Wisconsin Registry for Alzheimer's Prevention: Prospective Cohort Study of Preclinical AD

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BACKGROUND

Adult children of persons with Alzheimer's disease (AD) are at increased risk of developing AD due to hereditary, environmental and health risk factors shared with affected parents. Prospective studies of middle-aged adult children of persons with AD provide an opportunity to characterize early cognitive and neurobiological changes consistent with pre-clinical AD and to identify health and lifestyle variables that influence disease trajectory. Knowledge of factors that influence the development of the AD syndrome is essential if we are to develop strategies for early intervention and prevention of AD.

OBJECTIVE

To determine the neuropsychological profile, apolipoprotein ε (APOE) genotype and demographic, health and lifestyle characteristics of a cohort of adult children of persons with AD.

METHODS

To date, 471 adult children (ages 40-65) have been recruited into the Wisconsin Registry for Alzheimer's Prevention (WRAP) and have undergone extensive neuropsychological testing, APOE genotyping and health assessments. Entry into WRAP requires that an adult child provide either autopsy reports or medical records that must be reviewed to confirm the diagnosis of definite or probable AD in the parent.

SUMMARY OF RESULTS

Preliminary results of our first wave of data assessment indicate the following:

- The cohort has a mean age of 53, 71% are women.
- 45% have an APOE ε4 allele.
- The neuropsychological performance of APOE ε4 carriers and APOE ε4 non-carriers at baseline did not differ.
- Homocysteine levels were negatively correlated with verbal memory when controlling for age, education and gender, and WRAP participants taking statins had higher verbal fluency scores.
- Exercise and moderate alcohol consumption were positively correlated with performance on several cognitive measures.

CONCLUSIONS

The adult children of persons with AD have an increased prevalence of APOE ε4 allele, making them a high-risk group for developing AD. Our finding that the neurocognitive performance of APOE ε4 carriers and non-carriers is not different at baseline suggests that this is an ideal population to follow longitudinally as cognitive changes develop in future years. The finding that lifestyle and vascular risk factors are correlated with baseline cognitive performance raises the question about their influence on the future risk of developing AD.

PRELIMINARY RESULTS

CHARACTERISTICS

Demographics (N=468)	
Age (years)	53.01 (6.29)
Education (years)	16
Female gender, n (%)	331 (71)
White/Caucasian, n (%)	458 (98)
Health History (N=468)	
Heart disease, n (%)	44 (10)
Hypertension, n (%)	72 (16)
High cholesterol, n (%)	145 (32)
Diabetes, n (%)	5 (1)
Stroke	7 (2)
Head injury, n (%)	51 (11)
Neurological disorder, n (%)	26 (6)
Depression, n (%)	103 (22)
Subjective health rating[a]	3.81 (.84)
Life Style Variables (N=468)	
Exercise frequency per month[b]	3.62 (.75)
Alcohol use per week[c]	1.70 (1.40)
Smoked tobacco in past month, n (%)	35 (8)
Depression rating (CESD)	6.37 (6.79)

Laboratory Values/Vitals (N=468)	
Homocysteine	8.17 (2.40)
Creatinine	0.94 (.16)
Folic acid <20, n (%)	205 (45)
Cholesterol (nonfasting)	212.21 (33.65)
Body Mass Index	27.77 (5.82)
Systolic blood pressure	134.34 (16.29)
Diastolic blood pressure	77.24 (9.78)
Medications (Current) (N=468)	
Antidepressants, n (%)	96 (20)
Statins, n (%)	64 (13)
Nonsteroidals, n (%)	197 (41)
Estrogen, n (%)	72 (15)
Multivitamins, n (%)	244 (50)
Folate, n (%)	75 (16)
Vitamin E, n (%)	240 (50)

Values are means (SDs) unless otherwise noted.
a: 1=poor, 2=fair, 3=good, 4 = very good, 5=excellent
b: 1=never, 2=once per month, 3=1 to 4 times per month, 4=>once per week
c: 0=never, 1=<once per week, 2=1 to 2 days, 3=3 to 4 days, 4=5 to 6 days, 5=daily

APOE GENOTYPE

APOE Genotype (N=459)	N (%)
2,2	3 (.7%)
2,3	39 (8%)
2,4	14 (3%)
3,3	211 (46%)
3,4	173 (38%)
4,4	19 (4%)

About 4 million people in the United States have been diagnosed with Alzheimer's disease.

19 million Americans say someone in their family has Alzheimer's disease.

By 2050 nearly 14 million people in the United States will be diagnosed with Alzheimer's disease.

COGNITIVE PEFORMANCE AT BASELINE

Measure	WRAP ε4+ (N=204)	WRAP ε4- (N=248)
Intellectual Performance (WASI)		
Verbal IQ estimate	110.80 (9.01)	111.64 (9.16)
Performance IQ estimate	110.92 (9.34)	112.68 (10.47)
Full-Scale IQ estimate	113.69 (8.68)	114.24 (8.72)
Learning and Memory		
AVLT learning total (sum of 5 trials)	51.14 (8.51)	51.36 (7.87)
AVLT delayed recall	10.76 (2.96)	10.58 (2.97)
Face Recognition - immediate	38.25 (4.41)	37.57 (4.21)
Face Recognition - delayed	39.48 (4.31)	39.44 (3.86)
Verbal Ability and Language		
Vocabulary (WASI)	64.99 (5.74)	65.52 (5.40)
Similarities (WASI)	38.25 (4.20)	38.54 (4.05)
WRAT3 Word Reading	50.47 (4.35)	51.18 (4.25)
Boston Naming Test (# correct-spontaneous)	56.01 (2.86)	56.38 (3.08)
Verbal fluency (COWA)	42.42 (10.56)	41.91 (11.24)
Visual Spatial Ability		
Block Design (WASI)	43.91 (10.97)	46.62 (12.01)*
Matrix Reasoning (WASI)	25.63 (3.51)	25.62 (3.56)
Judgment of Line Orientation	25.72 (4.06)	25.99 (3.49)
Working Memory and Executive Function		
Working Memory Index Score (WAIS-III)	104.36 (12.81)	105.43 (13.13)
Stroop Color-Word (# items named)	110.81 (21.01)	111.51 (21.95)
Trail Making Test–B (seconds to complete)	61.86 (22.74)	62.28 (28.43)
Wisconsin Card Sort (total errors)	13.94 (7.02)	14.1 1 (7.43)

Tabled values are raw score means (SDs) unless otherwise noted. WASI=Wechsler Abbreviated Scale of Intelligence, WMS-III=Wechlser Memory Scale-III, AVLT=Rey Auditory Verbal Learning Test, COWA=Controlled Oral Word Associations, WRAT3=Wide Range Achievement Test, 3rd edition. *ε4+ < ε4- (p < .01) with age, education, and gender controlled.

PREDICTORS OF BASELINE COGNITIVE PERFORMANCE*

Predictor	Cognitive Domain	Outcome
Homocysteine	Learning and Memory Executive Function	Lower cognitive performance with higher (normal range) homocysteine scores
Exercise[b]	Executive Function	Inactive individuals had lower cognitive scores
Alcohol[c]	Executive Function Learning and Memory	Higher cognitive performance with higher (minimal to moderate range) alcohol use
Depression	Executive Function	Depressed persons had lower cognitive performance

*With age, education, and gender controlled