

Sniffing Out Dementia? Olfactory Dysfunction Test and Detection of Volatile Biomarkers for Early Diagnosis of Alzheimer's Disease

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Alzheimer's disease (AD) is the most common cause of dementia and a critical worldwide public health issue due to its significant socioeconomic burden on society, while the number of people with AD is rising exponentially due to the increasing life expectancy. A biomarker able to detect the disease in the early clinical stages is required urgently to facilitate earlier diagnosis and disease management, before irreversible brain damage or mental decline has occurred. However, the multifactorial nature of AD poses obstacles in finding a single biomarker. Probably a panel of biomarkers would offer the sensitivity and specificity needed in order to avoid false alarms, excessive testing and could also minimise emotional and/or financial harm that could result from misdiagnosis.

Currently, the most accurate diagnostic tests for AD are an amyloid PET scan or a spinal tap. Nevertheless, these tests are not available or easy to perform in any patient, are expensive and uncomfortable. In routine examination of neurological patients usually olfaction is underestimated, while it is considered that the olfactory nerve is a potential route through which the central nervous system might be harmed by pathogens and/or other environmental hazards. Olfactory dysfunction is an inevitable consequence among others in the natural aging process and is frequently linked to numerous neurodegenerative disorders, such as AD and Parkinson's disease. There is mounting evidence that odor identification is mainly affected in the preclinical stages of AD where the patient shows mild cognitive impairment. A study show that, older adults with olfactory dysfunction have more than twice the odds of developing dementia 5 years later controlling for age, sex, race and ethnicity, education, comorbidities and baseline cognitive function.

Despite the overwhelming evidence of above mentioned facts, the potential clinical and pre-clinical value of olfactory dysfunction in general is overlooked. Certainly, any biomarker must be validated prior using it in everyday clinical practice, provided that multiple studies in large groups of people established its accuracy and reliability to indicate the presence of the investigated disease. Furthermore, the laboratory methods used to measure the biomarker must be shown to be stable and reliable. However, the relatively inexpensive, easy to perform and non-invasive use of some odor identification test make's them superior to other under trial biomarkers of cognitive decline and AD.

Not only olfactory dysfunction could be used as a biomarker for early AD diagnosis, but remarkably the ability also, to detect certain volatile compounds emerging from body fluids or breath. Breath tests were used by physicians from the earliest ages of medicine because it was known that the odor of breath could be altered in individuals with certain diseases. Hundreds of volatile organic compounds (VOCs) are emitted from the human body and their components usually reflect the metabolic condition of an individual and often results in a change in body odor. Therefore, as there is the general assumption that any disease has a specific pattern of VOCs in the breath, if someone can detect them, then he can associate their unique breath print with that disease.

Review of the available literature confirmed that, the canine sophisticated olfactory system has the ability to detect in breath and urine a variety of different diseases through their characteristic scents, such as: melanomas, bladder cancer, lung and breast cancers. This provided theoretical evidence to create and use electronic nose devices (initially called artificial noses) in potential disease diagnosis. These

sensor devices, are capable of detecting, identifying and discriminating many types and sources of a wide diversity of chemical species and mixtures of compounds (including VOCs) present in volatiles of sampled air, derived from any source, even in exhaled breath. Blind experiments showed that 86% accuracy could be achieved in detecting and discriminating different diseases, when examined with the artificially intelligent nanoarray.

Inspired by canines, researchers tried to develop artificial intelligence that emulated dog decisions and to create and teach machine learning algorithms in order to sniff out diseases through synthetic analogs of animal olfactory receptors. In order to achieve this goal, cooperation between different scientific disciplines is needed by using gas chromatography combined with mass spectrometry for breath analysis, artificial intelligence, digital electronic sensors design and nanotechnology. In near future synthetic analogs of animal olfactory receptors should be used offering the sensitivity and accuracy required for diagnosing AD or other diseases. In the most optimistic scenario, an innovative electronic nose device could be portable and/or integrated with a smartphone.

Further research and clinical trials are required, in order to confirm the aforementioned data and validate the use of electronic nose for early AD diagnosis. Then it can be provided not only to primary care clinics, but family doctors also, where the test could be part of routine examination in people with altered cognition and/or behavior, even in mild form. Until then, simple olfactory testing may provide another opportunity for targeted early interventions to reduce morbidity and public health burden of dementia [1-12].

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