NEURONAL CHANGES IN PLAQUE BEARING AND NON-PLAQUE BEARING ANIMAL MODELS OF ALZHEIMER’S DISEASE

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Studies using transgenic mice that incorporate Alzheimer’s disease (AD) mutations are valuable for studying disease pathology. It is still undetermined what forms of amyloid aggregates are more pathologenic; insoluble fibrils or soluble oligomers. We examined the changes in total cell and neuronal populations in different mouse models of AD harboring different APP mutations and exhibiting different amyloid phenotypes.

TgCRND8 (K670M/N671L; V717F), and Dutch (E693Q) mice were used in this study. Total cell and neuronal populations in the neocortex, hippocampus and cerebellum were obtained using a derived cell counting method called isotropic fractionation. Total cell counts were determined by staining nuclei with DAPI and total neuron counts were determined by co-staining with the NeuN. We found no differences in total and regional brain weights as well as total cell numbers between transgenic and controls.

We found a decrease in the number of hippocampal neurons of TgCRND8 mice compared to controls and no difference between Dutch mice and their controls. When we normalized the data to the mean of respective control mice we found that TgCRND8 mice exhibited a decrease in hippocampal neurons compared to Dutch mice while Dutch mice exhibited a decrease in cortical neurons. No significant differences were observed in the cerebellum, however, TgCRND8 mice had fewer neurons compared to Dutch.

Our data suggests that mutations in APP that result in deposition of insoluble amyloid structures and plaques have a more detrimental effect on neuronal viability than mutations that cause an increase in soluble amyloid species and vascular amyloid.