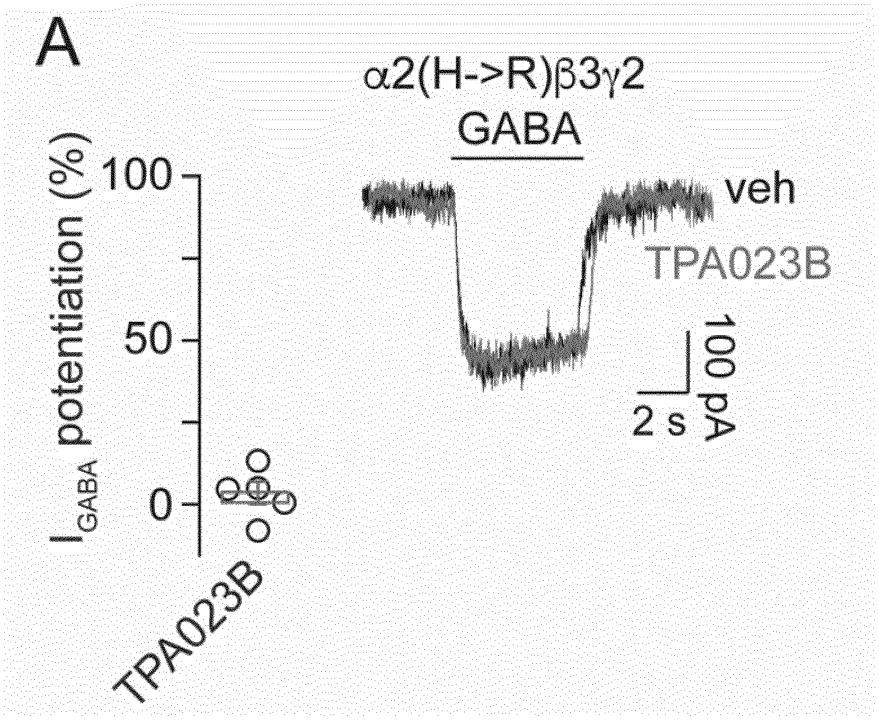

100
50
0
scratching bouts
vehicle
TPA023B
**
++
ns
wild-type
HRRR

Fig. 16


A
α2(H->R)β3γ2
GABA
veh
TPA023B
100 pA
2 s
I_{GABA} potentiation (%)
100
50
0
TPA023B

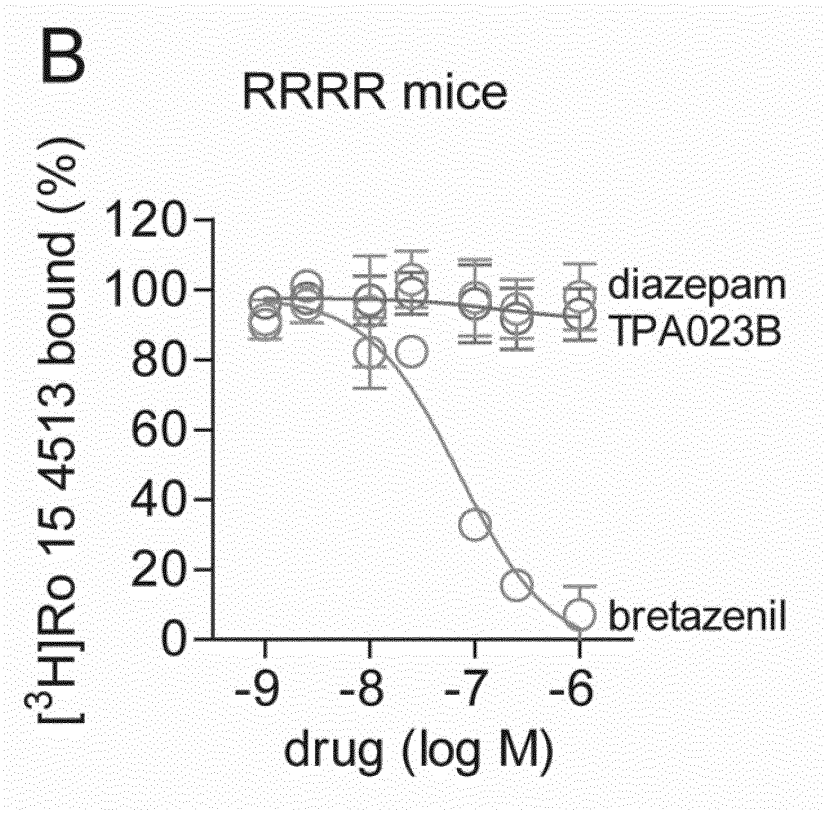
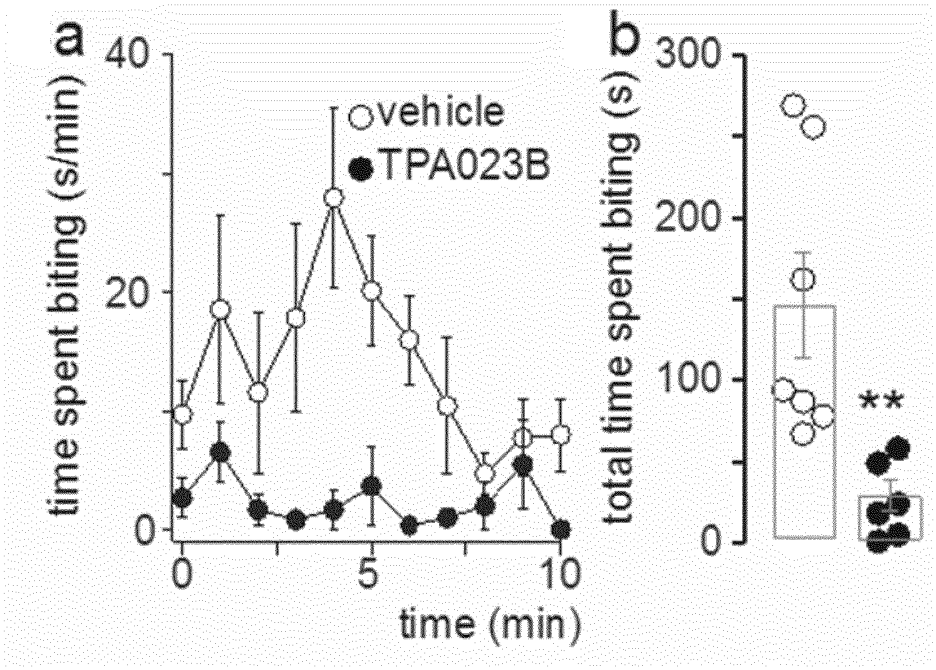
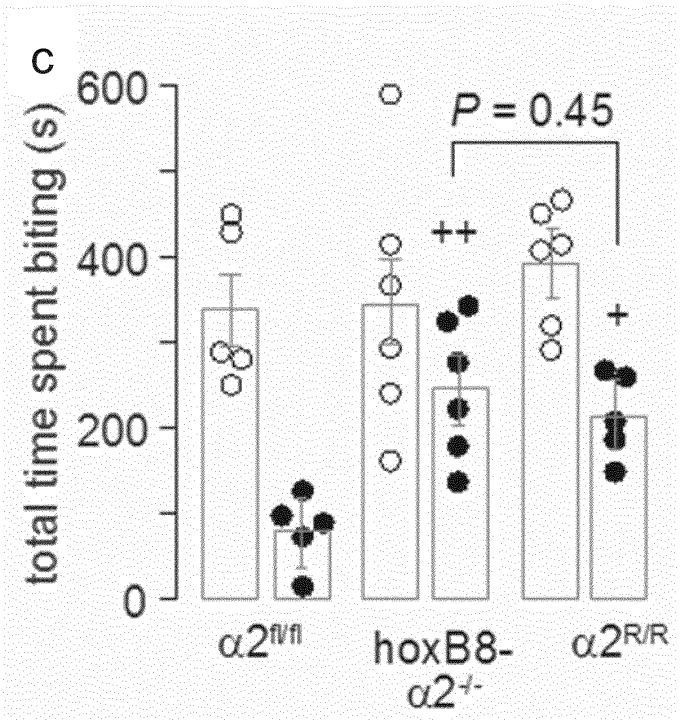

B
RRRR mice
[^{3}H]Ro 15 4513 bound (%)
120
100
80
60
40
20
0
diazepam
TPA023B
bretazenil
-9
-8
-7
-6
drug (log M)

Fig. 17a, b, c


a
time spent biting (s/min)
40
20
0
vehicle
TPA023B
0
5
10
time (min)
b
total time spent biting (s)
300
200
100
0
**


c
total time spent biting (s)
600
400
200
0
P = 0.45
++
+
α2fl/fl
hoxB8-
α2-/-
α2R/R