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Nine Risk Factors May Explain Two Thirds of AD Cases

Megan Brooks | |September 01, 2015

Nine potentially modifiable risk factors may explain two thirds of Alzheimer's disease (AD) cases globally, according to a comprehensive meta-analysis of published studies.

Risk factors include obesity, carotid artery narrowing, low educational achievement, hyperhomocysteine, depression, hypertension, frailty, current smoking, and type 2 diabetes (diabetes only in Asian populations).

According to the analysis, the population attributable risk (PAR) for each of the factors individually ranged from 0.175% to 24.5%, while a model combining all nine factors yielded a PAR of 66%.

Jin-Tai Yu, MD, PhD, from the Memory and Aging Center, Department of Neurology, University of California San Francisco, and colleagues report their findings online August 20 in the *Journal of Neurology, Neurosurgery and Psychiatry*.

"This is the first comprehensive systematic review and meta-analysis which takes into account almost all risk factors for AD suitable to be intervened via personal, clinical and public strategy; 16,906 articles were identified, of which 323 with 93 factors met the inclusion criteria for meta-analysis," Dr Yu noted in email to *Medscape Medical News*.

Dr Jin-Tai Yu

Strong Evidence

The research team pooled data from each of the studies and graded the evidence according to its strength.

Among the factors with relatively strong evidence (pooled population >5000), the researchers found grade I evidence for the protective effect of four medical exposures (estrogen, statin, antihypertensive medications, and nonsteroidal anti-inflammatory drug therapy) as well as four dietary exposures (folate, vitamins E and C, and coffee).

They also found grade I evidence for one biochemical exposure (hyperhomocysteine) and one psychological condition (depression) significantly increasing the risk for AD.

Grade I evidence also emerged pointing to "complex roles" for certain pre-existing conditions as either increasing or decreasing AD risk, Dr Yu said. Factors associated with increased risk include frailty, carotid atherosclerosis, hypertension, low diastolic blood pressure, and, in the Asian population, type 2 diabetes. Those tied to lower risk include history of arthritis, heart disease, metabolic syndrome, and cancer.

In terms of lifestyle factors, low education, and high or low body mass index (BMI) in midlife were associated with increased risk for AD, whereas high BMI later in life, cognitive activity, current smoking (in the Western population), light-to-moderate drinking, and stress were associated with decreased risk.

"We identified no evidence suggestive of significant association with occupational exposures," Dr Yu said.

"The current meta-analysis," he added, "indicated that the effective interventions in diet, medications, biochemical exposures, psychological condition, pre-existing disease and lifestyle may be promising options for preventative strategies. Moreover, further good-quality cohort studies and randomized controlled trials targeting these elements are necessary for clearing the exact direct relationship between the related modifiable risk factors and Alzheimer's risk."

New Nomenclature?

Reached for comment, Majid Fotuhi, MD, PhD, chairman, NeuroGrow Brain Fitness Center, McLean, Virginia, and Johns Hopkins Medicine, Baltimore, Maryland, told *Medscape Medical News*, "This study further supports publications by Kristine Yaffe, MD, and her team, which report up to half of AD cases around the world can be attributed to 7 modifiable risk factors, namely physical inactivity, obesity, smoking, diabetes, low education, depression, and hypertension."

Taken together, Dr Fotuhi said, the studies are "consistent with the concept that late-life 'Alzheimer's disease' is a manifestation of brain atrophy due to many different factors, and not just due to accumulation of plaques and tangles."

"Perhaps we should consider a new terminology which departs from an emphasis on Alzheimer's pathology as the sole cause of dementia in our elderly," Dr Fotuhi suggested. "This condition used to be called 'hardening of arteries' in 1930s and 40s, then 'senile dementia' in 1950s to 90s; the term gradually shifted to 'dementia of Alzheimer's type,' and now it is called 'Alzheimer's disease.' I favor a terminology that is broader and encourages clinicians to think of all the potential causes for cognitive decline in their patients," he noted.

Dr Fotuhi and two coauthors published a paper in *Nature Reviews Neurology* recently introducing a new hypothesis for late-life dementia called "dynamic polygon hypothesis," which emphasizes the heterogeneity and complexity of why people experience cognitive decline with aging.

"Appreciating that late-life cognitive deficits can be due to a number of different potentially treatable and preventable etiologies has hopeful implications for our healthcare system and economy," Dr Fotuhi said. "It is highly possible that a comprehensive assessment for identifying the culprits for cognitive decline in each middle-age patient followed by treating them aggressively over time should reduce his/her brain atrophy and risk of developing dementia."

The authors and Dr Fotuhi have disclosed no relevant financial relationships.

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