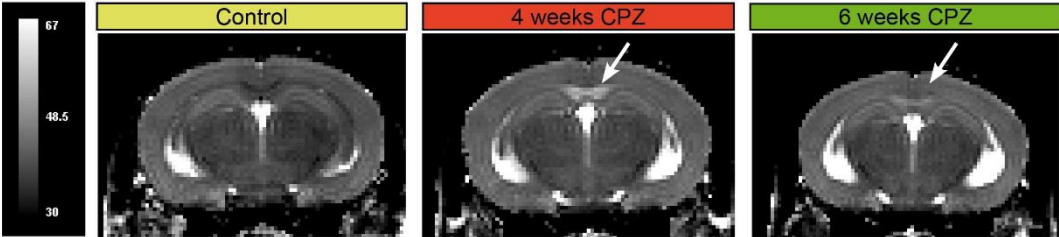
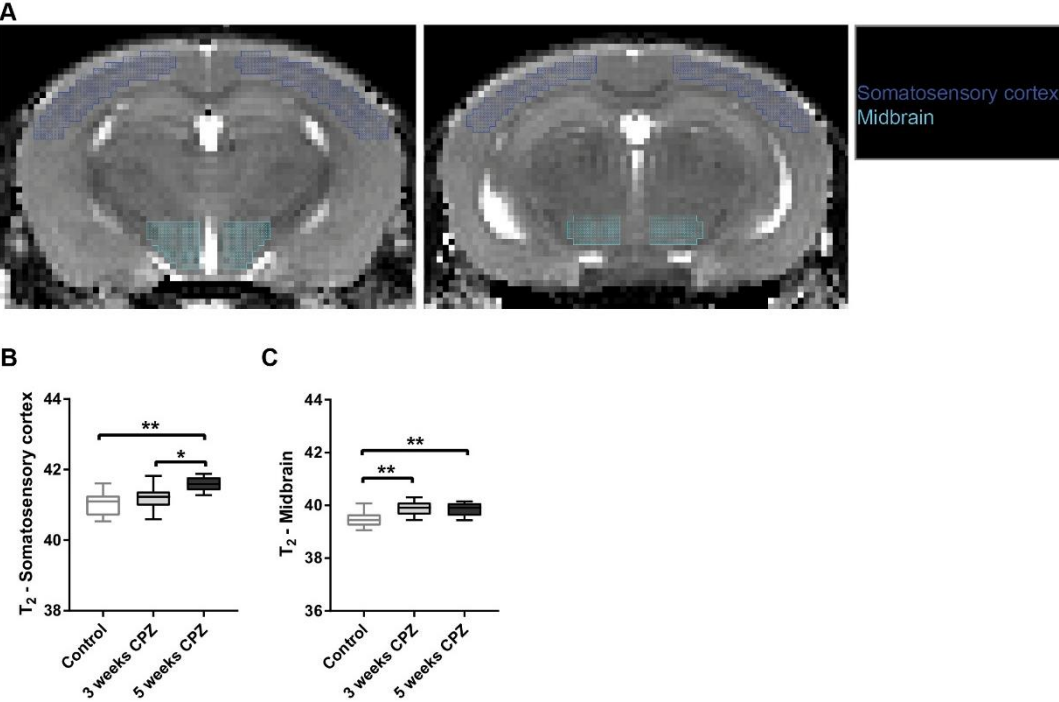


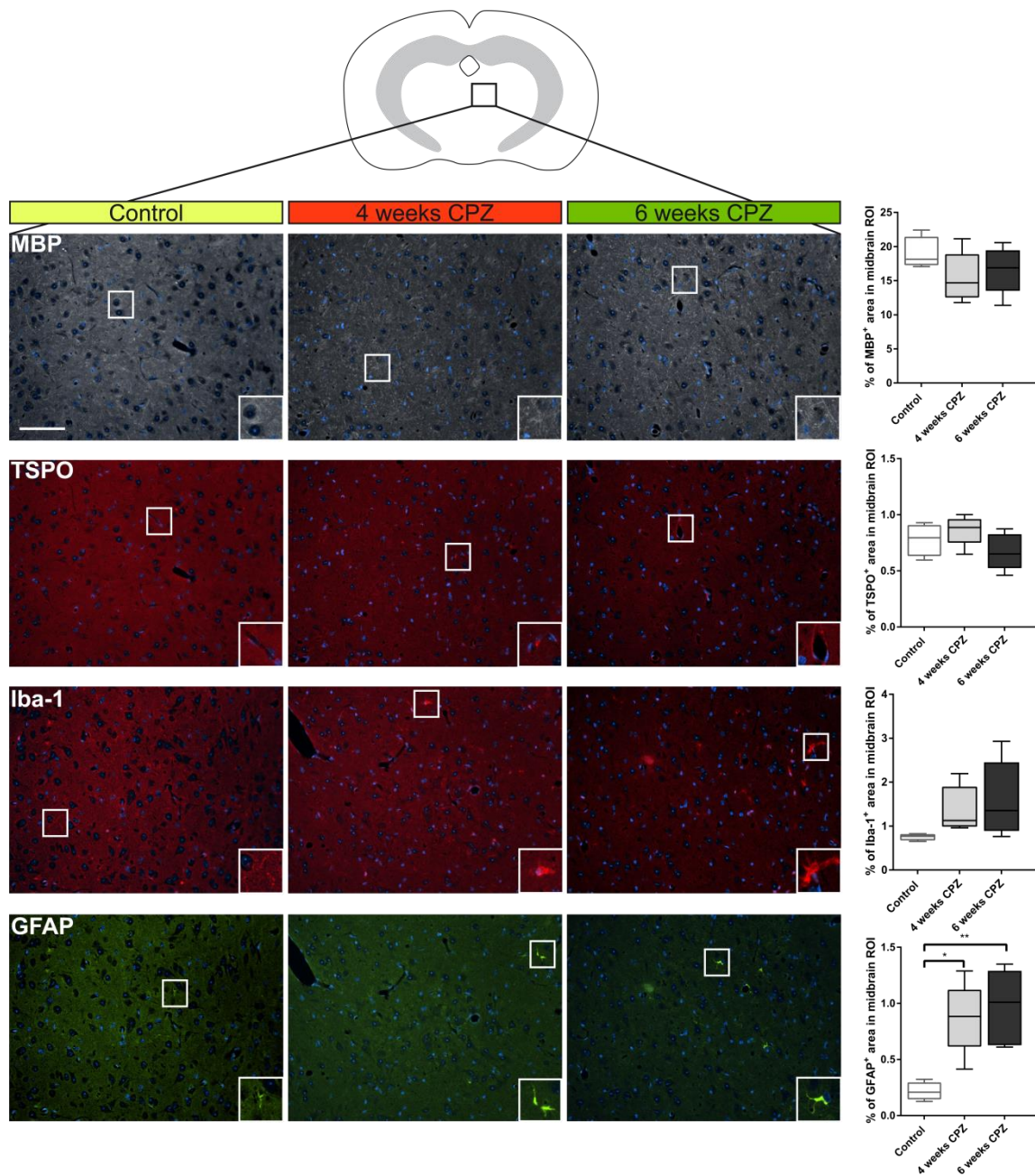
Supplementary material



Supplementary Figure 1: Representative T₂ maps showed that control mice displayed a dark, hypointense CC, while mice receiving three and five weeks of CPZ display a bright, hyperintense contrast in the CC (white arrows), indicative of demyelination, neuroinflammation and associated edema. Next, T₂ from the CC was decreased after five weeks compared to three weeks, suggesting partial recovery from the CPZ-induced injury.



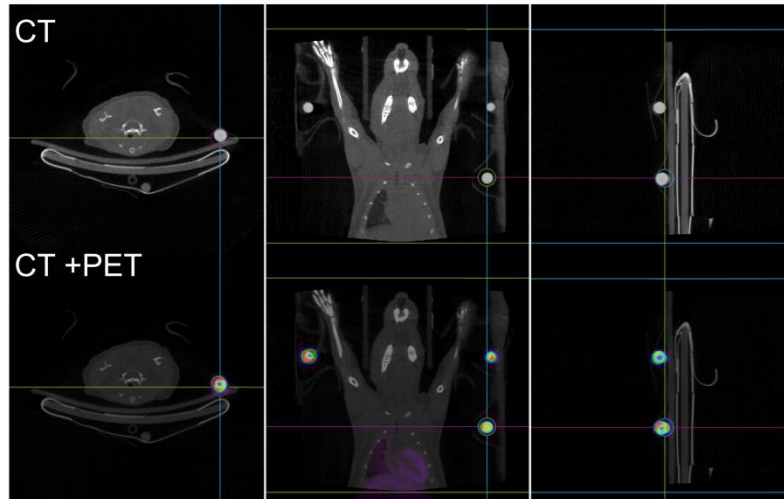
Supplementary Figure 2 : Quantification of mean T₂ values for control, CPZ-treated week 3, and CPZ-treated week 5 groups, in different brain regions (A). T₂ values were significantly increased in the (B) midbrain after three and five weeks of CPZ compared to control. T₂ values of the somatosensory cortex (C) were significantly increased only after five weeks of CPZ. (*One way ANOVA followed by Tukey multiple comparisons correction; *p < 0.05, **p<0.01, ***p < 0.001, ****p<0.0001*). Values are presented as Tukey box plots (mean ± SD). Abbreviations: CPZ, cuprizone.



Supplementary Figure 3: Investigation of the midbrain as pseudo reference region in the CPZ model. Analysis of the area of immunofluorescence for MBP, TSPO and Iba-1 does not show significant changes after CPZ treatment. Only a few TSPO and Iba-1 positive cells were observed (high magnification insets). The GFAP positive area in the midbrain was significantly elevated 4 and 6 weeks after CPZ induction, albeit at low levels (*One way ANOVA followed by Tukey multiple comparisons correction*; *p < 0.05, **p < 0.01). Values are presented as Tukey box plots (mean ± SD).

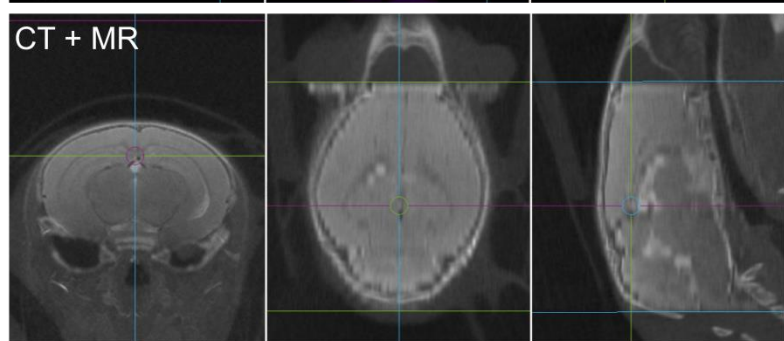
Step 1:
Co-registration of PET and CT using a landmark based approach

Outcome: PET and CT co-registered



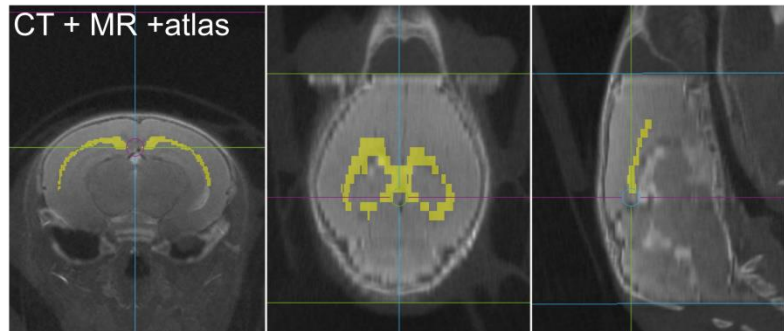
Step 2:
Co-registration of CT with MR using skull contours

Outcome: CT and MR co-registered



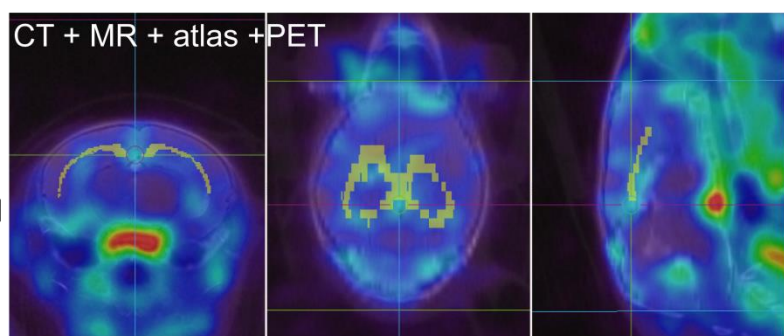
Step 3:
Co-registration of CT-MR with atlas using skull contours

Outcome: CT, MR and atlas co-registered



Step 4:
Translation of CT image transformation parameters to PET

Outcome: CT, MR, atlas and PET co-registered



Supplementary Figure 4: Overview of the co-registration work flow. First PET and CT images were co-registered in three dimensions using spheres as landmarks. In a second and third step CT images and the brain atlas were co-registered to MR images using the skull contour as reference. In a last step CT image transformation parameters were transferred to PET images leading to co-registered PET/MR images.