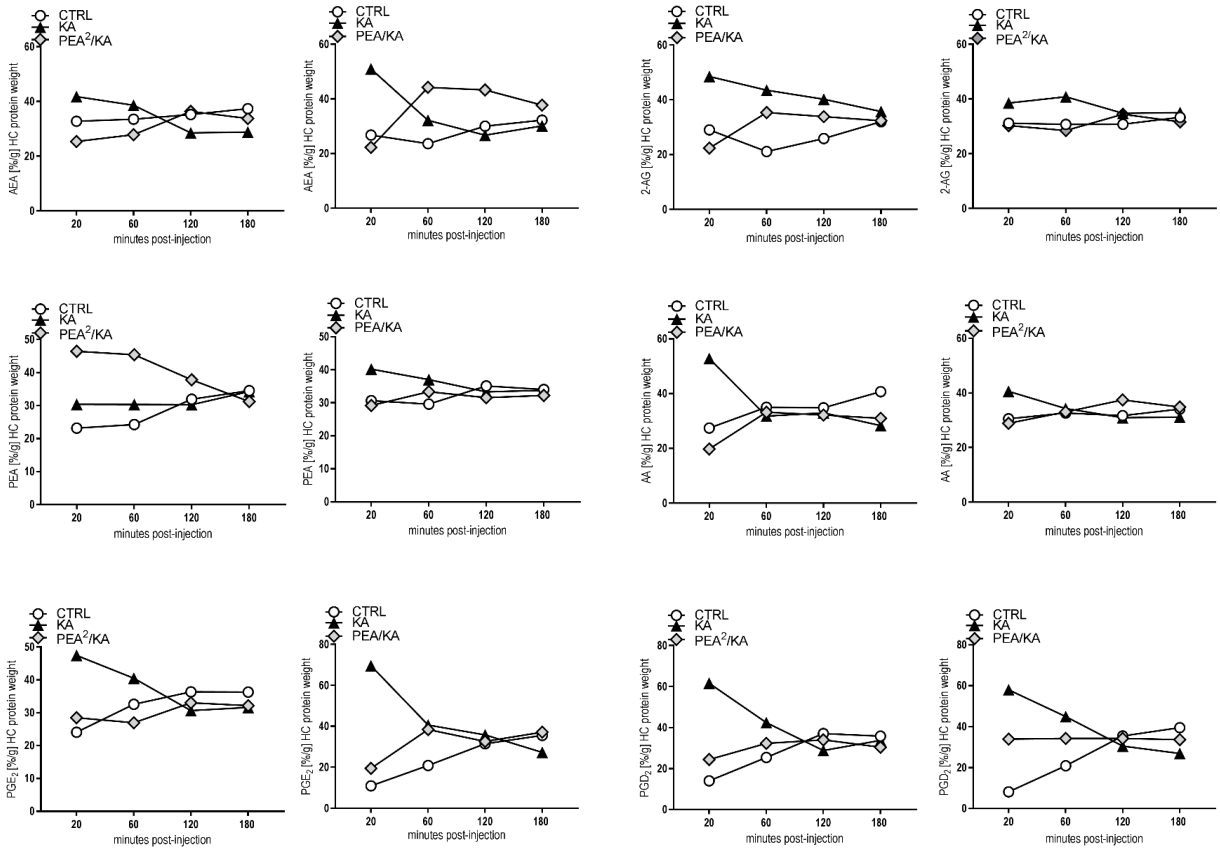
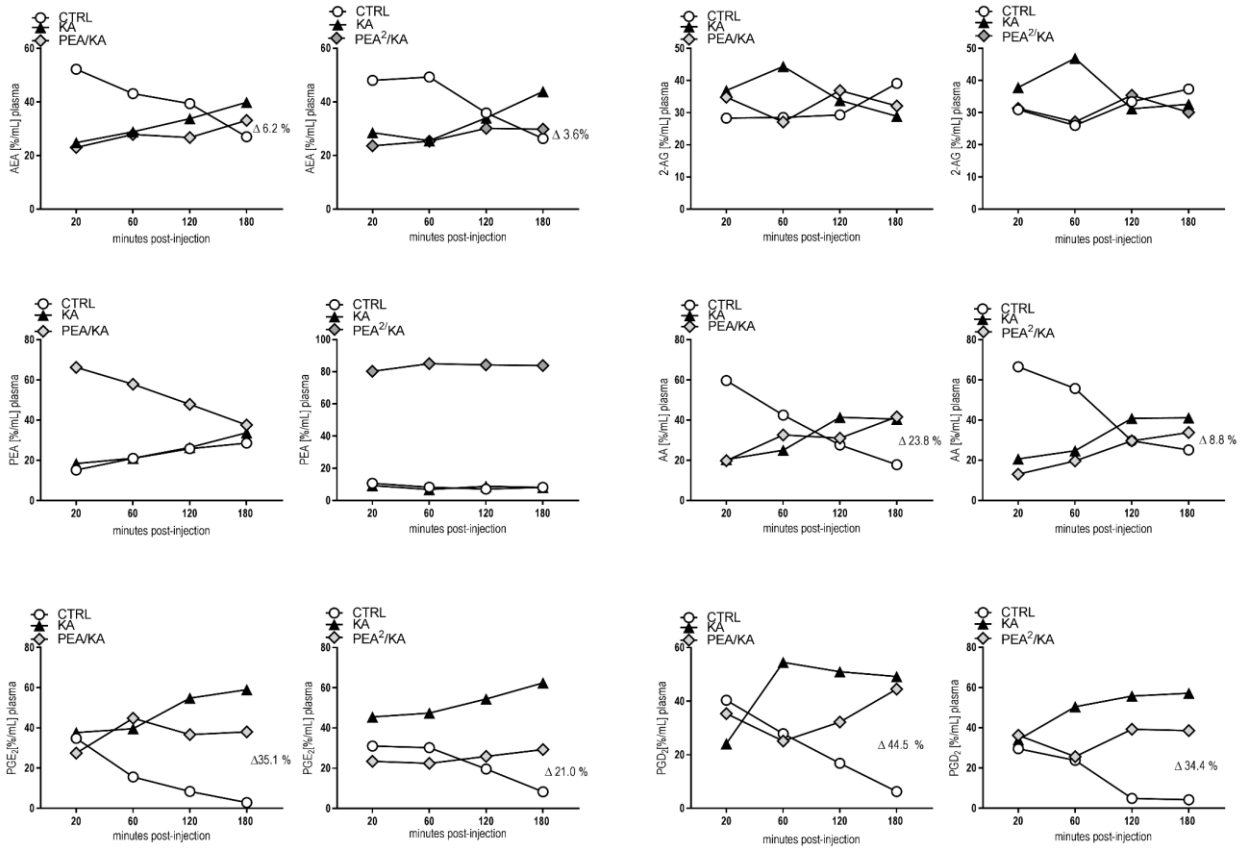
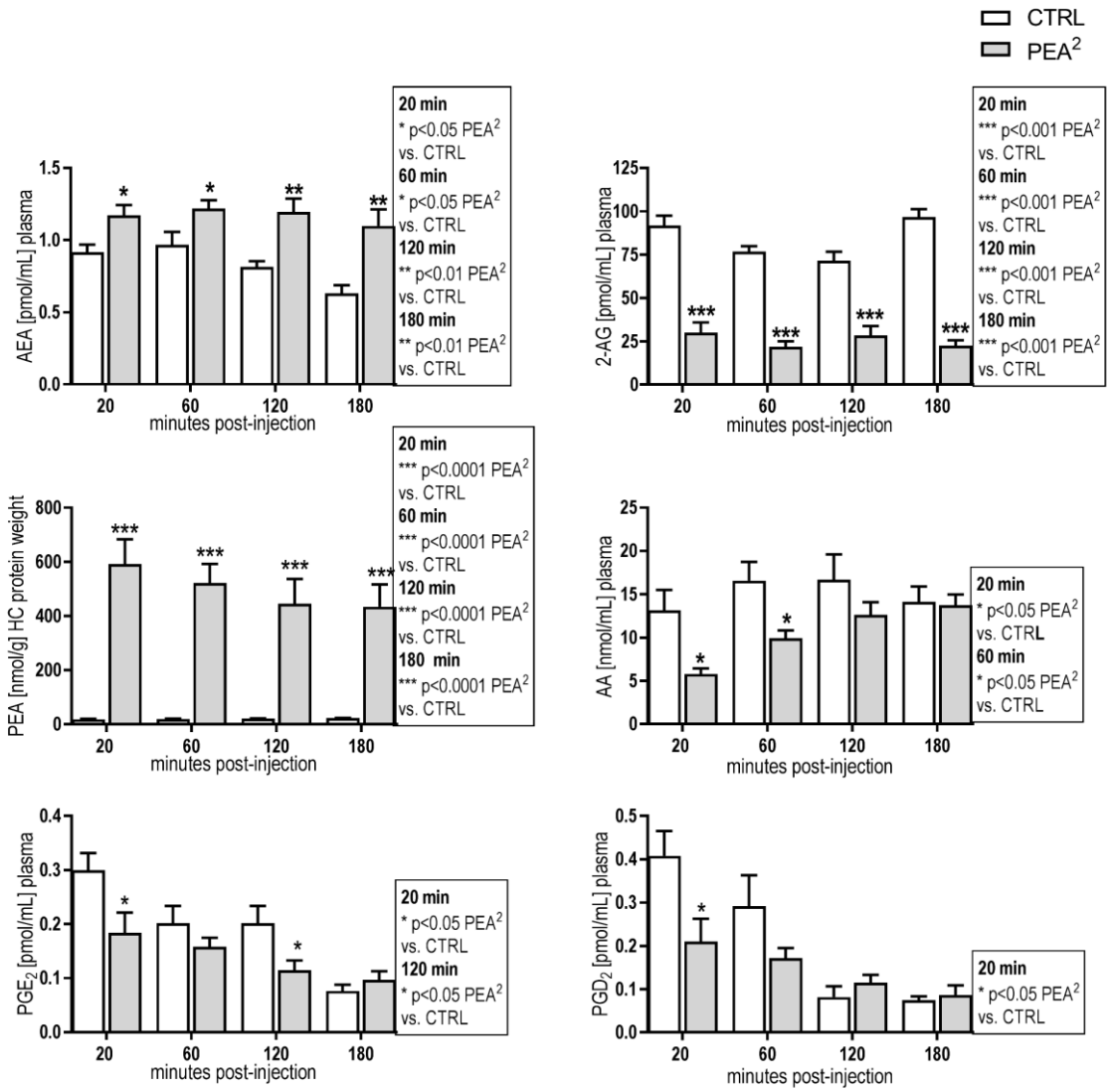
# Supplementary Material



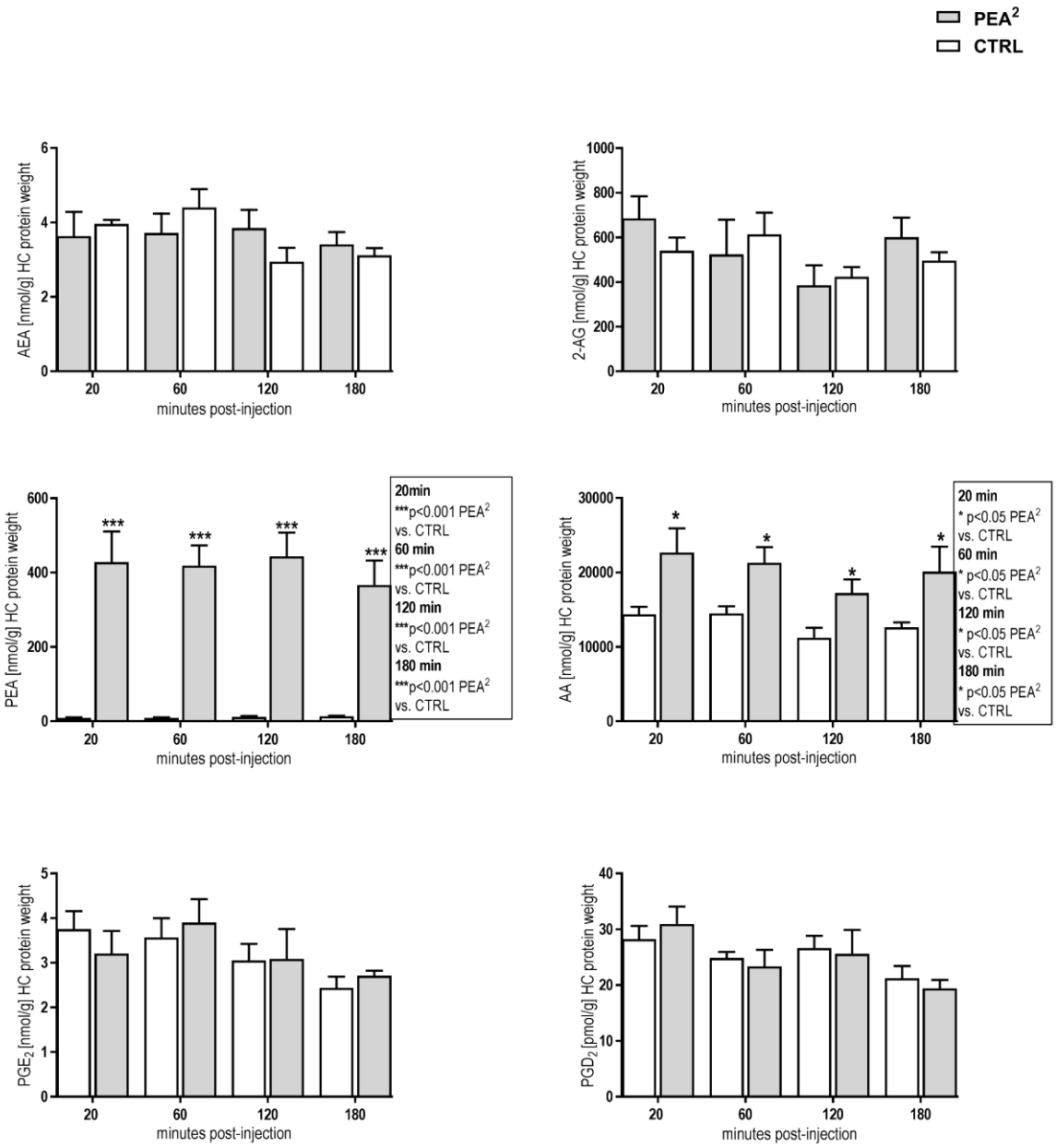

**Suppl. Figure 1.** Effect of acute and subchronic PEA-treatment on KA-induced epileptic seizures on hippocampal lipid (AEA, 2-AG, AA, PEA, $PGE_2$ and $PGD_2$) levels compared to vehicle injected controls over time course (20, 60, 120 and 180 min) post KA/vehicle-injection. Lipid levels are given in percentage, whereby the sum of average lipid levels of all three groups, at every time point was calculated and set to 100% and then percentages for every lipid level per time point and group were calculated. KA - kainic acid injected mice; PEA/KA - acute PEA-treated KA-injected mice; $PEA^2$/KA - subchronic PEA-treated KA-injected mice. Subchronic PEA-treatment modulates the lipid levels to an extent (%) closer to those of vehicle-injected group compared to acute PEA-treatment at the distinct time points.



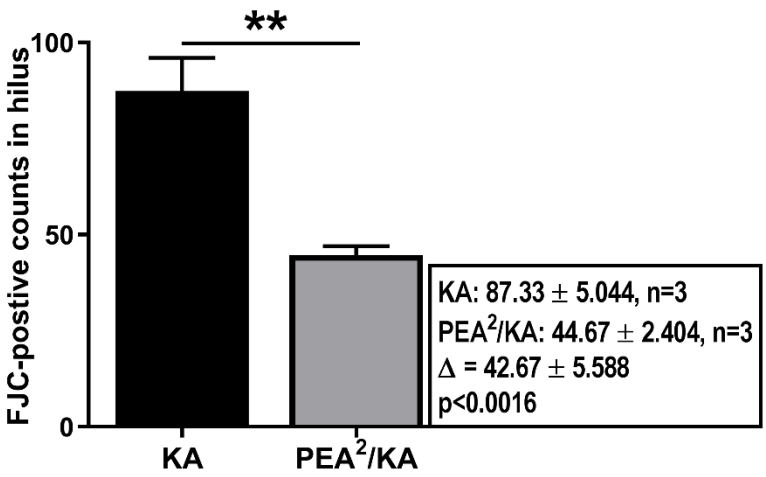

**Suppl. Figure 2** Effect of acute and subchronic PEA-treatment on KA-induced epileptic seizures on plasma lipid (AEA, 2-AG, AA, PEA, $PGE_2$ and $PGD_2$) levels compared to vehicle-injected controls over time course (20, 60, 120 and 180 min) post KA/vehicle-injection. Lipid levels are given in percentage, whereby the sum of average lipid levels of all three groups, at every time point was calculated and set to 100% and then percentages for every lipid level per time point and group were calculated. KA - kainic acid injected mice; PEA/KA - acute PEA-treated KA-injected mice; $PEA^2$ /KA - subchronic PEA-treated KA-injected mice. Subchronic PEA-treatment modulates the lipid levels to an extent (%) closer to those of vehicle-injected group compared to acute PEA-treatment at the distinct time points. Δ % depicts the variation in % of the lipid levels upon PEA-treatment from the vehicle-injected. The Δ % values depicted for AEA, AA, $PGE_2$, $PGD_2$ at 180 min are all superior for subchronic PEA-treatment compared to acute PEA-treatment.




**Suppl. Figure 3.** Plasma lipid (AEA, 2-AG, PEA, AA, $PGE_2$ and $PGD_2$) level changes of healthy controls upon subchronic administration of PEA ($PEA^2$) vs. vehicle-injected control mice. Error bars indicate SEM and asterisks in the figures indicate significant differences, *P < 0.05, **P < 0.01, ***P < 0.001.




**Suppl. Figure 4.** Hippocampal lipid (AEA, 2-AG, PEA, AA, $PGE_2$ and $PGD_2$) level changes of healthy controls upon subchronic administration of PEA ($PEA^2$) vs. vehicle-injected control mice. Error bars indicate SEM and asterisks in the figures indicate significant differences, *P < 0.05, ***P < 0.001.




**Suppl. Figure 5.** Semi-quantitative comparison of positive FJC signals in the hilus region from PEA-subchronically-treated ($PEA^2$/KA) vs. untreated (KA) epileptic mice. FJC signal were manually counted in three subsequent coronal brain sections distanced by 200 µm. Unpaired t-test revealed significant reduction ($p < 0.0016$) of FJC-sensitive neurodegeneration in ROI after subchronic PEA-treatment. Error bars indicate SEM and asterisks in the figures indicate significant differences, **$P < 0.001$.