EXPLORING THE OLFACTORY BRAIN MAPPING OF FUNCTIONAL NETWORKS IN THE NORMAL PROGRESSION OF AGING USING EEG

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Abstract: The olfactory system includes a large number of cortical components that contribute to normal odor perception and memory. Cerebral activation profiles during olfaction have been fairly well explored in healthy subjects, but little attention has been given to olfactory brain mapping in aging processes. To explore whether olfactory loss leads to deficits of olfactory profile by electroencephalogram (EEG) were used to investigate neural responses in healthy subjects. Participants smelled both pleasant (perfume, LANCOME TRESOR) and unpleasant (alcohol) odors. In the preliminary study, we report the results of using EEG to explore and map the cortical areas involved in sensing odorous molecules. Importantly, the intensity of the EEG signal elicited by olfactory chemosensory stimulation of cortical regions decreased following aging in healthy subjects. Moreover, we found that olfactory loss in normal subjects is correlated with several cerebral regions under aging. The fact that individuals with olfactory loss exhibited several signs of brain degeneration is in agreement with the postulation that olfactory loss could be a preclinical marker of aging. The purpose of the study will be to investigate the cerebral correlates of impairments in odor identification in a sample of healthy subjects following aging and to correlate the olfactory brain mapping of functional networks in the normal progression of aging by EEG. Here, we will focus on normal, nonpathological aging in humans and how it may affect the main olfactory system. In this study, we will also explore the possibility that olfactory dysfunctions in older persons could be associated not only with brain olfactory regions, but also with other brain regions which are sensitive to the aging processes.

Index Terms: Olfactory brain mapping, Functional networks, Aging, EEG

I. INTRODUCTION

The human olfactory system can detect and discriminate between a great variety of chemical molecules with high sensitivity and specificity (Angioly et al., 2003, Walker et al., 2003). This action occurs through anatomical, cellular, and molecular signal transduction that amplifies and integrates an enormous array of incoming olfactory information. Olfactory information is likely to be induced by the most peripheral particle of the odor, while identification and discernment are partly cognitive phenomena which are affected by the central olfactory structures.

The olfactory receptor cells project via the olfactory nerve to the olfactory cortex [1]. The brain structures involved in odor processing mainly consist of the primary olfactory cortex, which comprises the anterior olfactory nucleus, anterior cingulated gyrus, insula, amygdale, thalamus, hypothalamus, and hippocampus [2-10].

Testing olfaction gives critical information because olfactory problems are associated with sensory function, which is very important [11-12]. In 1984, an early study reported that smell identification ability changes with age [11]. The ability to detect odors peaks in humans between 20 and 40 years of age, and begins to decrease steadily thereafter. Murphy and colleagues (2002) illustrated that the prevalence of measured olfactory impairment is 24.5% overall, but among elderly people it can be as high as 70% [12].

These changes might alter the normal synaptic organization and damage olfactory processing during the age-related olfactory loss [13-14]. The aim of this project is to discuss the physiological basis of age-related olfactory loss and disordered olfactory transduction in the brain. Decreased olfactory function with age in humans parallels generalized age-related deficits in sensory functions and cognition that occur with a decrease in quality of life [15]. Neuroimaging tools, together with the abundance of information that exists on olfactory function, are helpful in analyzing the mechanisms that underlie age-related changes in the human brain [16-17]. However, studies of the mechanisms underlying olfactory function during normal physiological aging are few in number. In addition, instrumental approaches, such as EEG measurements, supported by evaluation of olfactory function will be implemented. The overall aim of this study will be to explore how olfactory loss under aging affects olfactory imaging. In this study, we will explore the physiology and plasticity of the olfactory system, the instrumental tools for assessing its function, and the aging process with which the olfactory dysfunction is intimately associated.

II. MATERIALS AND METHODS

Subjects: The sample will included 30 healthy subjects [Young subjects (n=10; mean age 20), Middle-aged subjects (n=10; mean age 40), and Older
subjects (n=10; mean age 60). All subjects had normal general cognitive performance according to the Mini-Mental State Examination (scores ≥ 26). All participants had undergone a widespread neuropsychological assessment. The protocol (C103016) has been approved by the Institutional Review Board of Fu Jen Catholic University.

**Odorous molecules:** For stimulation, non-toxic substances were used to generate smell sensations comprising both pleasant (perfume, LANCOME TRESOR) and unpleasant (alcohol) odors.

**Electroencephalogram (EEG):** Laboratory EEG (Fig. 1) recordings were performed using Neuron-Spectrum 3 (Neurosoft Lt, Russia) and 21-Channel Digital EEG Systems. Electrodes were situated according to the International 10-20 System. Digital EEG systems Neuron-Spectrum are modern, high-tech electronic medical devices commonly used by medical practitioners and neurophysiologist-researchers. The high quality of EEG recordings is achieved as a result of the component hardware and software. The sampling rate of the EEG signal is up to 5000 Hz per channel. The A/D converter is 16 bits, and the noise level is less than 0.3 µV. The mathematical processing of the received data allows for brain mapping, spectral, coherent, periodometric analysis and automatic report generation. The EEG display on the computer screen has a resolution up to 2560x1600 pixels, and images can be printed out on common paper. The impedance is indicated on the electronic unit’s front panel.

**Statistical analysis:** All data were expressed as means ± SEM. To establish significance, data were subjected to unpaired one-way ANOVA using the Sigma Stat 3.5 software statistical package (Systat SigmaStat V3.5.0.54 Software; San Jose, California, USA). The criterion for significance was set at P < 0.05. Differences between groups were assessed with Student’s t tests or one-way analysis of variance (one-way ANOVA) as indicated. The significance level was set at 0.05 or 0.001 as indicated.

III. RESULTS

EEG features real-time neuroimaging methods that provide measurements directly from neuronal activation [18-19]. Among the non-invasive approaches, EEG has emerged as the most viable option. Any activity in the brain is accompanied by changes in ion concentrations in neurons leading to polarization and depolarization.

EEG is advantageous in that it is portable and cost effective, although magnetic fields suffer far less degradation than electric fields from the spatial blurring effect of the skull. As it stands, a comprehensive picture of the interaction of odorous molecules with the brain’s functionality from a cognitive neuroscience perspective using EEG is still lacking. To fill this gap, participants completed one trial of the main experiment by smelling odorous molecules and performing an EEG imagery task. Participants smelled both pleasant (perfume, LANCOME TRESOR) and unpleasant (alcohol) odors. We report the results of the study using EEG (Fig. 2A) to map the areas of the cortex of the human brain involved in detecting odorous molecules (Fig. 2B).

Importantly, the EEG responses to chemosensory stimulation have been identified mainly using NET software in the topographic map. The intensity of the EEG signal elicited by olfactory chemosensory stimulation of cortical regions decreased following aging in healthy adults (Fig. 3). In this preliminary study, we found that olfactory loss in normal subjects was correlated with several cerebral regions following aging. The fact that individuals with olfactory loss had several signs of brain degeneration is in agreement with the postulation that olfactory loss could be a preclinical marker of aging.

![Figure 1. Electroencephalogram (EEG).](image)

EEG in laboratory instruments have available (Fig. 1A). Subjects accepted the experiment to detect the signal of EEG (Fig. 1B).
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IV. DISCUSSION

The olfactory receptor cells and the olfactory bulb help in the modification of the stimulus which is sensed and from the olfactory bulb; the information is transferred onto the primary olfactory cortex. The primary olfactory cortex includes regions of the temporal lobes which include the superior frontal cortex, insular cortex, limbic system, amygdala and hippocampus [1-5]. These areas determine the kind of chemosensory stimulation. Olfaction and memory are so infused that they allow us to make connections with experiences which are stored as memories. MRI studies have indicated that human olfaction declines with aging. Two studies that used MRI to compare aged adults to young adults found less brain activity in the olfactory structures of aged subjects, including the primary olfactory cortex, insular cortex, amygdala and hippocampus [20-21]. Importantly, data for the analysis of olfactory imaging comes from a body research including physiological, cognitive, and neuroimaging studies [4, 22-23]. Djordjevic and colleagues (2005) identified the key regions that are activated during olfactory perception, such as the piriform cortex, orbitofrontal cortex, and insula using positron emission tomography (PET) imaging [22].

Olfactory function can be evaluated through the use of specific instrumental approaches, including electrophysiological methods and neuroimaging techniques. Using these approaches, the aims of the present study were thus to characterize for the first time the topographic map and EEG intensity of olfactory stimulation and to examine whether this approach may be used to decrease the signal of the obtained EEG responses to study olfaction in subjects.

In this study, we indicate that olfactory loss in normal subjects is correlated with several brain measures of gray and white matter integrity under aging processes. Taken together, our study provide some evidence that the neural networks involved in the brain are organized into modules and that these modular partitions are linked to olfactory performance and personal quality of life in aging.

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