PRELIMINARY FINDINGS FROM THE WISCONSIN REGISTRY FOR ALZHEIMER'S PREVENTION (WRAP)

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BACKGROUND

The Wisconsin Registry for Alzheimer's Prevention (WRAP) is a longitudinal cohort study of asymptomatic middle-aged adult children of persons with Alzheimer's disease (AD). To be eligible for WRAP, a person must have a parent with either autopsy or medical record-confirmed AD, be between the ages of 40-65 and agree to longitudinal follow-up studies over a 20-year period of time.

METHODS

The primary objective of WRAP is to conduct a longitudinal cohort study to define the biological and neurocognitive course of pre-clinical AD in a high-risk cohort.

RESULTS

A total of 899 asymptomatic persons (mean age 53) with a family history and 332 controls without a family history have undergone baseline neuropsychological and laboratory testing including APOE genotyping. Baseline data indicate that the family history cohort has a high prevalence of APOE ε4 (41% vs. 16%) and higher self-reported memory problems (29% vs. 13%) when compared to controls. There are no significant differences between groups in demographic, health, laboratory or neuropsychological variables at baseline.

To date, a total of 330 family history subjects have undergone repeat neuropsychological and laboratory testing 4 years after baseline. Although there are no differences in mean test/re-test neuropsychological performance, 11% of the family history cohort (mean age 57) declined by more than 1 standard deviation in auditory verbal memory test (AVLT). In addition, 8% of the family history cohort now meets the criteria for mild cognitive impairment (MCI) defined as 1.5 standard deviations below age, gender and IQ adjusted norms on the AVLT.

TABLES & FIGURES

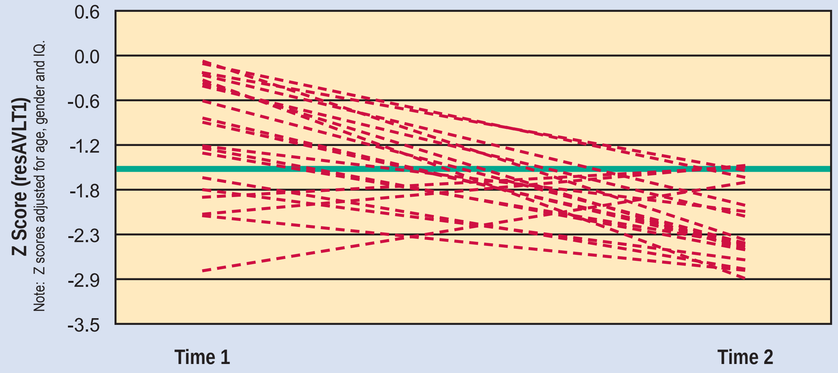
TABLE 1. WRAP PARTICIPANTS AND CONTROL CHARACTERISTICS

Demographics	WRAP Cohort (n=899)	Controls (n=332)
Age in years	52.4 (6.7)	55.8 (6.1)*
Education in years	15.9 (2.7)	16.7 (3.1)*
Male gender, % (n)	27.8 (839)	34.7 (308)
White/Caucasian, % (n)	96.7 (810)	95.1 (293)
Health History	**WRAP Cohort**	**Controls**
Heart disease, % (n)	9.2 (839)	9.7 (308)
Hypertension, % (n)	17.0 (839)	19.5 (308)
High cholesterol, % (n)	33.2 (837)	30.2 (308)
Diabetes, % (n)	2.9 (837)	2.60 (308)
Stroke, % (n)	1.1 (839)	0.97 (308)
Head injury, % (n)	13.4 (837)	13.3 (308)
Depression, % (n)	23.8 (808)	21.2 (288)
Subjective health rating	3.7 (0.8)	3.9 (0.8)

Laboratory Values/Vitals	WRAP Cohort	Controls
Homocysteine	7.9 (2.3)	7.8 (2.2)
Creatinine	0.9 (0.2)	1.0 (0.4)
Folic acid <21, % (n)	0.5 (829)	0.6 (302)
Cholesterol	207.3 (35.3)	197.9 (34.1)*
BMI	28.6 (6.2)	27.8 (5.6)
Systolic blood pressure	130.6 (75.9)	125.0 (16.6)*
Diastolic blood pressure	17.0 (9.8)	73.4 (10.2)
Life Style Variables	**WRAP Cohort**	**Controls**
Exercise frequency per month[a]	3.7 (0.7)	3.7 (0.6)
Alcohol use per week[b]	2.1 (1.2)	2.1 (1.2)
Memory problems self-report, % (n)	28.5 (836)	13.4 (306)*
Depression rating (CES-D)	6.74 (7.01)	5.1 (5.4)*

Note: Values are means (SDs) unless otherwise noted; *p < 0.0004 (Bonferroni correction for overall α = 0.01); a: 1=never, 2=<once per month, 3=1 to 4 times per month, 4=>once per week; b: 0=never, 1=<once per week, 2=1 to 2 days, 3=3 to 4 days, 4=5 to 6 days, 5=daily

FIGURE 1. INDIVIDUALS WITH 1.5 SD OR MORE BELOW THE MEAN IN AVLT AT TIME 2



CONCLUSIONS

A substantial proportion of the family history cohort show declines in verbal learning over a 4-year interval. These findings may be consistent with published data suggesting that there are neurocognitive, fMRI and cerebrospinal fluid changes suggestive of pre-clinical AD in this cohort. Our failure to find differences in mean test scores over the 4-year interval suggest that a substantial number of research subjects also improved in their test performance. The significance of these findings will be better defined once we complete T_2 testing of the control group.

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