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A Smell Test for Alzheimer's?

Megan Brooks

May 25, 2012 – There is a large body of evidence for an association between hyposmia and Alzheimer's dementia (AD), but the predictive value of olfactory dysfunction in the development of Alzheimer's disease (AD) is uncertain, a new review of the topic concludes.

"We establish through a systematic review the lack of proven evidence that loss-of-smell tests can be used to clinically predict future AD," Cyrus A. Raji, MD, PhD, from University of Pittsburgh Medical Center Mercy Hospital in Pennsylvania, who worked on the study, told *Medscape Medical News*.

"It's a big public health message. This has been a huge topic in recent years, and some popular websites even promote smell tests for Alzheimer's," Dr. Raji added.

The study was published online May 2 in *Laryngoscope*.

Longitudinal Data

For this review, the researchers searched PubMed, Ovid, MEDLINE, EMBASE, ISI Web of Science, PsychINFO, the Cochrane Database of Systematic Reviews and the Cochrane Register of Controlled Trials for relevant studies describing the predictive value of olfactory testing for conversion to AD.

They failed to identify any randomized controlled trials on the usefulness of olfactory testing for prediction of conversion to dementia. In the 2 prospective longitudinal cohort studies they identified, hyposomia had only moderately predictive value, they say.

In 1 longitudinal study, 126 patients with mild cognitive impairment (MCI) were followed for 3-years. During this time, 33 (26%) converted to AD and 93 (74%) did not.

After adjustment for potential predictors of conversion to AD, baseline scores on the University of Pennsylvania Smell Identification Test (UPSIT) were significantly lower among AD-converters than nonconverters (25.8 vs 33.2; $P < .0001$). The study authors estimated that UPSIT testing had a sensitivity of 48.5% for predicting the development of AD.

In the other longitudinal study, 21 participants without AD at baseline (8 controls and 13 patients with amnestic MCI) completed the Brief Smell Identification Test 12 months after enrollment. Six of the 13 with MCI (46%) met formal criteria for AD at this time.

Those study authors did not report the conversion rate of participants with normal cognition to AD. Among the participants with baseline MCI, AD converters had worse olfactory identification scores than did nonconverters (2.33 vs 3.44), although this difference was not statistically significant. Six of the 7 nonconverting participants with MCI showed significantly lower total olfactory scores than the control group ($P < .001$).

Susceptible to Confounding

Dr. Raji and colleagues also identified 30 cross-sectional studies that compared participants with or without baseline MCI to patients with preexisting AD. These studies demonstrated a positive association between poorer performance on a variety of olfactory identification tests and AD.

The cross-sectional evidence "corroborates the association between hyposmia and AD but does little to validate the use of olfactory identification as a clinical screening or prognostic instrument," the investigators say. They note that both AD and hyposmia in cognitively normal adults increase in frequency with age.

"The extensive cross-sectional body of research," they add, "is particularly susceptible to confounding" because one third of these studies failed to control for age.

A simple, accurate, and inexpensive method of predicting the onset of AD "remains a valuable but elusive target for clinicians," the authors conclude.

Susan Bookheimer, PhD, professor of Cognitive Neurosciences, Department of Psychiatry and Biobehavioral Sciences, University of California, Los Angeles, who reviewed the analysis for *Medscape Medical News*, made the point that loss of olfaction is a "non-specific sign of cognitive, particularly frontal lobe, impairment. It is found in Parkinson's, AD, fronto-temporal dementia, traumatic brain injury, etc."

The conclusions of the current analysis, Dr. Bookheimer said, are "appropriate, basically saying we need more studies." Overall, the currently available data for anosmia as a predictor of AD are "lacking," she added.

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

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