Longitudinal investigation [1] of neuroinflammation and metabolite profiles in the $APP_{swe} \times PS1_{\Delta e9}$ transgenic mouse model of Alzheimer's disease.

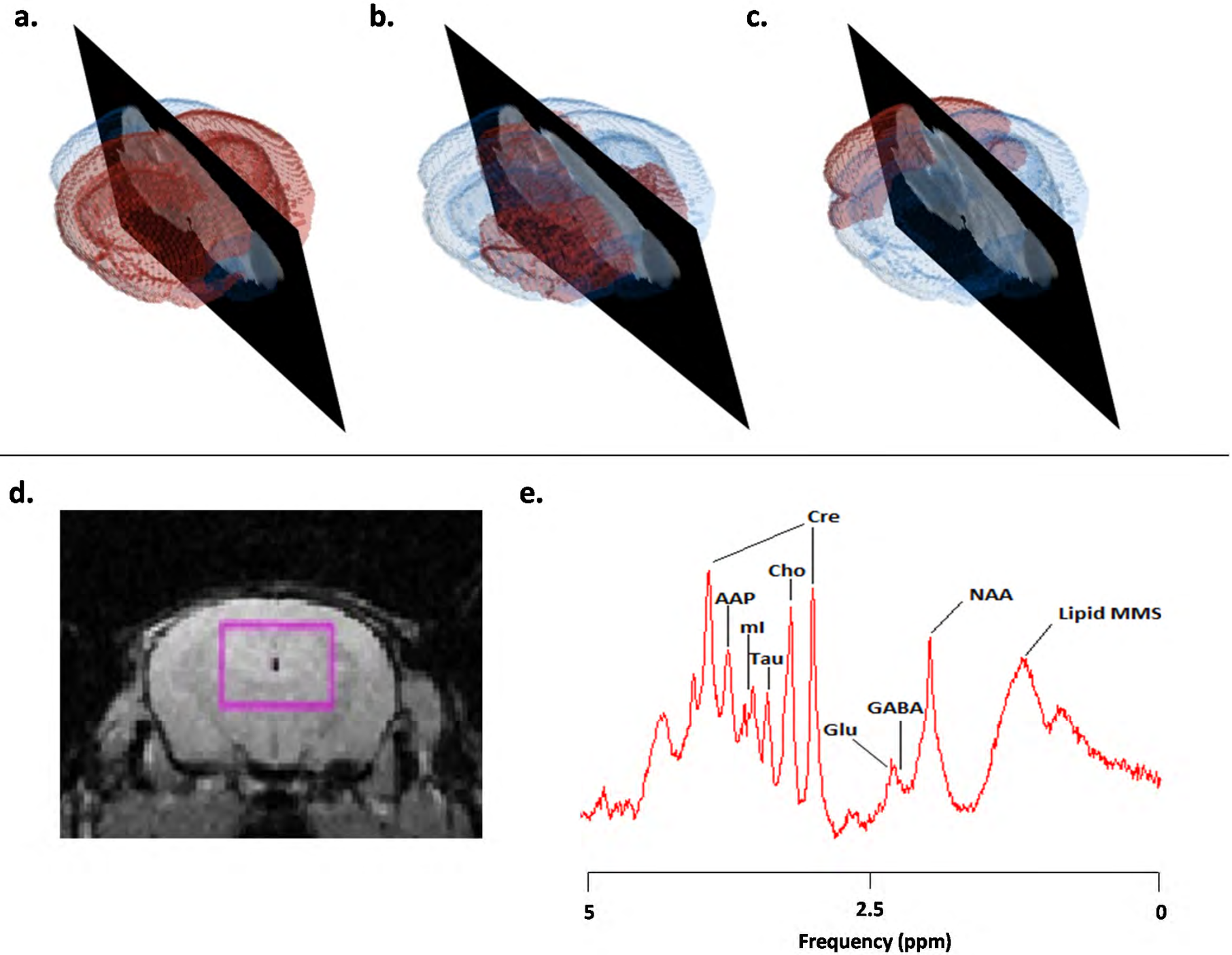
Chaney A.[1,2]*, Bauer M.[3†], Bochicchio D.[2†], Smigova A.[1,2], Kassiou M.[4], Davies K.E.[1]4 , Williams S.R.[1], Boutin H.[1,2].

[1] Centre for Imaging Science, Faculty of Biology, Medicine and Health and Manchester Academic Health Sciences Centre University of Manchester, Manchester, M13 9PT, UK
[2] Wolfson Molecular Imaging Centre, Faculty of Biology, Medicine and Health and Manchester Academic Health Sciences Centre, University of Manchester, Manchester, M20 3LJ, UK.
[3] Medical University Vienna, Department of Clinical Pharmacology, Waehringer Guertel 18-20, 1090 Vienna, Austria.
[4] School of Chemistry, University of Sydney, NSW 2006 Australia.

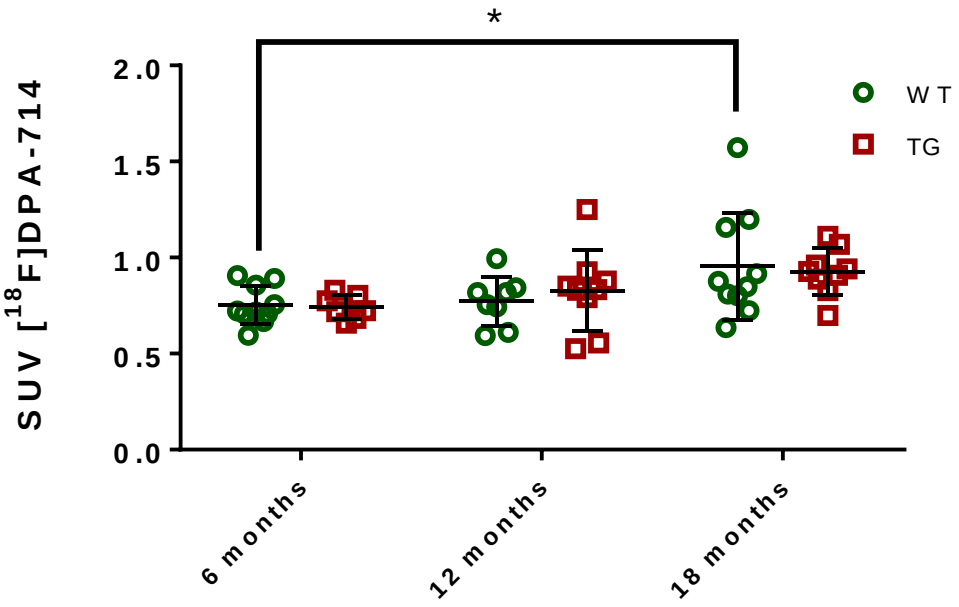
† Contributed equally to the work

* Current address: 3165 Porter Drive, Stanford University, Palo Alto, CA, 94304.

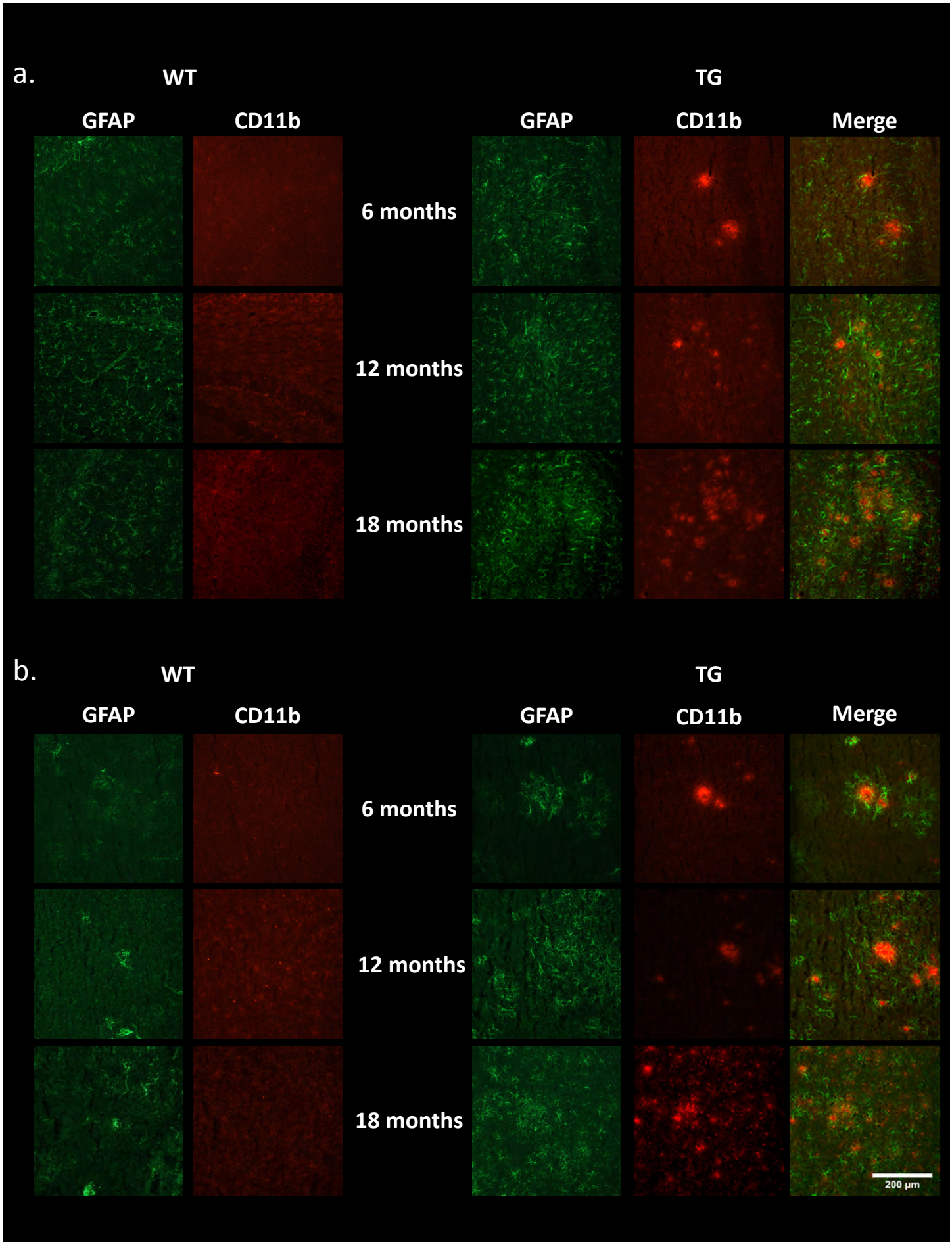
Corresponding Author:
Dr Hervé Boutin,
Wolfson Molecular Imaging Centre,
27 Palatine Road, Manchester, M20 3LJ, UK
Email: herve.boutin@manchester.ac.uk
Tel: +44 161 275 0078
Fax: +44 161 275 0003



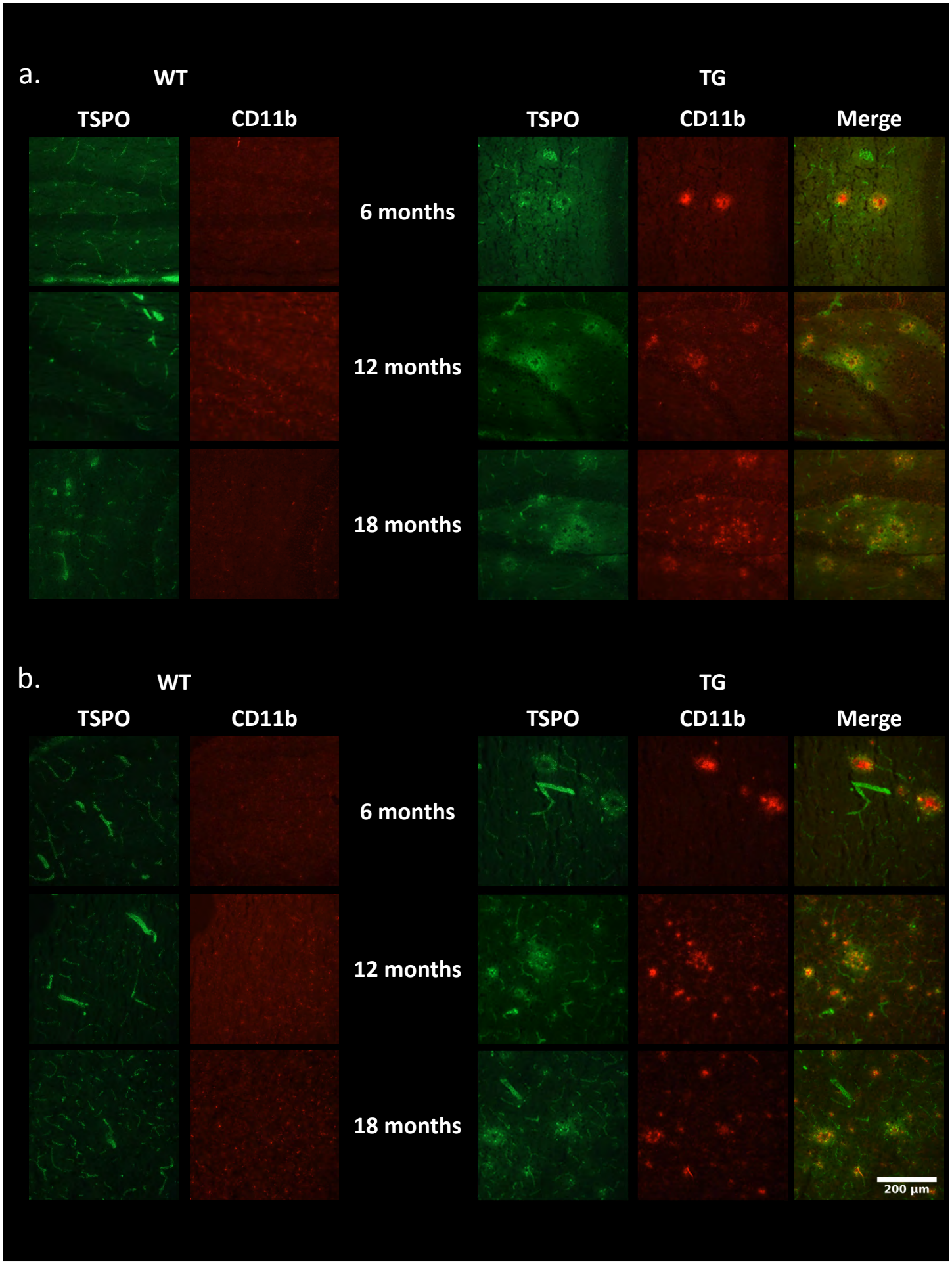
Supplementary figure 1: Whole brain was segmented into the hippocampus and cortex (**a**), other subcortical (**b**) and cerebellum (**c**) regions of interest for PET quantification using a modified version of the Waxholm space template (Johnson et al. 2010). The MRS voxel was centred at bregma -2.30mm according to the Paxinos mouse brain atlas and encompassed hippocampal and thalamic regions (**d**). Example of an MRS spectrum i*n vivo* with the main metabolites highlighted (**e**). AAP-amino acid proton, mI-myo-Inositol. Tau-taurine, Cho-choline containing compounds, Cre- creatine+phosphocreatine, Glu- glutamate, GABA- γ-aminobutyric acid, NAA- N-acetylaspartate, Lipid MMS- lipid and macromolecules.



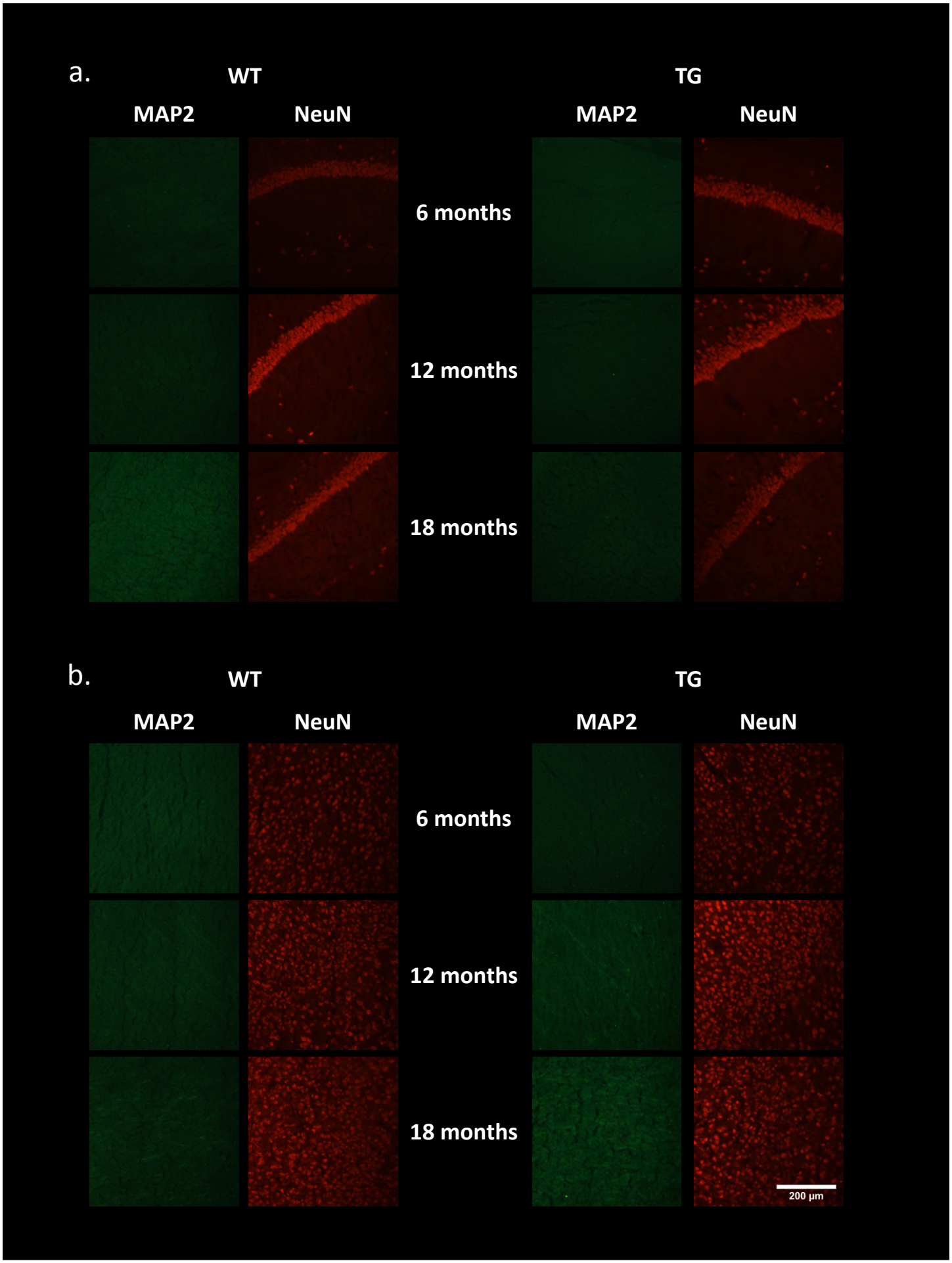
Supplementary Figure 2: [^{18}F]DPA-714 standard uptake value in the cerebellum of WT and APP_{swe}×$PS1_{\Delta e9}$ mice at 6 (WT n=10, TG=7), 12 (WT n=8, TG=9) and 18 months (WT n=10, TG=9) of age. Results are expressed as mean±SD. Statistical analysis was performed using two-way ANOVA followed by Sidak's post-hoc analysis (*p≤0.05).



Supplementary figure 3: Immunoreactivity of GFAP (green) and CD11b (red). Representative images of double staining in the hippocampus (**a**) and cortex (**b**) of WT and $APP_{swe} \times PS1_{\Delta e9}$ mice at 6, 12 and 18 months of age. Pictures were taken at **20×** magnification between bregma -2.06mm and -2.30mm. Scale bar represents 200µm.



Supplementary figure 4: Immunoreactivity of TSPO (green) and CD11b (red). Representative images of double staining in the hippocampus (a) and cortex (b) of WT and APPswe×PS1Δe9 mice at 6, 12 and 18 months of age. Pictures were taken at **20×** magnification between bregma -2.06mm and -2.30mm. Scale bar represents 200µm.



Supplementary figure 5: Immunoreactivity of MAP2 (green) and NeuN (red). Representative images of double staining in the hippocampus (**a**) and cortex (**b**) of WT and APP_{swe}×$PS1_{\Delta e9}$ mice at 6, 12 and 18 months of age. Pictures were taken at **20×** magnification between bregma -2.06mm and -2.30mm. Scale bar represents 200µm.