# Depression in Children of Persons with Alzheimer's Disease: The Wisconsin Registry for Alzheimer's Prevention

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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. Because of caregiving demands or neurobiological factors, they may also have an increased risk for depression, which can further contribute to abnormal cognitive decline (e.g., Green et al., 2003; Jorm et al., 1991; Wilson et al., 2002; Yaffe et al., 1999).

## OBJECTIVES

To examine depressive symptoms, self-reported diagnoses of depression, use of antidepressant medications, and neuropsychological performance among middle-aged children of persons with AD.

## METHODS

572 middle-aged children (ages 40 to 65 years) of persons with AD and 85 control subjects without a family history of dementia enrolled in a prospective study of risk and protective factors for Alzheimer's disease (Wisconsin Registry for Alzheimer's Prevention – WRAP) and underwent extensive baseline neuropsychological testing, APOE genotyping, laboratory testing, and health history assessments. Entry into WRAP was based on autopsy confirmation or clinical diagnosis of AD in a parent; parents of controls survived to age 70 or older without significant memory problems.

## SUMMARY OF RESULTS

**Compared to controls, children of AD parents...**

- were more likely to report a depression diagnosis, currently or in the past (22% vs. 12%).
- were taking antidepressant medications more often at the time study entry (21% vs. 9%).
- reported a higher level of depressive symptoms on the 20-item Center for Epidemiologic Studies-Depression scale (CES-D) (mean = 6.46 + 6.68 vs. 3.96 + 4.38).

**Among children of AD parents...**

- CES-D scores correlated significantly with measures of learning and memory, executive function, speeded visuoconstruction, and retrieval from semantic memory, with demographics and relevant health history factors covaried.
- 8% had CES-D scores in the clinically significant range (≥ 16).
- neither history of depression nor CES-D scores varied by APOE genotype.

## RESULTS

TABLE 1. CHARACTERISTICS OF CHILDREN OF AD PARENTS AND CONTROLS

| Demographics | WRAP (n = 572) | Controls (n = 85) |
|---|---|---|
| Age (years) | 52.74 (6.47) | 55.72 (5.82)** |
| Education (years) | 16.03 (2.64) | 16.69 (2.74)* |
| Female gender, % (n) | 71 (403) | 62 (53) |
| White/Caucasian, % (n) | 98 (562) | 99 (84) |
| **Health History** | | |
| Heart disease, % (n) | 9 (5) | 13 (11) |
| Hypertension, % (n) | 15 (85) | 15 (13) |
| High cholesterol, % (n) | 31 (176) | 26 (22) |
| Diabetes, % (n) | 2 (10) | 2 (2) |
| Stroke, % (n) | 1 (7) | 1 (1) |
| Head injury, % (n) | 11 (63) | 7 (6) |
| Neurological disorder, % (n) | 6 (32) | 1 (1) |
| Depression, % (n) | 22 (125) | 12 (10)* |
| **Laboratory Values/Vitals** | | |
| Homocysteine | 7.99 (2.33) | 7.46 (1.66)* |
| Creatinine | 0.94 (0.17) | 0.96 (0.15) |
| Folic acid ≤ 20, % (n) | 46 (262) | 41 (35) |
| Cholesterol (non-fasting) | 208.68 (35.20) | 200.80 (33.83) |
| Body Mass Index | 28.51 (6.21) | 27.77 (6.11) |
| Systolic blood pressure | 132.84 (16.64) | 127.12 (18.98)** |
| Diastolic blood pressure | 76.64 (9.88) | 73.84 (10.71)* |
| **Medications (current)** | | |
| Antidepressants, % (n) | 21 (120) | 9 (8)* |
| Statins, % (n) | 14 (80) | 17 (14) |
| Nonsteroidals, % (n) | 35 (202) | 27 (23) |
| Estrogen, % (n) | 14 (78) | 8 (7) |
| Multivitamins, % (n) | 52 (298) | 52 (44) |
| Vitamin B, % (n) | 16 (93) | 18 (15) |
| Vitamin E, % (n) | 45 (259) | 32 (27) |
| **Lifestyle Variables** | | |
| Exercise frequency per month[a] | 3.62 (0.72) | 3.85 (0.36)* |
| Alcohol use per week[b] | 1.76 (1.37) | 1.74 (1.31) |
| Smoked tobacco in past month, % (n) | 8 (44) | 6 (5) |
| **Depression rating (CES-D)** | 6.46 (6.68) | 3.96 (4.39)** |

Values are means (SDs) unless otherwise noted.
WRAP = participants with one or both parents diagnosed with Alzheimer's disease
Controls = participants with parents free of dementia to age 75
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
*$p$ < .05 **$p$ < .01

TABLE 2. CES-D SCORES AND NEUROPSYCHOLOGICAL PERFORMANCE AMONG CHILDREN OF AD PARENTS

| Cognitive Measure | P Value for CES-D Effect |
|---|---|
| **Learning and Memory** | |
| AVLT learning total (sum of 5 trials) | .03 |
| AVLT delayed recall | |
| Face Recognition - immediate | < .01 |
| Face Recognition - delayed | < .01 |
| **Verbal Ability and Language** | |
| Vocabulary (WASI) | |
| Similarities (WASI) | |
| WRAT-III Word Reading | |
| Boston Naming Test (# correct-spontaneous) | .04 |
| Verbal Fluency (COWA) | .02 |
| **Visual Spatial Ability** | |
| Block Design (WASI) | < .01 |
| Matrix Reasoning (WASI) | |
| Judgment of Line Orientation | |
| Clock Drawing | |
| **Working Memory and Executive Function** | |
| Working Memory Index Score (WAIS-III) | |
| Stroop Color-Word (# items named) | .01 |
| Trail Making Test-B (seconds to complete) | < .01 |
| Wisconsin Card Sort (total errors) | |

Tabled values are from linear regression analyses with demographics (age, education, and gender) and significant health and lifestyle measures (history of heart disease, systolic blood pressure, and strenuous exercise per week) entered as predictors, in addition to CES-D scores. Only statistically significant ($p$ < .05) values are shown. If the Bonferroni correction is applied, CES-D effects were significant for Face Recognition-Immediate and Trail Making Test-B only.

AVLT = Rey Auditory Verbal Learning Test
WASI = Wechlser Abbreviated Scale of Intelligence
WRAT-III = Wide Range Achievement Test, 3rd edition
COWA = Controlled Oral Word Associations
WAIS-III = Wechlser Adult Intelligence Scale

## FURTHER INTERPRETATION

Current symptoms of depression, as measured by the CES-D, affected performance on about one-half (8 of 17) of the cognitive measures. Although CES-D scores accounted for only 1% to 3% of variance in cognitive scores, the strength of the depression effect was equal to the combined effect of several health and life-style measures (history of heart disease, systolic BP, and frequency of strenuous exercise). Relationships were likely attenuated by the generally good health and relatively low depression ratings of WRAP participants.

The strongest associations between CES-D scores and cognitive performance were on tests that required rapid processing of visual details (e.g., face recognition) or timed tests where scores depended on speed of response (e.g., Trails B).

The mild elevations in depressive symptoms noted among children of AD parents may have been secondary to caregiving stress. Data on caregiving are now being collected and will be included in longitudinal follow-ups.

Longitudinal data will be needed to determine if depression increases the risk of AD or mild cognitive impairment as this sample ages.

## CONCLUSIONS

Among individuals whose parent(s) had AD, depressive symptoms were mildly elevated, and these symptoms were associated with lower performance on cognitive tests. Longitudinal follow-up is planned to evaluate the stability of depression-cognition associations and to determine if depression at midlife affects dementia onset in later years.

## SIGNIFICANCE OF WRAP

➲ the neurobiological substrates of AD develop decades before cognitive and functional symptoms become severe enough to be clinically apparent.

➲ the role and timing of various risk and protective factors in the development of AD can only be determined by prospective longitudinal studies that track development from midlife or earlier.

➲ first-degree relatives of persons with AD are at increased risk for developing the disease, and as a result, they are an especially valuable group to further understanding of how this disease may be delayed or prevented.

***WRAP is the largest cohort of AD offspring currently under study.***