Anosmia - Marker Of Cognitive Decline In Elderly

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Neurodegeneration is an important health problem in elderly. Significant decrements in the ability to smell are present in over 50% of the population between 65 and 80 years of age and in 75% of those 80 years of age and older. Olfactory impairment has been described in number of neurodegenerative diseases viz. Parkinson's Disease, Alzheimer's Disease, dementia with Lewy bodies (DLB), multiple system atrophy, corticobasal degeneration, and frontotemporal dementia. Olfactory impairment in Parkinson's Disease often predates the clinical diagnosis by at least 4 years. In staged cases, studies of the sequence of formation of abnormal α-synuclein aggregates and Lewy bodies suggest that the olfactory bulbs may be, along with the dorsomotor nucleus of the vagus, the first site of neural damage in Parkinson's Disease.[1] In post mortem studies of patients with very mild "presymptomatic" signs of Alzheimer's Disease, poorer smell function has been associated with higher levels of AD-related pathology.

Worldwide, about half of the older persons in need of care (two-thirds of the dependent population age 90 and above) suffer from dementia or cognitive impairment. One estimate (World Alzheimer's Report 2010) projected that the 36 million people with dementia worldwide in 2010 would increase to 115 million by 2050. The largest increases would occur in low and middle income countries where about two-thirds already live.

Brain atrophy occurs with aging after the age of 60 years and is associated with cognitive decline. Atrophy proceeds at varying rates indifferent parts of the brain. In mild cognitive impairment, atrophy has been found mostly in the prefrontal cortex and hippocampus. In the early stages of typical amnestic AD, the memory loss may go unrecognized or be ascribed to benign forgetfulness of aging. Once the memory loss becomes noticeable to the patient and spouse and falls 1.5 standard deviations below normal on standardized memory tests, the term mild cognitive impairment (MCI) is applied. This construct provides useful prognostic information, because approximately 50% of patients with MCI (roughly 12% per year) will progress to AD over 4 years. Mini-Mental State Examination (MMSE), the Montreal Cognitive Assessment (MOCA), and Cognistat can be used to capture dementia and follow progression Increasingly, the MCI construct is being replaced by the notion of early symptomatic AD[2].

Because of the suggestion that olfactory impairment may be an early indicator for cognitive impairment, there has been interest in the possibility of using olfactory testing to assist in diagnosis of AD or predict who will develop AD or cognitive impairment. However there has been limited research on the association of olfaction and cognition in a general population of older adults not at high risk for AD or cognitive impairment. Some studies have reported that olfaction impairment appears to precede clinical signs of cognitive impairment or AD and have hypothesized that it may be an early indicator of brain changes.[3] Olfactory impairment has been reported in both preclinical and clinical phases of AD. Autopsy studies have found neurofibrillary tangles, pathology thought to be associated with AD, appear first in the entorhinal cortex and olfactory bulb areas of the brain both in people with AD and / or dementia as well younger people with no clinical signs of dementia.[4] A recent study found the density of tangles present in the central olfactory system was inversely related to odor identification ability.[5] Neuropathological studies have revealed that brain regions and subsystems involved in odor information processing, including the olfactory bulb, piriform

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and orbital prefrontal cortices, have direct projections to perirhinal and entorinal cortices. These, in turn, have extensive projections to the hippocampus,[6] known as the primary brain region involved in initial memory formation, and also one of the first regions affected in AD neurodegeneration. In addition, the anterior olfactory nucleus and olfactory bulb are the two primary brain regions commonly affected in AD. Indeed, change in olfactory identification has been strongly associated with pathological changes in the medial temporal lobe structures.[7,8] These studies strongly imply a primary role for olfactory dysfunction as an indicator of pathological cognitive decline and dementia.

Observational and clinical studies have found a significant association between olfactory impairment and subsequent cognitive decline. For example, a large-scale study (N=1920) on the relationship between olfactory identification ability and general cognitive functioning (as measured by Mini Mental State Examination (MMSE)) indicated that olfactory dysfunction at baseline was significantly predictive of future cognitive impairment after 5 years (odds ratio (OR) = 6.62; confidence interval (CI) = 4.3610.04) Schubert *et al*[9] have also reported low sensitivity of 55.1% but high specificity (84.4%) for olfactory assessment in predicting cognitive decline.

A number of standardized olfactory and taste tests are commercially available. Most evaluate the ability of patients to detect and identify odors or tastes. For example, the most widely used of these tests, the 40 item University of Pennsylvania Smell Identification Test (UPSIT. The Indian Smell Identification Test (INSIT) uses the essence of 10 commonly used items as odorants (cardamom, kewra, khus, lemon, mango, orange, pineapple, rose, thinner, vanilla) which represent familiarity in day to day life. A score of ≤ 4 indicate anosmia .

Wilson *et al* has reported that impairment in olfactory identification at baseline was significantly associated with the incidence of mild cognitive impairment.

Olfactory abilities are primarily assessed by measuring threshold (lowest detectable concentration of odors), discrimination (ability to differentiate between odors) and identification (ability to identify odors). H. R. Sohrabi *et al*[10] studied association f cognitive decline and olfactory dysfunction in community dwellingsubjects. The major novel finding of the study was that olfactory discrimination rather than odour identification (as measured by Sniffin' Sticks D) was a significant predictor of future cognitive decline over a 3-year period. However, concluded that, the predictive value of olfactory assessment in screening those at a higher risk for AD needs further research to improve its sensitivity and specificity.

In the current issue of this journal Gaurav *et al*[11] in his hospital based observational study, reported cognitive impairment in 50% of elderly subjects and anosmia to be prevalent in 64% of cases and also documented association of anosmia and cognitive impairment ($p < 0.0001$) in elderly. Anosmia was detected bu INSIT test which is easy to perform, cheap and is suitable for Indian patients because the agents used are familiar. The test has been standardised by George *et al* and has already been used in some studies.

However, local causes and other conditions causing anosmia needs to be ruled out anddtetailed neurological assessment and neuroimaging studies or PET scan may throw additional light on the association of anosmia with cognitive impairment and other neurodegenerative disorders. Large sample sized prospective studies are essential to find out the steps in preventing the progress of disease and improve quality of life in elderly.

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