

# Supplementary Information

## Roles of Toll-like receptor 2/4, monoacylglycerol lipase, and cyclooxygenase in social defeat stress-induced prostaglandin E<sub>2</sub> synthesis in the brain and their behavioral relevance

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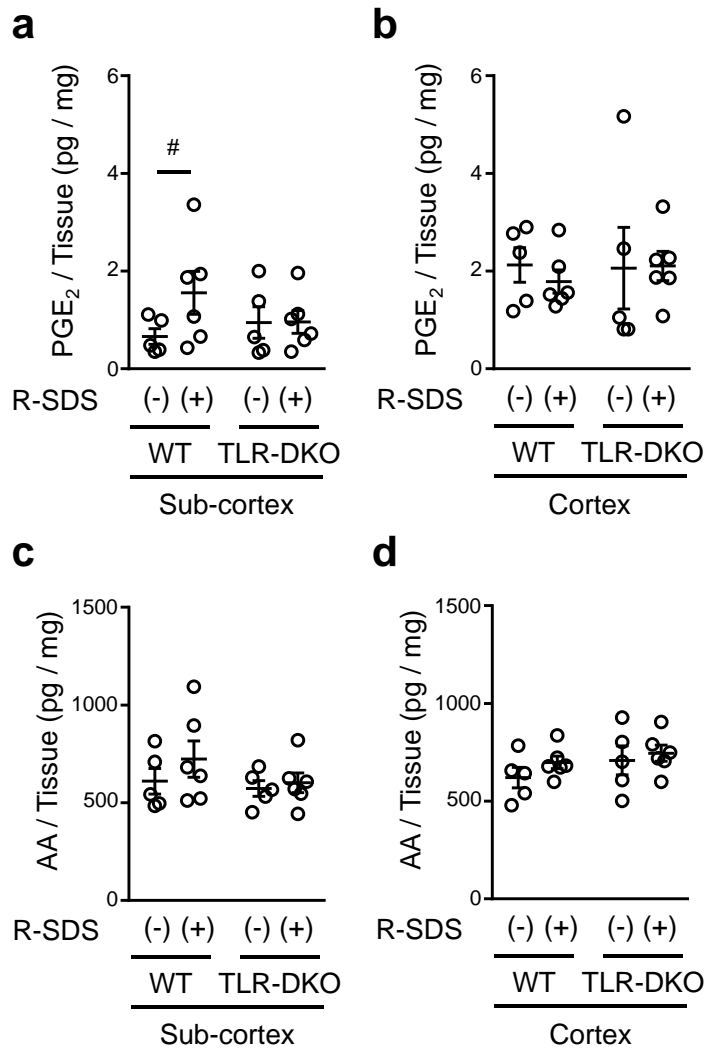
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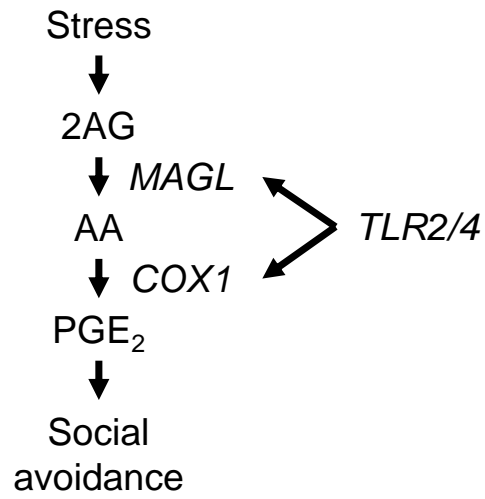
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**Supplementary Figure S1.** LC-MS/MS confirmed that social defeat stress increases the PGE<sub>2</sub> contents in subcortical tissues in a TLR2/4-dependent manner. The contents of PGE<sub>2</sub> (a, b) and free arachidonic acid (AA) (c, d) in subcortical (a, c) and cortical (b, d) tissues of wild-type (WT) and TLR2/4 double knockout (TLR-DKO) mice with or without repeated SDS (R-SDS). #*P* = 0.09 for unpaired *t* test. Data are shown as means ± SEM.



**Supplementary Figure S2.** Our proposal about stress-induced PGE<sub>2</sub> synthesis in the brain and its behavioral significance based on this study. Our findings suggest that stress increases the PGE<sub>2</sub> synthesis in subcortical regions of the brain through enzymatic activities of MAGL and COX1, the expression of which is enhanced by TLR2/4 activity, thereby leading to social avoidance. 2AG, 2-arachidonoylglycerol; AA, arachidonic acid; COX1, cyclooxygenase-1; MAGL, monoacylglycerol lipase; PGE<sub>2</sub>, prostaglandin E<sub>2</sub>; TLR, Toll-like receptor.