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Olfactory Response as a Marker for Alzheimer's Disease: Evidence from Perceptual and Frontal Oscillation Coherence Deficit

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1 Works for me dx.doi.org/10.17504/protocols.io.bi2qkgdw

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ABSTRACT

High-frequency oscillations of the frontal cortex are involved in functions of the brain that fuse processed data from different sensory modules or bind them with elements stored in the memory. These oscillations also provide inhibitory connections to neural circuits that perform lower-level processes. Deficit in the performance of these oscillations has been examined as a marker for Alzheimer's disease (AD). Additionally, the neurodegenerative processes associated with AD, such as the deposition of amyloid-beta plaques, do not occur in a spatially homogeneous fashion and progress more prominently in the medial temporal lobe in the early stages of the disease. This region of the brain contains neural circuitry involved in olfactory perception. Several studies have suggested that olfactory deficit can be used as a marker for early diagnosis of AD. A quantitative assessment of the performance of the olfactory system can hence serve as a potential biomarker for Alzheimer's disease, offering a relatively convenient and inexpensive diagnosis method. This study examines the decline in the perception of olfactory stimuli and the deficit in the performance of high-frequency frontal oscillations in response to olfactory stimulation as markers for AD. Two measurement modalities are employed for assessing the olfactory performance: 1) An interactive smell identification test is used to sample the response to a sizable variety of odorants, and 2) Electrophysiological data are collected in an olfactory perception task with a pair of selected odorants in order to assess the connectivity of frontal cortex regions. Statistical analysis methods are used to assess the significance of selected features extracted from the recorded modalities as Alzheimer's biomarkers. Olfactory decline regressed to age in both healthy and mild AD groups are evaluated, and single- and multi-modal classifiers are also developed.

The novel aspects of this study include: 1) Combining EEG response to olfactory stimulation with behavioral assessment of olfactory perception as a marker of AD, 2) Identification of odorants most significantly affected in mild AD patients, 3) Identification of odorants which are still adequately perceived by mild AD patients, 4) Analysis of the decline in the spatial coherence of different oscillatory bands in response to olfactory stimulation, and 5) Being the first study to quantitatively assess the performance of olfactory decline due to aging and AD in the Iranian population.

THIS PROTOCOL ACCOMPANIES THE FOLLOWING PUBLICATION

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MATERIALS TEXT

Electroencephalogram, Olfactometer, University of Pennsylvania Smell Identification Test (UPSIT)

participants criteria


- 1 Participants were selected among the individuals referring to the memory clinic with memory performance complaints.
- 2 Two expert neuropsychologists assessed all the participants and recorded their smoking history, preferred hand, age, level of education, as well as any past olfactory problem. Demographic and medical history data were also collected for each participant.
- 3 The Mini-Mental State Examination (MMSE), the Clock Drawing Test (CDT), and a verbal fluency test were performed.
- 4 An expert neurologist diagnosed probable Alzheimer's disease according to the latest guideline of the NIA-AA.

UPSIT Test

- 5 The test kit consists of 24 odors which are each exposed by scratching its corresponding strip.
- 6 After presenting each scent to the participant, four options to select from are provided, and the participant is asked to identify the closest match among these options to the odor that they perceived. As some participants in the study were not able to read the list of options printed in the kit, either because of vision problems or due to illiteracy, the list of options for each odor presentation was read loudly and clearly to the participants, once before and once after the presentation of each odor.

Olfactory EEG Test

- 7 EEG signals were recorded using a 32-channel Mitsar amplifier. Data were recorded from the Fz, Cz, Pz, and Fp1 electrodes.

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- 8 Participants performed an olfactory perception task. During this task, the participant is presented with a sequence of stimuli composed of two different odors, one of which occurring more frequently (lemon, $p=0.75$) and the other being presented rarely (rose, $p=0.25$).
 - 9 Our experimental protocol consisted of a two-second stimulus presentation followed by 8 seconds of rest (pure water) interval. The odors were delivered to the participants using a laboratory olfactometer.