









Supplementary Materials (SF)

Figure S1: The treatment with DMF induces mRNA expression of late-kinetic enzymes of the NRF2 pathway in the hippocampus of CaMKII-TDP-43 mice. RT-qPCR determination of mRNA levels of (A) *Nfe2l2*, (B) *Hmox1*, (C) *Nqo1*, (D) *Gpx1* and (E) *Txn1* genes at the hippocampus of WT mice and CaMKII-TDP-43 mice treated with VEH or DMF, n = 4–5 samples ± SEM. The asterisks represent the difference in significance: * $p < 0.05$, ** $p < 0.01$, comparing each group according to a one-way ANOVA followed by Tukey's post-test.

Figure S2: DMF does not have a neuroprotective effect on CA1 and CA2 areas of hippocampus. (A) Immunofluorescence staining of DAPI and CALBINDIN-D28K of 30 µm-thick sections of CA1 of the hippocampus from WT, and mice treated with vehicle or DMF. (B) Quantification of the neuronal cells stained with DAPI in CA1 from WT, and CaMKII-TDP-43 mice treated with vehicle or DMF. (C) Quantification of the intensity of the area stained with CALBINDIN-D28K in CA1 from WT, and CaMKII-TDP-43 mice treated with vehicle or DMF. (D) Immunofluorescence staining of DAPI and CALBINDIN-D28K of 30 µm-thick sections of CA2 of the hippocampus from WT, and CaMKII-TDP-43 mice treated with vehicle or DMF. (E) Quantification of the neuronal cells stained with DAPI in CA2 from WT, and CaMKII-TDP-43 mice treated with vehicle or DMF. (F) Quantification of the intensity of the area stained with CALBINDIN-D28K in CA2 from WT, and CaMKII-TDP-43 mice treated with vehicle or DMF. Bars indicate the mean of n = 4–5 samples ± SEM. Asterisks show significant differences with * $p < 0.05$ comparing each group according to a one-way ANOVA followed by Tukey's post-test.

Figure S3: The treatment with DMF does not exert a neuroprotective effect on CA3 area of hippocampus. (A) Immunofluorescence staining of DAPI and CALBINDIN-D28K of 30 µm-thick sections of CA3 of the hippocampus from WT, and CaMKII-TDP-43 mice treated with vehicle or DMF. (B) Quantification of the neuronal cells stained with DAPI in CA3 from WT, and CaMKII-TDP-43 mice treated with vehicle or DMF. (C) Quantification of the intensity of the area stained with CALBINDIN-D28K in CA3 from WT, and CaMKII-TDP-43 mice treated with vehicle or DMF. Bars indicate the mean of n = 4–5 samples ± SEM. Asterisks show significant differences with * $p < 0.05$ comparing each group according to a one-way ANOVA followed by Tukey's post-test.

Figure S4: DMF treatment does not modulate neuroinflammation in CA2, CA3 and dentate gyrus of hippocampus of CaMKII-TDP-43 mice. (A) Immunofluorescence of IBA1 (red) and GFAP (green), microglial and astrocytic markers, respectively, of 30 µm-thick sections in the CA2-CA3 regions of hippocampus of WT mice and CaMKII-TDP-43 mice treated with VEH or DMF, n = 4–5 samples ± SEM. (B) Quantification of number of IBA1⁺ microglial cells and (C) GFAP⁺ astrocytes cells at the CA2-CA3 regions of WT mice and CaMKII-TDP-43 mice treated with VEH or DMF, n = 4–5 samples ± SEM. (D) Immunofluorescence of IBA1 (red) and GFAP (green) of 30 µm-thick sections in the dentate gyrus area of hippocampus of WT mice and CaMKII-TDP-43 mice treated with VEH or DMF, n = 4–5 samples ± SEM. (E) Quantification of number of IBA1⁺ microglial cells and (F) GFAP⁺ astrocytes cells at the dentate gyrus of WT mice and CaMKII-TDP-43 mice treated with VEH or DMF, n = 4–5 samples ± SEM. The asterisks represent the difference in significance: * $p < 0.05$, ** $p < 0.01$, comparing each group according to a one-way ANOVA followed by Tukey's post-test.