Moderate-to-high intensity physical training does not alter the cerebrospinal amyloid-β_{1-42} levels in patients with Alzheimer’s disease

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**Background:** Alzheimer’s disease (AD) is a progressive neurodegenerative disease, for which there are very few therapeutic option available. Previous studies have indicated that β-amyloid_{1-42} (Aβ42) levels in brain in a transgenic mouse model for AD, and in serum in humans, can be altered in response to physical exercise.

**Objective:** To investigate whether 16 weeks of supervised moderate-to-high intensity physical exercise influences the CSF Aβ_{1-42} levels in patients with AD.

**Methods:** In a randomized, controlled multicenter trial conducted at 8 memory clinics in Denmark (the ADEX study), we recruited 200 patients with mild AD to a supervised aerobic exercise group (60-minute exercise sessions three times a week for 16 weeks) or to a control group. The exercise aimed to achieve an intensity of 70-80\% of maximal individual heart rate. In a subgroup of subjects (n=37, 24 males/13 females; mean age: 67.2 years +/- 6.7, (54-79), mean MMSE: 24.7 +/- 5.0 (18-30)), we analysed CSF for Aβ42 before and after 16 weeks of physical exercise. Analysis was performed with Meso Scale Discovery systems β-Amyloid 38, 40 & 42 triplex. Statistical Analysis of Aβ42 levels in the four groups was performed using one-way analysis of variance (ANOVA), and for two group comparison the paired t-test was chosen.

**Results:** At baseline, mean levels of Aβ_{1-42} were comparable in the two groups (168 pg/ml in intervention group, 147 pg/ml in control group) and no significant difference (p = 0.206) in CSF levels of Aβ42 was found between the two groups, after 16 weeks of moderate-to-high intensity physical exercise (184 pg/ml in intervention group, 188 pg/ml in control group). However, a non-significant trend was found when comparing delta values (baseline – follow up) for the two groups (p = 0.18).

**Conclusion:** We could not detect changes in CSF levels of Aβ42 after 16 weeks of moderate-to-high exercise in mild AD patients, which may suggest that physical exercise cannot reduce cerebral amyloid load.
Figure 1: Concentration of Aβ1-42 in CSF in controls and intervention, at baseline and after 16 weeks of moderate-to-high exercise, respectively. In the overall cohort no significant difference in Aβ1-42 is observed. When comparing controls at baseline and follow up, no significant difference is observed (mean: 147 pg/ml at baseline vs. 188 pg/ml at follow up). Further when comparing intervention at baseline and follow up, no significant difference is observed either (mean: 168 pg/ml at baseline vs. 184 pg/ml).
Figure 2: Delta (Baseline – Follow up) concentration Aβ1-42 in CSF in controls and intervention. No significant difference in Aβ1-42 is observed.