

Ability to recognize and recall odors may identify those at risk for Alzheimer's disease

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Diagram of the brain of a person with Alzheimer's Disease. Credit: Wikipedia/public domain.

A non-invasive protocol testing the ability to recognize, remember and distinguish between odors was able to identify older individuals who - according to genetic, imaging and more detailed memory tests - were at increased risk of Alzheimer's disease. The report of a study by a team of Massachusetts General Hospital (MGH) investigators has been published online in *Annals of Neurology*.

"There is increasing evidence that the neurodegeneration behind Alzheimer's disease starts at least 10 years before the onset of memory symptoms," says Mark Albers, MD, PhD, of the MGH Department of

Neurology, the principal investigator and corresponding author of the report. "The development of a digitally-enabled, affordable, accessible and non-invasive means to identify healthy individuals who are at risk is a critical step to developing therapies that slow down or halt Alzheimer's disease progression."

It is well known that brain circuits that process olfactory information can be affected by Alzheimer's disease, and several studies have documented a diminished ability to identify odors in affected individuals. Other studies have associated deficits in odor identification with established Alzheimer's disease biomarkers and with greater rates of cognitive decline, but the most commonly used test of olfactory ability - the University of Pennsylvania Smell Identification Test - has a number of limitations and does not take into account the great variation in olfactory ability among healthy individuals.

The battery of four tests developed by the MGH team addresses both olfactory and cognitive functions:

- In the OPID (Odor Percept IDentification)-10 test, [participants](#) are presented with a battery of 10 odors - menthol, clove, leather, strawberry, lilac, pineapple, smoke, soap, grape or lemon. After experiencing each odor for two seconds, they are asked whether the scent is familiar and then asked to choose among four words - from the names listed above - for the one that best describes the odor.
- Participants then complete the Odor Awareness Scale (OAS), a previously validated questionnaire that assesses their overall attention to environmental odors and how they are affected emotionally and behaviorally by scents.
- The OPID-20 test includes the 10 odors previously presented and an additional 10 - banana, garlic, cherry, baby powder, grass, fruit punch, peach, chocolate, dirt and orange. Participants are

first asked whether a presented odor was included in the OPID-10 test and then asked which word best describes the [odor](#). Their ability to remember odors from the first test determines their POEM (Percepts of Odor Episodic Memory) score.

- In the Odor Discrimination (OD) test, participants are presented with two consecutive odors and asked whether they were different or the same, a process that is repeated 12 times with different paired scents.

The study recruited 183 participants, most of whom were enrolled in ongoing studies at the MGH-based Massachusetts Alzheimer's Disease Research Center. At the time of the olfactory testing, 70 were cognitively normal, 74 tested normal on cognitive tests but were personally concerned about their cognitive abilities, 29 had mild cognitive impairment and 10 had been diagnosed with possible or probable Alzheimer's disease. As part of the studies they were enrolled in, all of them had comprehensive medical and neurological examinations - including annual tests of their memory and cognitive abilities - and several had brain imaging studies of Alzheimer's-associated factors.

Results of the OPID-20 test significantly differentiated among the four groups of participants, and those results correlated with the thinning of two brain regions - the hippocampus and the entorhinal cortex - previously associated with Alzheimer's risk. Participants' ability to remember a previously presented aroma, as reflected in the POEM score, also showed significant differences between the two cognitively normal groups and participants with Alzheimer's disease, whose results were no better than chance.

Because the ability of normal individuals to recognize and discriminate between odors can vary by as much as 40 times, the POEM scores of the two cognitively normal groups were compared with what would have

been predicted based on their ability to identify and differentiate between odors, as reflected in the OAS and OD tests. That comparison determined whether each individual was a good or poor POEM performer, and poor POEM performers were more likely to have the variant of the APOE gene associated with increased Alzheimer's risk. While results of an annual test of short-term memory improved year-to-year for the good POEM performers, no such improvement was seen among the poor performers, who also showed thinning of the entorhinal cortex.

Albers and his colleagues are currently recruiting participants for a larger-scale study to validate these results. "It is well recognized that early diagnosis and intervention are likely to produce the most effective therapeutic strategy for Alzheimer's disease - preventing the onset or the progression of symptoms," he says. "If these results hold up, this sort of inexpensive, noninvasive screening could help us identify the best candidates for novel therapies to prevent the development of symptoms of this tragic disease."

More information: Alefiya Dhillal Albers et al, Episodic Memory of Odors Stratifies Alzheimer Biomarkers in Normal Elderly, *Annals of Neurology* (2016). [DOI: 10.1002/ana.24792](https://doi.org/10.1002/ana.24792)

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