

Supplemental Fig. S1. C57BL/6 mice were exposed to two electric foot shocks and subsequently received treatment with either fluoxetine (flx, 20mg/kg/day) or vehicle (drinking water). On day 28, generalized fear response was measured to investigate fluoxetine treatment efficacy, by exposing the mice to neutral environment (cylinder plus tone displayed, data not shown). After a 28-day drug-washout period, generalized and/or sensitized fear was assessed by exposing mice to cylinder plus tone (day 56), hexagonal context containing the grid floor as major shock-context reminder and shocking chamber without shock application (day 57). Mice were sacrificed one week after conditioned fear response evaluation.

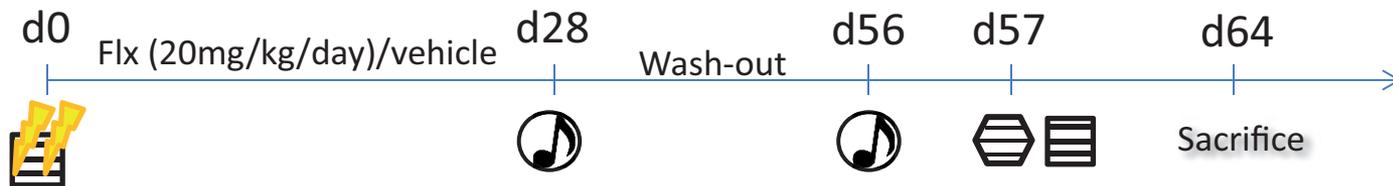
Supplemental Fig. S2. Graphic illustration of the one-sided KS test based GSEA/MSEA. All the quantified proteins/metabolites are ranked based on the correlation between their expression pattern and the group distinction pattern. The distribution of ranks of proteins/metabolites involved in a pathway is compared with the even distribution to estimate the significance of enrichment.

Supplemental Table S1. Proteomic comparison between shocked and control mice.

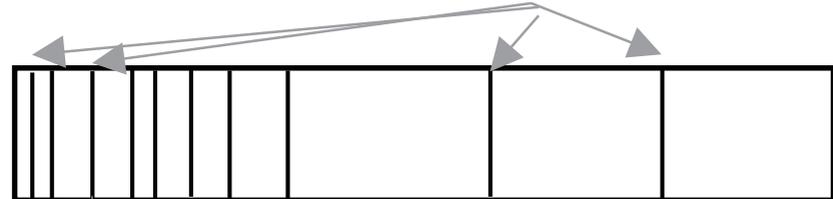
Supplemental Table S2. Altered cellular pathways enriched by Gene Set Enrichment Analysis (GSEA) from proteomics analysis in different brain regions.

Supplemental Table S3. Normalized abundance of measured metabolites.

Supplemental Table S4. Metabolic pathways enriched by Metabolite Set Enrichment Analysis (MESA) in different brain regions.



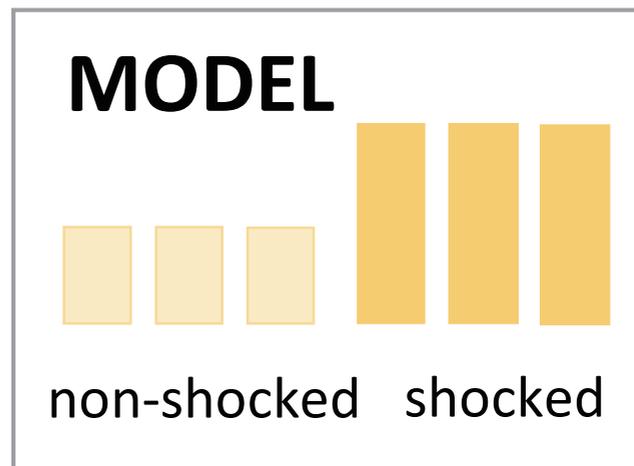
Proteins/metabolites in the pathway



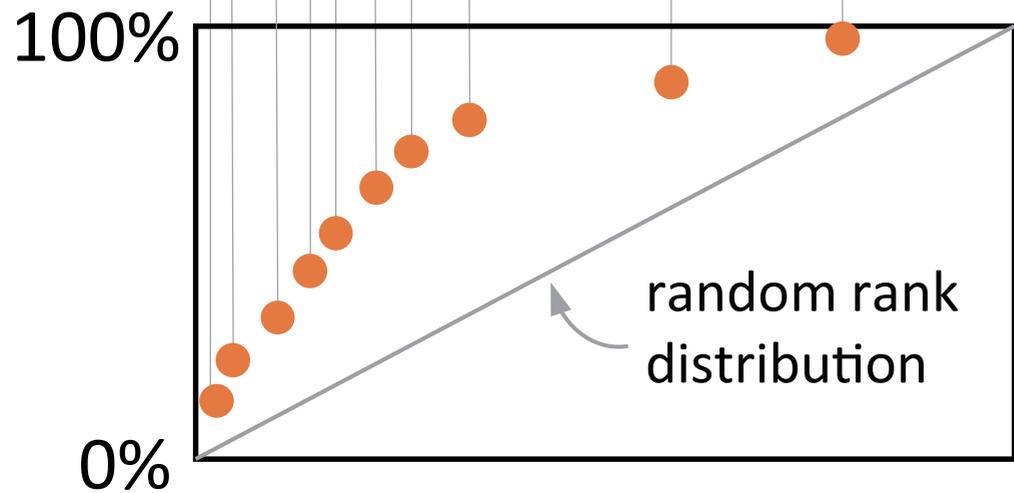
Ranked protein/metabolite list



PCC to the model



Cumulative distribution



Rank

One-sided KS-test

Pathway enriched for change

↑ YES

Metabolites in the pathway tend to have higher/lower ranks?

↓ NO

No enrichment