Type of presentation: Poster

LS4-P-11 Post mortem degradation of ferritin and its significance for determining the iron content of the human brain

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There are several ways of visualizing iron in the human brain. Most of the iron is stored in ferritin's iron core, and these cores can be visualized on iron (L-) maps using energy filtered transmission electron microscopy. MRI allows iron quantification by applying R_2* mapping. R_2* is strongly dependent on the paramagnetic properties of ferritin. However, the relationship between magnetic configuration of the iron core in ferritin is still incompletely understood and could influence the accuracy of iron quantification using MRI. It is generally believed that most of the signal from R_2* mapping is picked up from the iron cores of ferritin, and not from cytoplasmic iron.

We aimed to use small brain samples of human donors in order to relate the R_2* signal with numbers of ferritin and total iron content. For this, we combined iron mapping using electron microscopy with R_2* mapping using quantitative fMRI, and determined the total iron content using mass spectrometry. The number of ferritin cores was determined from iron maps of postmortem brain samples from six deceased human subjects. The mean iron content of adjacent human samples were obtained using mass spectrometry, and quantitative MRI at 3 Tesla was used for R_2* mapping of the same samples. Analyses focused on three gray matter regions: the frontal cortex, putamen, and globus pallidus. The post mortem intervals of the human donors had ranged from 6 to 24 hours. We demonstrated that autolysis led to a rapid degradation of ferritin iron cores, with fewer than one-third remaining detectable via EFTEM after 24 hours postmortem. The degradation followed a single-exponential decay pattern, suggesting that approximately 94% of the total brain iron is stored in ferritin in fresh tissue. However, R_2* relaxation rates did not follow this degradation pattern but instead correlated strongly with total iron content as measured by mass spectrometry. This signifies that R_2* mapping-derived magnetic susceptibility for iron appeared to be independent of the structural and magnetic organization of the ferritin iron core and shows a linear relationship with total iron content.

grant sponsor: FWF, grant 10.55776/P29370; ethics votum Medical University of Graz, 28-549 ex 15/16