Effect of moderate-high intensity aerobic exercise on beta-amyloid accumulation measured with $^{11}$C-PIB-PET in patients with mild to moderate Alzheimer´s disease

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**Introduction:** Physical exercise may be an important adjunct to pharmacological and other non-pharmacological treatment of Alzheimer’s disease (AD). Several studies have indicated a beneficial effect of physical activity on symptoms of AD, but biological mechanisms underlying this effect remains relatively uninvestigated. Such mechanisms include induction of neurogenesis, effects on vascular risk factors as well as reduction of deposits of beta-amyloid. The objectives of the present study was to investigate whether moderate-high intensity aerobic exercise reduces the accumulation of beta-amyloid in AD.

**Methods:** The ADEX study is a multi-center randomized, controlled trial which aimed to investigate the impact of a supervised aerobic exercise program on symptoms and biomarkers of AD. A total of 200 patients with mild AD were randomized to either an exercise group (60-minute exercise sessions three times a week for 16 weeks) or to a control group (usual care). Of these a subgroup of patients underwent $^{11}$C-PIB-PET and 3-Tesla MRI for the quantification of beta-amyloid deposition. The regional PET standardized uptake value (SUV) was measured. Data were normalized to gray matter cerebellum standardized uptake value, resulting in a region-to-cerebellar ratio (SUVR). Between-group difference in change in global SUVR (lateral temporal cortex, posterior cingulate gyrus, anterior cingulate gyrus, precuneus, parietal cortex, and lateral prefrontal cortex) from baseline was assessed using un-paired t-test.

**Results:** A total of 34 participants ((mean; ± SD) Age: mean; SD, baseline MMSE: 25.6; ±2.7, gender (f/m): 16/18) underwent MRI and $^{11}$C-PIB-PET at baseline. At baseline 15 subjects were randomized to the intervention, 19 to the control group. There was no significant difference between groups in baseline variables (age, gender, MMSE). Baseline SUVR was for the intervention group 2.32 (1.18-2.79), and for usual care group 2.04 (range: 1.15-2.65) There was an increase in SUVR from baseline to follow-up (intervention group: 0.040; ±0.033 vs. usual care group: 0.025; ± 0.029, respectively) in both groups but no significant between-group difference in change from baseline between the intervention and control group (p=0.74).

**Conclusion:** The present findings do not support an effect of physical exercise on global beta-amyloid deposition in patients with AD. Longer duration of interventions, either of each exercise schedule or trial period, as well as higher intensity of exercise, may be needed in order to affect global beta-amyloid deposition, but further analysis are needed to investigate regional effects and associations to other biochemical markers and cognitive function. Other mechanisms than amyloid accumulation may also underlie the effects of physical exercise on symptoms of AD.