A Clinical Precision Medicine Approach Reduces Alzheimer’s, Dementia and Vascular Risk and Improves Cognition: A Prospective Cohort Study from the Alzheimer’s Prevention Clinic at Weill Cornell Medicine and New York-Presbyterian

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Background

The Alzheimer’s Prevention Clinic provides direct clinical care to patients who receive evidence-based, individualized early interventions applying principles of pharmacogenomics, nutrigenomics and clinical precision medicine.

Objectives

Our primary outcome measure was change in six AD, dementia, and vascular risk scales in response to multi-modal interventions. Secondary outcome measures include overall and differential effectiveness of interventions on blood biomarkers and cognition (based on genotype and physician & patient-reported adherence).

Study Design & Participants

This prospective cohort study includes patients with family history of AD and no or minimal cognitive complaints, and preclinical AD or MCI. 166 participants met inclusion criteria (mean age 63±4.6, 50.6% female). Using SPSS, paired sample t-tests were computed to compare changes in risk scales in subjects with blood biomarker data at baseline and six-months. Changes in blood biomarkers were compared using ANOVA within and across different genotype and adherence groups. Multiple repeated measures general linear models were computed to compare changes in cognition per genotype and adherence. NIH Toolbox cognitive scores were corrected for age, gender, ethnicity, and education to account for multiple comparisons across groups.

Measures

Clinical assessment
- Visit with neurologist & neurological exam
- Anthropometrics: vital signs/biometric assessment
- Laboratory measures: blood biomarkers and genetics

Cognitive assessment
- Traditional tests: MMSE; FAS; ANT; Trails B; Boston Naming
- WHTB-CB tests: RAVLT Auditory Verbal Learning (Trials 1-3); RAVLT Delayed Recall & Recognition; Dimensional Change Card Sort (DDCS); Flanker Inhibitory Control and Attention; Pattern Comparison Process Speed; Odor Identification; Oral Symbol Digit (OSD); Picture Vocabulary; Oral Reading Recognition

Lifestyle & nutritional recommendations
- Recommendations refined based on clinical measures (see Biomarker-Intervention Paradigm below)

Behavioral assessment
- Adapted MIND-DIET questionnaire (Patient-reported)
- Rapid Assessment of Physical Activity (RAPA) (Patient-reported)
- Adherence to recommendations (Physician-reported & Patient-reported)

Education via Asu.org
- Evidence-based course on AD prevention

RESULTS

Change in Risk Scales

Risk Scales: After 6 months, improvements were observed in all risk scales (CAIDE Midlife, p<.046; MLDRI, p=.006; LDDRI, p<.001; MADO MCI, p<.001; Late-onset AD, p<.001; ANU-ADRI, p<.001).

Change in Blood Biomarkers & Cognition Mediated by ApoE and MTHFR Status

Mediation by genotype: Stratification by ApoE and MTHFR genotypes resulted in variations in response for a host of blood biomarkers and cognitive tests.

Biomarker-Intervention Paradigm

These data suggest a clinical precision medicine approach toward AD prevention reduces AD, dementia and vascular risk and improves cognition. Differential effects were observed based on genotype and adherence. These results are encouraging and warrant further evaluation via randomized trial utilizing AD-specific biomarkers pre vs. post-intervention. In addition to neuroimaging, we also plan to include an expanded genetics panel (including mitochondrial DNA) and microbiome assessments.

Conclusion