

Olfactory Deterioration in Mild Cognitive Impairment

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Abbreviations: MCI: Mild Cognitive Impairment, aMCI: amnesic Mild Cognitive Impairment, UPSIT: Pennsylvania Smell Identification Test, VAS: Visual Analogue Scale

ABSTRACT

Olfaction is important for many everyday activities, ranging from feeding to detecting dangerous situations. It is the main reason older adults complain about loss of flavor in food. Olfactory deterioration is common in older individuals and has been associated with early onset of several neurodegenerative diseases. Olfaction deteriorates from normosmic, which is normal smell ability to hyposmia (decreased ability) and anosmia (complete loss) and is often quantified in threshold, discrimination and identification scores through standardized smell tests. Identifying the true cause of smell decline is often difficult and problematic, because there are many factors that affect the ability to smell like age, gender, smoking, genetic predisposition, head injuries and sinonasal diseases. Several studies have supported that the risk for MCI patients to progress to Alzheimer's disease is 4 times greater than other older persons for older adults with olfactory deficits. Finally, as the underlying pathology and mechanisms need further research and clarification, focusing on different MCI subtypes might prove useful in revealing these mechanisms.

Keywords: Olfactory; Smell; Cognitive Impairment; MCI

Mini Review

Olfaction is important for many everyday activities, ranging from feeding to detecting dangerous situations and its loss affects even more facets of everyday living [1]. It is the main reason older adults complain about loss of flavor in food. Olfactory deterioration is common in older individuals and has been associated with early onset of several neurodegenerative diseases (e.g. Alzheimer's disease, Parkinson's, Huntington's, Lewy Body, etc.) [2]. Smell loss has been found in 80% of individuals over 80 years old [3] and it has been associated with higher mortality rates in the older population [4] and more with men than women [5]. Cognitive and, specifically, episodic memory decline seems to be affected in people with impaired smell identification and for this reason olfactory impairment is often investigated as a predictor of early cognitive impairment, as it is the case for Mild Cognitive Impairment (MCI) [6]. Thus, it is considered as an early-stage and progression clinical marker.

Measuring the Olfactory Ability

Olfaction deteriorates from normosmic, which is normal smell ability to hyposmia (decreased ability) and anosmia (complete loss) and is often quantified in threshold, discrimination and

identification scores estimated through standardized smell tests. In threshold tests, participants must detect the smell across different concentrations. The threshold is set when the odour is detected in the lowest concentration. Discrimination is related to the differentiation between smells. The participant must identify the smell among other ones. Two of the most well-known and widely administered psychophysiological smell tests are the Pennsylvania Smell identification Test (UPSIT) [7] and the Sniffin' Sticks Test [8]. Both tests have been validated in different languages and countries and age and gender stratified normative values exist. Certain cultural adaptations have been applied to ensure the face validity of the tests is not affected. The Visual Analogue Scale (VAS) has been used to assess olfactory deficit and is significantly correlated to UPSIT for Parkinson's disease [9], making it an easy and quick instrument to investigate olfactory deterioration. Further research is necessary to ensure reliability and replicability of the findings. Identifying the true cause of smell decline is often difficult and problematic because there are many factors that affect the ability to smell like age, gender, smoking, genetic predisposition, head injuries and sinonasal diseases [10]. Further research on the exact role and effect of these factors on olfactory decline will shed more

light on the actual process of deterioration in neurodegenerative disorders and early cognitive impairment.

Olfactory Decline in MCI

Mild Cognitive Impairment (MCI) is a term coined over 40 years ago and still pertains literature and research, perplexing researchers and health professionals alike and places emphasis on early identification of cognitive deficits. Initially, the term was used to describe slight memory impairment that did not meet dementia criteria, but over the years many terms were used to define and describe MCI. Current research focuses on the MCI subtypes (e.g. amnesic and non-amnesic) and to other symptoms, apart to the ones related to memory decline. It is also clear that not all MCI patients will progress to dementia. Neuroanatomic and neurophysiological changes in the primary olfactory cortex and system in general result in decline in the ability to identify smells and those are often large in MCI patients [11-13], as well as the changes in the hippocampus and the entorhinal cortex [14]. Several studies have demonstrated that olfactory deterioration occurs before the onset of dementia and can distinguish MCI patients from the control group and, thus, have a predictive power on who will progress to dementia or not [15-18]. Lack of homogeneity in MCI terminology, diagnosis methods, and olfactory tests applied as well as differences in the conduction methodologies and procedures does not allow for consistent and easily generalizable inferences [13]. Targeting research on different MCI subtypes -with inherent clinical heterogeneity- could lead to identification of prodromal dementia and distinguish it from healthy aging changes before it happens. For example, memory loss is the predominant characteristic of amnesic MCI (aMCI) with 10%-15% of patients later progressing to Alzheimer's disease [19]. Non-amnesic patients (naMCI) will most probably progress to Lewy Body or vascular dementia [20]. Several studies have supported that the risk for MCI patients to progress to Alzheimer's disease is 4 times greater than for other older persons, when olfactory deterioration is present during baseline assessment [21,22]. Based on the meta-analysis conducted by Rahayel and colleagues (2012), the combination of imaging biomarkers, neuropsychological and clinical assessment and smell identification tests could be useful and effective in order to detect Alzheimer's disease and to predict the transition from MCI to Alzheimer's disease [23].

Conclusion

This mini review was conducted focusing on olfactory impairment measuring instruments and the relation between olfactory decline and MCI. Although smell diminishes early in older individuals with diverse types of neurodegenerative diseases, the reasons are still unclear and not known. It has been hypothesized that disruptions on the primordial neuropathological substrate might be related to decline in the ability to detect, distinguish and identify smells [9,10]. As the olfactory dysfunction can appear earlier in non-MCI persons, this dysfunction can be a 'messenger' of

preclinical cognitive decline and neurodegenerative disease. Hence, other clinical, neuroimaging or even self-reported complaints can act as a proactive strategy. Finally, as the underlying pathology and mechanisms need further research and clarification, focusing on different MCI subtypes might prove useful in revealing these mechanisms.

Acknowledgment

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Conflict of interest

The authors declare that they have no conflict of interest.

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