Supplementary Figure 1 (SFig.1)



**Supplementary Figure 1. Representative images of the RAW flow cytometry.** A, Representative images of the RAW flow cytometry in Figure 5. C, Representative images of the RAW flow cytometry in Figure 6. F, Representative images of the RAW flow cytometry in Figure 7. D. RS + IS = restraint stress plus ice-water swimming. GC: glucocorticoid. NSA: Necrosulfonamide (a GSDMD inhibitor).

Supplementary Figure 2 (SFig.2)



**Supplementary Figure 2. The effects of NSA on the behavior of stressed rats in open-field test (n = 6).** A, the motion trajectory in the open field. B, the total movement distance in the open field. C, the movement distance in the central area of the open field. D, the cumulative duration in the central area of the open field. E, the number of feces in the open field. The results are shown as the mean ± SEM, \*\*P < 0.01 vs. the control group. NSA: Necrosulfonamide (a GSDMD inhibitor).

**Supplementary Material 1**

Original western blots for GSDME in Figure 6 (n = 6)

Six repetitions of GSDME and β-actin expression levels in hypothalamus.

GSDME (55kDa)



180

130

100

70

55

40

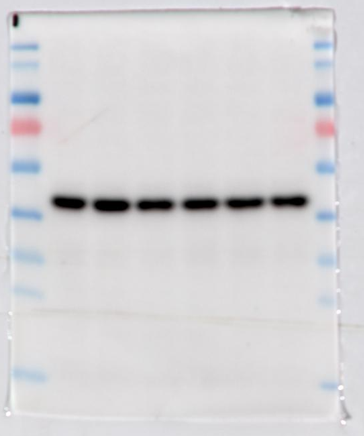
35

25

15

1 2 3 4 5 6

β-actin (43kDa)



180

130

100

70

55

40

35

25

15

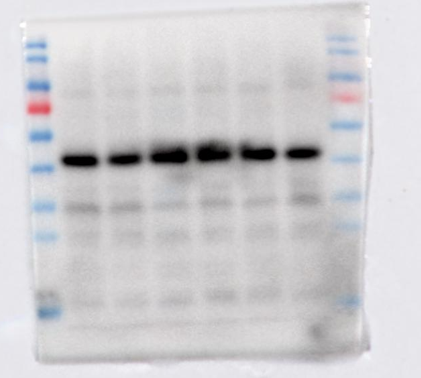
1 2 3 4 5 6

1, 2, 3, 4, 5, and 6 respectively represent the expression levels of GSDME and β-actin of six rats in the control group. Six repetitions in total.

Original western blots for GSDMD in Figure 6 (n = 6)

Six repetitions of GSDMD and β-actin expression levels in hypothalamus.

GSDMD (53kDa)



180

130

100

70

55

40

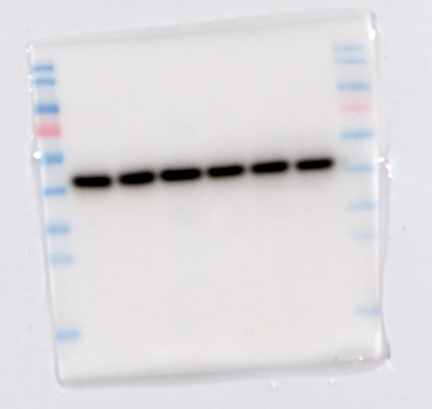
35

25

15

1 2 3 4 5 6

β-actin(43kDa)



180

130

100

70

55

40

35

25

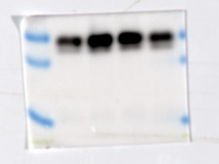
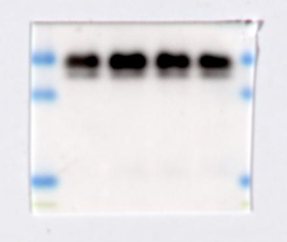
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1 2 3 4 5 6

1, 2, 3, 4, 5, and 6 respectively represent the expression levels of GSDMD and β-actin of six rats in the control group. Six repetitions in total.

Original western blots for GSDMD-NT in Figure 6 (n = 6)

GSDMD-NT (31kDa)

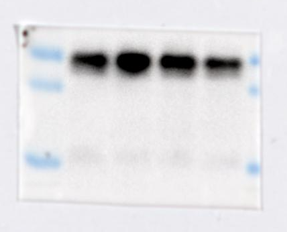
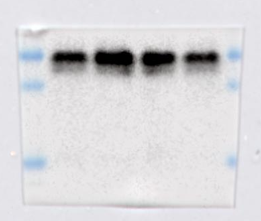
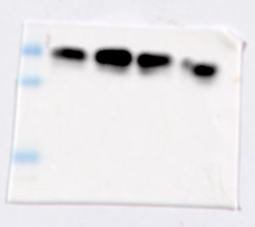


1 2 3 4

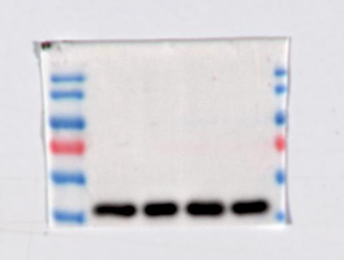
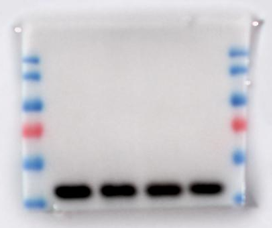
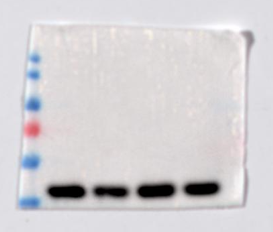
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25

15



β-actin (43kDa)



180

130

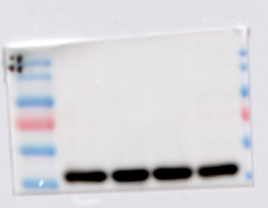
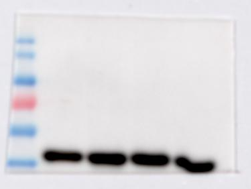
100

70

55

40

1 2 3 4

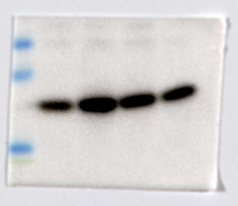
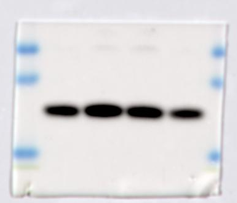
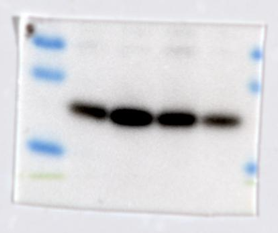


1, 2, 3, and 4 respectively represent the expression levels of GSDMD-NT and β-actin in the control group, stress group, stress + NSA group, and NSA group. Six repetitions in total.

**Supplementary Material 2**

Original western blots for Cleaved-caspase-1 and NLRP3 in Figure 8 (n = 6)

Cleaved-caspase-1(22kDa)



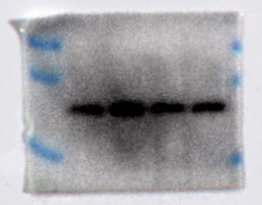
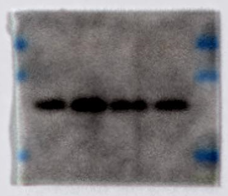
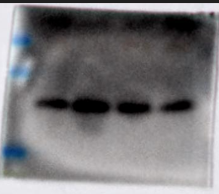
35

25

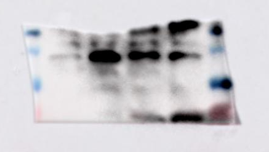
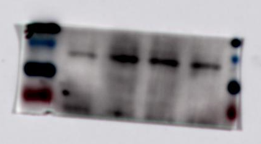
15

10

1 2 3 4



NLRP3 (118kDa)



1 2 3 4

180

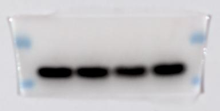
130

100

70





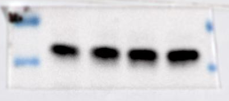
β-actin (43kDa)



1 2 3 4

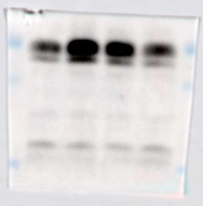
55

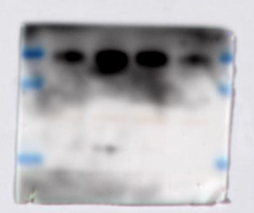
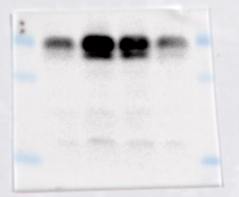
40



1, 2, 3, and 4 respectively represent the expression levels of Cleaved-caspase-1, NLRP3 and β-actin in the control group, stress group, stress + GC (1mg/kg) group, and GC (1mg/kg) group. Six repetitions in total.

Original western blots for GSDMD-NT in Figure 8 (n = 6)

GSDMD-NT (31kDa)

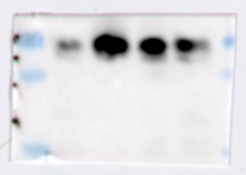
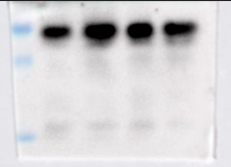


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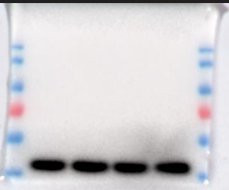
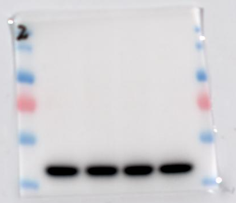
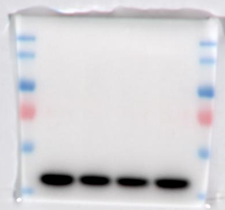
25

15

1 2 3 4



β-actin (43kDa)



180

130

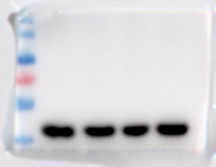
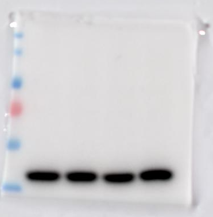
100

70

55

40

1 2 3 4



1, 2, 3, and 4 respectively represent the expression levels of GSDMD-NT and β-actin in the control group, stress group, stress + GC (1mg/kg) group, and GC (1mg/kg) group. Six repetitions in total.