

**OBJECTIVE**

To determine if changes in arterial and venous cerebral blood flow (CBF) and pulsatility index (PI) predict changes in Aβ in preclinical AD.

**METHODS**

**Participants and Protocol:**

- **Recruitment from Wisconsin Alzheimer’s Disease Research Center or community**
- **Inclusion Criteria:** Middle-aged adults (aged 40-72 years) with a potential history of AD
- **Exclusion Criteria:** dementia or mild cognitive impairment on baseline screening, use of or contraindications to use of acetylcholinesterase inhibitors, use of or contraindications to use of statins, or any history of cardiovascular disease that would contraindicate participation in an MRI study

**Baseline:**

- **Aβ42** Enriched, Randomized n=4 per group, stratified by sex and APOE allele status
- **All baseline, month 12, and month 18 MRI with PC-POWER, and LP and cognitive assessments.**

**RESULTS**

**Baseline Group Differences:**

- **No differences at baseline between APOE4 carriers and non-carriers (all p-values > 0.19).**
- **Baseline straight sinus CBF (p = 0.036) and working memory performance (p = 0.035) were greater in the treatment group than placebo group.**
- **Women performed better on memory and learning tasks than men (p = 0.046).**

**Effects of Simvastatin on Outcomes (Table 2):**

- **The simvastatin group trended towards increased pica CBF (p = 0.063).**
- **The simvastatin group had decreased PI in venous segments at month 18 (SSS, p = 0.012; SSF, p = 0.042).**
- **The simvastatin group showed trends towards decreased PI in multiple arteriolar vessels (pica, p = 0.06; cica, p = 0.07).**

**Relationship between PC-POWER measures and CSF Aβ:**

- **Change in CBF or PI over time did not predict change in CSF Aβ over time (all p-values > 0.24).**
- **Change in cica PI predicted change in CSF Aβ at month 12 (p=0.005).**

**CONCLUSIONS**

- **18-month simvastatin therapy in a middle aged population with a family history of AD reduced PI but did not significantly affect Aβ burden.**
- **Simvastatin treatment decreased pulsatility index in cerebral veins.**
- **Simvastatin treatment showed trends towards beneficially lowering pulsatility index and increasing blood flow in cerebral arteries.**
- **This study supports the hypothesis that cerebrovascular changes precede detectable change in AD neurotoxins in healthy, middle aged adults.**
- **This study provides novel evidence supporting a cascade from increased vessel stiffness to increased Aβ burden.**

**REFERENCES & ACKNOWLEDGEMENTS**

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Full reference list: goo.gl/mGREb

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