Alzheimer’s Disease (AD) Prevention

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Outline

• Risk Factors
• Lifestyle modifications
  • Mediterranean Diet
  • Multidomain Intervention Trials
  • Cognitive Training
  • Sauna
  • Exercise
• Summary
Risk Factors

• Not Modifiable
  • Age
  • Genetics (ApoE4, APP, Presenilin)

• Modifiable
  • Central obesity, hyperlipidemia, hypertension, insulin resistance, diabetes (3x), smoking, MDD, CAD, CVD, physical inactivity, elevated homocysteine and low B12, and low education
  • 1/3 AD cases may be prevented by controlling these factors
  • Antihypertensive meds may result in 19-55% reduction in cognitive decline, vascular dementia, and AD
  • Insomnia or excess sleep (>9 hours)
  • Hearing loss

• Sometimes Modifiable
  • TBI – number and age
Mediterranean Diet

• Systematic review$^2$ of 18 studies (5 RCTs)
  • Improvements in global cognitive functioning, memory, language, and executive function
  • No impact on incident dementia
  • Hybrid diet with DASH - decreased risk for cognitive decline and incident AD
• Less atrophy on MRI and less amyloid-B protein accumulation$^6$
Multidomain Lifestyle Intervention Trials

• PreDIVA$^3$ – 6 yr open cluster RCT that included 3500 cognitively healthy pts 70-78 years old
  • Intervention – Nurses gave advice every 4 months on nutrition and exercise, managed cardiovascular diseases vs. control received general health advice
  • Results – No reduction in dementia or disability score

• Multidomain Alzheimer Prevention Trial (MAPT)$^3$ – 3 yr double-blind RCT that included 1600 >70 yr old with subjective memory complaint, slow walking speed, and limitations in IADLs
  • Intervention – Nutritional and exercise advice, cognitive training, management of cardiovascular diseases and DHA 800mg/day
  • Results – No effect on cognitive decline initially, post-hoc analysis showed those with a positive amyloid scan showed a significant benefit from the intervention
Multidomain Lifestyle Intervention Trials

- Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER)\(^6\) – 2 yr RCT that included 1200 adults from 60-77 at risk for dementia
  - Intervention – Advice on nutrition and GUIDED physical activity and cognitive training, cardiovascular risk management or control receiving general health advice
  - Results – Both groups showed cognitive improvements, 2 yrs post the intervention group showed 25% greater improvement in memory, processing speed and executive function\(^7\)
  - Ongoing 5 year follow up
Cognitive Training

• ACTIVE³ – RCT with 2800 cognitively healthy pts > 65
  • Intervention – 10 group sessions over 6 weeks that included training in either memory or reasoning/speed of processing + a few sessions before 1ˢᵗ and 3ʳᵈ year follow up (control group had no intervention)
  • Results
    • Domain specific training was beneficial in the targeted domain
    • Improvements in cognitive performance were maintained at 5 years
    • Self reported improvement in ADLs
    • 10 years - intervention group had less functional decline and dementia rates were significantly lower in participants in the speed of processing intervention group
Sauna

• Prospective cohort of 2315 men 42-60 yo were followed for median of 20 years – 204 diagnosed with dementia and 123 with AD
  • Intervention – Observe sauna use over time and risk for AD
  • Controlled for age, alcohol, BMI, systolic BP, smoking, Type 2 DM, previous MI, resting heart rate, LDL-C, physical activity, and socio-economic status
  • Results – HR for dementia and AD was significant at 4-7x/week: 0.34 (95% CI: 0.16–0.71 P = 0.004) and 0.35 (95% CI: 0.16–0.90 P = 0.029), respectively
  • Reduces blood pressure and increases vascular compliance
Exercise

- Mental Activity and eXercise (MAX)\(^2\) trial
  - Intervention – all received mental activity and exercise for 60min/day for 3 days/week for 12 weeks
  - Results – Improved health-related quality of life

- Meta-analysis of 18 RCTs in those with dementia found aerobic exercise (with or without nonaerobic exercise) may improve cognitive function\(^2\)

- Systematic review of 24 studies (16 moderate quality) excluding those with dementia – 18 showed decreased risk of AD\(^8\)
Future Research

• Studies are currently being done assessing lifestyle interventions and looking at the impacts in individuals with different genotypes (ex. ApoE and MTHRF)
Summary

• Up to 1/3 of AD cases may be prevented by lifestyle modifications including:
  • Mediterranean / DASH diet
  • Regular Exercise
  • Sauna Use
  • Sleep
  • Smoking Cessation
  • Controlling/preventing chronic diseases
  • Hearing Loss
  • TBI
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