

**Table S1. Mean  $\pm$ SEM values & statistical tests for sex-interaction.**

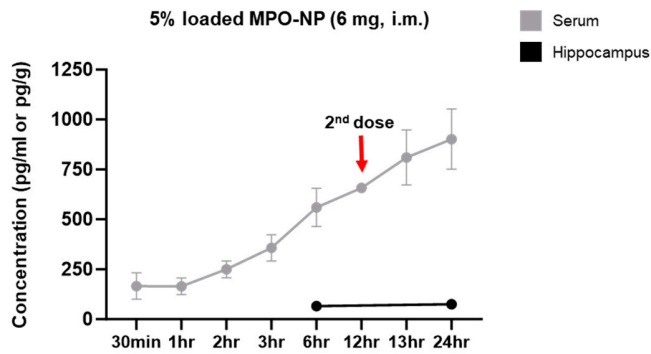
| Figure 3B | Control                | DFP+ VEH              | DFP +<br>MPO-oral     | Interaction<br>effects P<br>value | Statistical analysis                         |
|-----------|------------------------|-----------------------|-----------------------|-----------------------------------|--|
| CA1       | 1.269 $\pm$<br>0.313   | 18.24 $\pm$<br>4.749  | 24.63 $\pm$ 7.17      | 0.2176                            | 2-way ANOVA (Tukey's multiple<br>comparison) |
| CA3       | 1.413 $\pm$<br>0.4040  | 17.14 $\pm$<br>4.399  | 29.30 $\pm$ 6.844     | 0.3146                            | 2-way ANOVA (Tukey's multiple<br>comparison) |
| DG        | 1.337 $\pm$<br>0.2446  | 27.48 $\pm$<br>6.971  | 31.17 $\pm$ 12.47     | 0.0154                            | 2-way ANOVA (Tukey's multiple<br>comparison) |
| AMY       | 1.569 $\pm$<br>0.3224  | 73.63 $\pm$<br>18.16  | 48.00 $\pm$ 13.30     | 0.2084                            | 2-way ANOVA (Tukey's multiple<br>comparison) |
| PC        | 2.561 $\pm$<br>0.5447  | 63.98 $\pm$<br>19.76  | 38.49 $\pm$ 11.93     | 0.3046                            | 2-way ANOVA (Tukey's multiple<br>comparison) |
| Figure 3D | Control                | DFP+ VEH              | DFP +<br>MPO-oral     | Interaction<br>effects P<br>value | Statistical analysis                         |
| CA1       | 172.0 $\pm$<br>14.28   | 167.6 $\pm$<br>6.341  | 133.1 $\pm$ 12.92     | 0.3438                            | 2-way ANOVA (Tukey's multiple<br>comparison) |
| CA3       | 276.0 $\pm$<br>17.48   | 166.8 $\pm$<br>11.73  | 223.5 $\pm$ 21.58     | 0.5437                            | 2-way ANOVA (Tukey's multiple<br>comparison) |
| DG        | 185.8 $\pm$<br>16.82   | 165.6 $\pm$<br>9.870  | 156.9 $\pm$<br>14.77  | 0.0016                            | 2-way ANOVA (Tukey's multiple<br>comparison) |
| AMY       | 357.2 $\pm$<br>45.07   | 264.2 $\pm$<br>19.23  | 280.5 $\pm$ 40.81     | 0.0090                            | 2-way ANOVA (Tukey's multiple<br>comparison) |
| PC        | 364.6 $\pm$<br>20.78   | 268.4 $\pm$<br>15.16  | 311.0 $\pm$ 29.78     | 0.6318                            | 2-way ANOVA (Tukey's multiple<br>comparison) |
| Figure 4B | Control                | DFP+ VEH              | DFP +<br>MPO-oral     | Interaction<br>effects P<br>value | Statistical analysis                         |
| CA1       | 6.726 $\pm$<br>1.188   | 3.381 $\pm$<br>0.5512 | 5.952 $\pm$<br>0.4017 | 0.3701                            | 2-way ANOVA (Tukey's multiple<br>comparison) |
| CA3       | 6.286 $\pm$<br>1.012   | 4.238 $\pm$<br>0.7401 | 3.202 $\pm$<br>0.7537 | 0.1586                            | 2-way ANOVA (Tukey's multiple<br>comparison) |
| DG        | 4.702 $\pm$<br>0.3201  | 3.643 $\pm$<br>0.7161 | 4.548 $\pm$<br>0.9023 | 0.0653                            | 2-way ANOVA (Tukey's multiple<br>comparison) |
| AMY       | 10.96 $\pm$<br>1.500   | 2.098 $\pm$<br>0.4483 | 5.893 $\pm$ 1.760     | 0.6707                            | 2-way ANOVA (Tukey's multiple<br>comparison) |
| PC        | 10.46 $\pm$<br>2.108   | 2.279 $\pm$<br>0.7183 | 5.876 $\pm$ 1.483     | 0.2004                            | 2-way ANOVA (Tukey's multiple<br>comparison) |
| Figure 5B | Control                | DFP+ VEH              | DFP +<br>MPO-oral     | Interaction<br>effects P<br>value | Statistical analysis                         |
| CA1       | 1.424 $\pm$<br>0.6641  | 30.16 $\pm$<br>7.040  | 22.09 $\pm$ 3.969     | 0.6868                            | 2-way ANOVA (Tukey's multiple<br>comparison) |
| CA3       | 0.8694 $\pm$<br>0.3904 | 28.36 $\pm$<br>6.836  | 24.48 $\pm$ 4.935     | 0.7271                            | 2-way ANOVA (Tukey's multiple<br>comparison) |
| DG        | 0.5643 $\pm$<br>0.3796 | 26.66 $\pm$<br>4.915  | 28.60 $\pm$ 5.300     | 0.6095                            | 2-way ANOVA (Tukey's multiple<br>comparison) |
| AMY       | 1.798 $\pm$<br>1.045   | 63.04 $\pm$<br>10.61  | 47.17 $\pm$ 8.564     | 0.2019                            | 2-way ANOVA (Tukey's multiple<br>comparison) |
| PC        | 2.000 $\pm$<br>0.9350  | 62.58 $\pm$<br>10.36  | 72.43 $\pm$ 9.984     | 0.6973                            | 2-way ANOVA (Tukey's multiple<br>comparison) |

| <b>Figure 6<br/>AMY</b> | <b>Control</b>     | <b>DFP+ VEH</b>      | <b>DFP +<br/>MPO-oral</b> | <b>Interaction<br/>effects P<br/>value</b> | <b>Statistical analysis</b>               |
|-------------------------|--------------------|----------------------|---------------------------|--|---|
| #                       | 49.56±             | 30.63±               | 21.30± 3.361              | 0.2309                                     | 2-way ANOVA (Tukey's multiple comparison) |
| Branch/cell             | 4.966              | 5.273                |                           |  |   |
| Average                 | 61.15±             | 37.73±               | 20.90± 4.012              | 0.0523                                     | 2-way ANOVA (Tukey's multiple comparison) |
| branch/cell             | 4.644              | 6.509                |                           |  |   |
| Max                     | 90.56±             | 57.37±               | 33.00± 5.818              | 0.3545                                     | 2-way ANOVA (Tukey's multiple comparison) |
| branch                  | 6.915              | 10.09                |                           |  |   |
| length                  |                    |                      |                           |  |   |
| # end point             | 40.45±             | 24.85±               | 15.42± 2.579              | 0.5017                                     | 2-way ANOVA (Tukey's multiple comparison) |
| voxels                  | 3.915              | 4.234                |                           |  |   |
| <b>Figure 6<br/>CA1</b> | <b>Control</b>     | <b>DFP+ VEH</b>      | <b>DFP +<br/>MPO-oral</b> | <b>Interaction<br/>effects P<br/>value</b> | <b>Statistical analysis</b>               |
| #                       | 15.36±             | 15.27±               | 12.21±                    | 0.6659                                     | 2-way ANOVA (Tukey's multiple comparison) |
| Branch/cell             | 2.348              | 1.612                | 0.6777                    |  |   |
| Average                 | 23.28±             | 19.40±               | 14.52± 1.661              | 0.8540                                     | 2-way ANOVA (Tukey's multiple comparison) |
| branch/cell             | 1.659              | 1.786                |                           |  |   |
| Max                     | 32.25±             | 27.90±               | 21.87± 2.267              | 0.7849                                     | 2-way ANOVA (Tukey's multiple comparison) |
| branch                  | 2.735              | 3.250                |                           |  |   |
| length                  |                    |                      |                           |  |   |
| # end point             | 13.60±             | 12.30±               | 9.580±                    | 0.7141                                     | 2-way ANOVA (Tukey's multiple comparison) |
| voxels                  | 1.607              | 1.187                | 0.6965                    |  |   |
| <b>Figure 7B</b>        | <b>Control</b>     | <b>DFP+ VEH</b>      | <b>DFP +<br/>MPO-oral</b> | <b>Interaction<br/>effects P<br/>value</b> | <b>Statistical analysis</b>               |
| CA1                     | 0.7813±<br>0.2611  | 29.50±<br>5.703      | 4.417± 2.365              | 0.2006                                     | 2-way ANOVA (Tukey's multiple comparison) |
| CA3                     | 0.5417±<br>0.2813  | 28.33±<br>5.698      | 3.028± 1.150              | 0.4261                                     | 2-way ANOVA (Tukey's multiple comparison) |
| DG                      | 0.6250±<br>0.2777  | 35.14±<br>6.307      | 4.472± 2.512              | 0.2099                                     | 2-way ANOVA (Tukey's multiple comparison) |
| AMY                     | 0.7500±<br>0.5261  | 32.40±<br>5.949      | 2.833± 2.007              | 0.4943                                     | 2-way ANOVA (Tukey's multiple comparison) |
| PC                      | 0.6042±<br>0.4106  | 43.62±<br>5.888      | 1.389±<br>0.7119          | 0.1935                                     | 2-way ANOVA (Tukey's multiple comparison) |
| <b>Figure<br/>7D</b>    | <b>Control</b>     | <b>DFP+ VEH</b>      | <b>DFP +<br/>MPO-oral</b> | <b>Interaction<br/>effects P<br/>value</b> | <b>Statistical analysis</b>               |
| CA1                     | 73.80±<br>4.972    | 110.5±<br>8.653      | 70.00±<br>10.22           | 0.3544                                     | 2-way ANOVA (Tukey's multiple comparison) |
| CA3                     | 63.93±<br>4.224    | 105.0±<br>5.875      | 71.15±<br>9.909           | 0.1045                                     | 2-way ANOVA (Tukey's multiple comparison) |
| DG                      | 70.17±<br>7.750    | 113.8±<br>5.645      | 70.27±<br>9.892           | 0.0521                                     | 2-way ANOVA (Tukey's multiple comparison) |
| AMY                     | 84.06±<br>5.071    | 126.0±<br>6.064      | 70.97±<br>10.08           | 0.0880                                     | 2-way ANOVA (Tukey's multiple comparison) |
| PC                      | 75.91±<br>6.903    | 122.5±<br>5.592      | 64.83±<br>6.966           | 0.0788                                     | 2-way ANOVA (Tukey's multiple comparison) |
| <b>Figure<br/>8B</b>    | <b>Control</b>     | <b>DFP+ VEH</b>      | <b>DFP +<br/>MPO-oral</b> | <b>Interaction<br/>effects P<br/>value</b> | <b>Statistical analysis</b>               |
| CA1                     | 0.1007±<br>0.01377 | 0.04144±<br>0.006908 | 0.03371±<br>0.005008      | 0.6941                                     | 2-way ANOVA (Tukey's multiple comparison) |

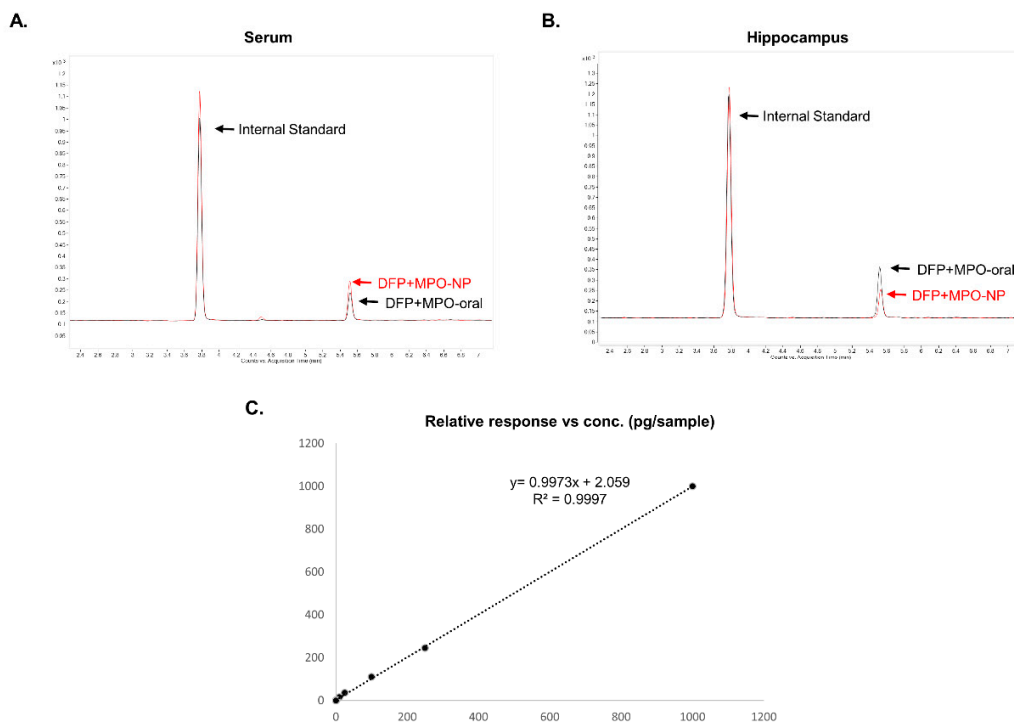
|     |                      |                      |                      |        |   |
|-----|----------------------|----------------------|----------------------|--------|---|
| CA3 | 0.08086±<br>0.01273  | 0.02800±<br>0.008461 | 0.02638±<br>0.005094 | 0.3785 | 2-way ANOVA (Tukey's multiple comparison) |
| DG  | 0.07462±<br>0.007553 | 0.02911±<br>0.009264 | 0.02700±<br>0.007901 | 0.7929 | 2-way ANOVA (Tukey's multiple comparison) |
| AMY | 0.1202±<br>0.01048   | 0.03300±<br>0.008893 | 0.02350±<br>0.005301 | 0.7073 | 2-way ANOVA (Tukey's multiple comparison) |
| PC  | 0.07760±<br>0.009383 | 0.02544±<br>0.004901 | 0.02576±<br>0.004396 | 0.6537 | 2-way ANOVA (Tukey's multiple comparison) |

**Table S2. Antibodies used for IHC.**

| Primary Antibody                              | Source                      | Catalogue number | Dilution factor |
|---|-----------------------------|------------------|-----------------|
| Anti-NeuN (rabbit)                            | EMD Millipore               | ABN78            | 1:200           |
| Anti-IBA1 (goat)                              | Abcam                       | Ab5076           | 1:300           |
| Anti-GFAP (mouse)                             | Sigma Aldrich               | G3893            | 1:300           |
| Anti-KIR4.1 (goat)                            | Santa Cruz<br>Biotechnology | Sc-23637         | 1:100           |
| Anti-GP91 <sup>phox</sup> (mouse)             | Santa Cruz<br>Biotechnology | sc-130543        | 1:100           |
| Anti-C3 (rat)                                 | Novus Biologicals           | NB200-540        | 1:80            |
| Anti-parvalbumin (rabbit)                     | Abcam                       | Ab11427          | 1:1000          |
| Secondary Antibody                            | Source                      | Catalogue number | Dilution factor |
| AMCA blue streptavidin                        | Jackson<br>ImmunoResearch   | 016-150-084      | 1:60            |
| Cy3 <sup>TM</sup> -conjugated<br>Streptavidin | Jackson<br>ImmunoResearch   | 016-160-084      | 1:80            |
| Biotinylated donkey anti-<br>goat             | Jackson<br>ImmunoResearch   | 711-295-152      | 1:100           |
| Biotinylated donkey anti-<br>rat              | Jackson<br>ImmunoResearch   | 712-065-153      | 1:100           |
| AlexaFluor 488 anti-<br>mouse                 | Jackson<br>ImmunoResearch   | 115-545-003      | 1:300           |
| AlexaFluor 488 anti-rabbit                    | Jackson<br>ImmunoResearch   | 711-545-152      | 1:200           |
| Rhodamine Red X anti-<br>rabbit               | Jackson<br>ImmunoResearch   | 111-295-144      | 1:300           |
| Rhodamine Red X anti-<br>mouse                | Jackson<br>ImmunoResearch   | 715-295-151      | 1:300           |



**Figure S1:** Serum and hippocampal MPO concentrations. In control animals given 5% loaded MPO-NP, serum (pg/mL) concentrations increased over 24 h while hippocampal (pg/g) maintained from 6 h to 24 h. n=4, data are represented as mean  $\pm$  SEM.



**Figure S2:** Method validation for MPO LCMS. Chromatograms of MPO and the internal standard in the serum (A) and hippocampus (B) on day 8. (C) The response linearity of MPO.