EFFECTS OF SPECIFIC DHA AND CHOLESTEROL CONTAINING DIETS ON SYNAPTIC DENSITY AND NEUROGENESIS IN 10-13 MONTHS-OLD APP/PS1, APOE4 AND APOE KNOCKOUT MICE

X. Fang\textsuperscript{1,2}, D. Jansen\textsuperscript{1,2}, A. Rijpma\textsuperscript{1,2}, M. Wiesmann\textsuperscript{1,2}, I.A.C. Arnoldussen\textsuperscript{1,2}, C.I.F. Janssen\textsuperscript{1,2}, V. Zerbi\textsuperscript{1,2}, P. Schipper\textsuperscript{1,2}, L.M. Broersen\textsuperscript{3}, J.P. Dederen\textsuperscript{1,2}, A.J. Kiliaan\textsuperscript{1,2}

\textsuperscript{1}Anatomy, \textsuperscript{2}Cognitive Neuroscience, Donders Centre for Neuroscience, Radboud University Nijmegen Medical Centre, Nijmegen, \textsuperscript{3}Danone Research, Wageningen, The Netherlands

Introduction: Alzheimer's disease (AD) is a progressive neurodegenerative disorder, and early phenomenons in the neurodegenerative process are synaptic damage and impaired neurogenesis. It has been shown that high cholesterol and docosahexaenoic acid (DHA) intake affect the course of AD, possibly by influencing the cerebral circulation and neuronal membrane integrity with herewith related synaptic density and neurogenesis.

Aim: We therefore investigate the effects of DHA and cholesterol containing diets on synaptic density and neurogenesis in a 10-13 months-old male AD mouse model (APPswe/PS1dE9) and mouse models for hypercholesterolemia and atherosclerosis (ApoE4 mice and ApoE knockout (-/-)).

Methods: From 2 months of age, mice were fed a standard diet, a diet enriched with 1% cholesterol, or a multi-nutrient diet containing precursors and cofactors in brain membrane synthesis, such as DHA, phospholipids, uridine monophosphate, choline, B-vitamins and antioxidants (Fortasyn). Synapses were visualized with synaptophysin antibody. Neurogenesis was examined with doublecortin immuno-labeling. Synaptic density (SD) and doublecortin-positive cells were quantified in the hippocampus.

Results: Synaptophysin and doublecortin stainings are currently being analyzed and will be presented.

Conclusions: We expect to find increased SD and neurogenesis in the transgenic animal models and an even higher increase in cholesterol fed mice, suggesting a compensatory mechanism for impaired synaptic function and neurodegeneration. We hypothesize that a high cholesterol intake may cause impaired cerebral blood flow (as shown in earlier studies) inducing ischemia, fortifying the above mentioned hypothesis of a compensatory mechanism.