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ALZHEIMER DISEASE

Sniffing out a marker of early Alzheimer disease

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Severe olfactory impairment correlates with imaging markers of brain pathology that are present in preclinical Alzheimer disease (AD), new work has shown. The findings suggest that olfactory impairment could be a clinically useful marker of early AD in cognitively normal elderly people.

Olfactory impairment has previously been associated with several neurodegenerative diseases and with the presence of brain pathology, but studies of the association between olfactory impairment and neuroimaging markers of pathology have previously proved inconclusive. Rosebud Roberts and colleagues previously showed that olfactory impairment was associated with the development of mild cognitive impairment (MCI) and progression to AD dementia, and have now investigated the association with imaging markers.

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“We investigated the association of impaired olfactory function with imaging biomarkers of brain pathology: abnormal amyloid accumulation, reduced brain cortical thickness, brain hypometabolism and reduced hippocampal volume,” explains Roberts. “We aimed to determine whether olfactory impairment could be a marker of brain pathology that underlies cognitive impairment.”

The study included 829 participants aged 70–89 years who were cognitively normal. For all participants, olfactory function was measured with the Brief Smell Identification Test, and cortical thickness and hippocampal volume were assessed with MRI. PET was used to assess amyloid accumulation in 306 participants, and brain metabolism in 305 patients.

Of all participants, 78 had anosmia and 503 had hyposmia. Abnormalities in amyloid accumulation, cortical thickness and hippocampal volume were all more common among participants with olfactory impairment than in those without, and statistical analysis showed that these imaging markers were significantly associated with anosmia, but not with hyposmia.

“Abnormal brain imaging biomarkers that are known to be associated with MCI and AD were associated with severe olfactory impairment,” says Roberts. “Our findings are in keeping with studies that have shown an association between olfactory impairment and cognitive impairment.”

The researchers acknowledge that their findings need validation in longitudinal studies. However, the results suggest that testing for anosmia has clinical potential.

“Imaging is expensive, invasive, time-consuming and requires specialists to perform and interpret the scans, whereas a smell test is simple to administer and easy to interpret,” says Roberts. “If longitudinal studies prove that abnormal imaging biomarkers are causally related to impaired olfactory function, olfactory function could be used to identify people who are at increased risk of developing MCI and people with amnestic MCI who are likely to progress to AD dementia.”

Ian Fyfe

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