# Development of the Objective Method for Detection and Analysis of Disorders in the Olfactory Event-Related Potentials

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***Abstract*—This paper presents an objective method for early diagnosis of disorders and diseases of olfactory system. To achieve this goal the author designed a fragrance dosing prototype, which is synchronized with the dedicated recorder of olfactory evoked potentials. Automatic synchronization of registration of olfactory event-related potentials with dosing of stimulus fragrances enables precise determination of latency occurring between stimulation and response of the central nervous system. Obtained results allow to prove that developed prototype enables the evaluation of the olfactory system disorders in the context of neurodegenerative disorders. However it is necessary to establish a standardization procedures, before a wide implementation in a clinical practice. That is why the developed method requires a broader research which is an issue of a much larger group of patients and significantly longer duration of the study.**

***Index Terms*—event-related potentials (ERP), olfactory system diagnosis, brain activity, microprocessor**

## I. Introduction

THE surrounding world supplies us with a stream of odour perceptions, which are described as smell. With the loss or impairment of smell, many pleasant life experiences disappear. The sense of smell was a long time the most unrecognized among other our senses due to the fact that it is less essential than vision, audition or the somatic senses. Development of research in the olfactory area can be observed starting from 2004. In this year Richard Axel and Linda Buck were awarded the Nobel Prize for their research on "discoveries of odorant receptors and the organization of the olfactory system". They gave us explanation concerning recognition and memorization of about 10000 different odours. Such complicated process engages about 3 % of our genes (it means about 1000 genes). Each gene is responsible for only one olfactory receptor type. It is possible to recognize such a big number of odours due to the fact that one odour can activate several receptors but with different intensity.

Currently, most of researches are concentrated on chemical structures and processes declining in olfactory system. However, some works are also devoted to modeling of electrical behavior for olfactory explanation.

A lot of scientists are convinced that a deterioration of the sense of smell is a significant handicap. We cannot perceive the different qualities of food - when something tastes good it is mainly the result of olfactory system activation. Moreover we cannot detect warning signals, for example smoke from a fire or leaking gas. A unique odour can also induce very old remembrance, concerning even our childhood.

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## II. Anatomy of Olfactory System

The human olfactory epithelium is located in the superior nasal cavity and encompasses a portion of superior turbinate, the superior nasal septum, and the region of the cribriform plate. It contains several millions of receptors (olfactory bipolar neurons), sending messages directly to the olfactory bulb of the brain through the perforations in the cribriform plate.The olfactory bulb lies on the ventral aspect of the frontal lobes [1]. The odour sensitivity varies in people [2]. Within a broad range, the sensory threshold is related to the administered substances.

It is necessary to notice, that olfactory receptor cells are exposed directly to the external environment. Therefore, they can be easily damaged during our life as a result of skull fractures or other pathology in this region.

## III. Olfactory Event-Related Potentials

An external effect of the smelling process can be measured as olfactory event-related potentials (called also more generally as olfactory evoked potentials - OEP). The olfactory evoked potentials are a class of the event-related potentials and according to the present measurement approach they are a variant of the electroencephalography EEG. It should be stated that these potentials are measured on a skull and not on or in the nose. The amplitude of the potentials is in the range of single microvolts. Unfortunately, the precision of such potential measures is low, because of existing "body" noises. Additionally, other brain activities and even human emotion variations can distort the result. Therefore, further researches of electrical properties must be continued. Today's measurement methods of olfactory event-related potentials need several repetition cycles to obtain average values of the necessary potential. Because it is necessary to take into account olfactory weariness (attenuation), a repetition frequency is low and as a consequence, a patient survey is long (usually 20 - 30 min. using existing equipment). Additionally, the precision of such average calculations gives often insufficient accuracy for malfunction detection of a brain behavior.

## IV. Olfactory Disorders as Diagnostic Indicators

The assessment of the olfactory function in human live is currently recognized as an established diagnostic method useful in the detection of early stages of many laryngological and neurological diseases in which abnormal olfaction is the early sign (Alzheimer's disease, Parkinson's disease) [3]. At this point in time there is no approved method and equipment designed for direct and objective assessment of the olfactory function. Indirect methods are inaccurate and are used only for detection of advanced olfactory diseases. For this reason the early objective diagnose could have a great impact on the treatment effectiveness and increase comfort of patient life. This paper presents an objective diagnosis method and its advantages in comparison with nowadays long-time and often invasive diagnosis methods.

Disturbances in human olfactory system are observed in several brain disorders, but proper recognition and precise measurement of such pathology in olfactory regions is extremely challenging.

## V. Overview of Diagnosing Methods of Smell System

The research methodology of smell in humans develops today in two directions. In the first case the modifications lead to maximal method simplification and at the same time to the study duration shortening. These changes reduce costs, which in turn results in easier and more widespread introduction of these studies to everyday clinical practice. Second direction is headed toward their liability and accuracy growth.

Disorder diagnosing methods of smell in human scan be divided into two major groups. The first are subjective methods(quantitative, qualitative and screening), and the second group includes objective methods[4].

Currently, the most popular methods for evaluation of the quality of olfactory system are psychophysical methods. They belong to the subjective methods. Among them the most popular are:

- University of Pennsylvania Smell Identification Test (UPSIT);
- the Connecticut Chemosensory Clinical Research Center Test (CCCRC test);
- Cross-Cultural Smell Identification Test (CC-SIT);
- the Sniffin' Sticks test.

However these methods demand a close collaboration of a medical staff with patient.

Objective methods are still in the development and need a standardization procedures, before a wide implementation in a clinical practice.

Therefore, the main goal of presented project was to build a prototype of measurement system with enhanced precision (sensitivity) dedicated uniquely to olfactory potentials. It is also necessary to understand and to separate more precisely distortion of event-related potentials. The delay between the stimulus and cortical response is the most important parameter (the latency), that must be measured with the use of microprocessor system. To obtain the sufficient resolution, a smart system for precise detection of the time instant, when odour stimulus starts to excite nerve receptors, must be designed. During the project four different odour samples were used (Table 1).The odour is evoked using the following elements: coffee, aniseed oil (olfactory receptor neurons will be induced), lemon oil, peppermint oil (olfactory receptor neurons and trigeminal nerve will be induced).

TABLE I
Odour Samples and Induced Nerves

| Odour samples | Nerve excitation |
|---|---|
| lemon oil | olfactory and trigeminal nerves |
| peppermint oil | olfactory and trigeminal nerves |
| coffee | olfactory nerve |
| aniseed oil | olfactory nerve |

## VI. Methodology

Since imaging methods (computed tomography - CT scan, magnetic resonance imaging - MRI) have become widely used in the analysis of the brain electrical activity [4], the use of the olfactory evoked potentials has not been developed. However it must be noted that the olfactory evoked potentials have two main advantages:

- the measure is entirely noninvasive;
- the method is not so expensive as CT scan and MRI.

Realization of the project was conducted in two main steps (briefly described in [5]:

- design and realization of a new registration system of olfactory event-related potentials (ERP), based on high-gain amplifiers and high-resolution analog-to-digital converters with dedicated software for noise cancelation (Fig. 1 presents signal path);
- design and construction of an accurate, precise odour sample dispenser. Very important feature is the synchronization of a pump action with the ERP registration system.

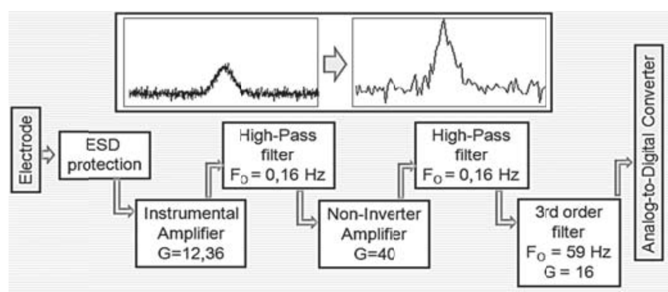


Fig. 1. Olfactory evoked potentials signal path

### A. The registration system

The author decided to use the ModularEEG including one digital board with isolated microcontroller/ADC ATmega8 and three 2-channel EEG amplifier boards (Fig. 2). Furthermore, author decided to use active electrodes. Such electrodes contain a built-in circuitry which amplifies the electrical current. It improves the signal quality received by the ModularEEG and avoids the skin preparation and conductive paste, required by normal passive electrodes applied usually in EEG systems [6]. Technical parameters of the ModularEEG are presented in Table II.

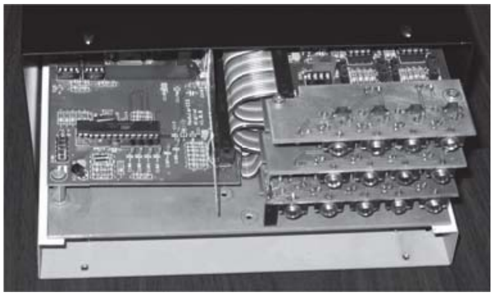

Fig. 2. Prototype of olfactory ERP registration system.

TABLE II
GENERAL SPECIFICATION OF MODULAREEG

| | |
|---|---|
| Number of channels | 2 - 6 |
| Resolution | 8 bits |
| Input Voltage Resolution | 0.5 µV |
| Input Voltage Full Scale | +/- 256 µV |
| Wideband noise | ~ 1 $\mu V_{p-p}$ |
| Supply Current | 70 mA (2 channels) |
| Sampling frequency | 256 Hz |

### B. *Odour sample dispenser*

The accurate and precise odour sample dispenser, with controlled odour parameters, is necessary to obtain a proper nervous excitation. The principle of operation is similar to the principle of pneumatic dispenser. Compressed air pushes the piston in the dispenser fragrance. The substance dosing time, its quantity and repeat cycle are performed by a solenoid valve control that ensures a constant and even flow. The construction is characterized by durability, portability and quiet operation (Fig. 3). Synchronization of a pump action with the ERP registration is one of the most important features. It is achieved with the use of shared microswitch. It is connected directly to electrovalve and to the ERP registration system.

Fig. 3. Prototype of odour sample dispenser.

An increase of latency of nerve activation can be observed in the case of deterioration of a smell system. The latency is visible for both olfactory and trigeminal nerves. To obtain a proper result it is necessary to minimize noise coming from measurement system and, what is very important, to be sure, that other nerves are inactivated, for example, the patient must be isolated from acoustic signals.

## VII. RESULTS

Conducted research showed great impact of muscle electrical activity on EEG signal. It was due to the eyes movement. Fig. 4 presents the EEG waveform (first channel) while the patient was looking to the right and then looking forward. This situation is obviously connected with electrodes placement. According to the literature to record ERP electrodes should be placed in FP (first channel) and between T and F (second channel) positions – frontal and temporal lobes.

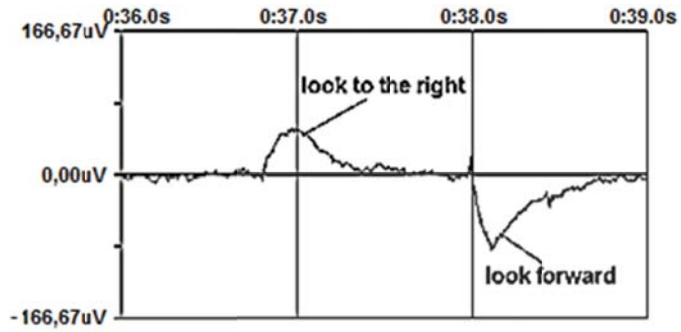


Fig. 4. Eye movements registered in EEG waveforms - look to the right and forward.

According to these results, test conditions were specified. Patient has to be very calm, relaxed and cooperative during the test. To avoid brain and other disturbances patient should be tested in lying position. Moreover he has to have blindfolded eyes and blocked ears.

Fig. 5 presents the results of olfactory nerve excitation due to the coffee smell stimulation. In this case latency between stimulation and central nervous system response was 480 ms. Fig. 6 presents the results of olfactory and trigeminal nerves excitations due to the peppermint oil smell stimulation. In this case latency between stimulation and central nervous system

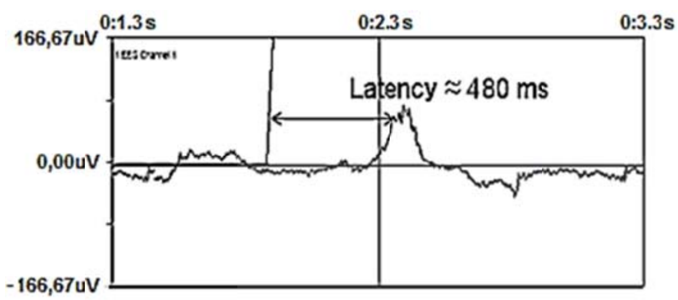


Fig. 5. Reconstruction of olfactory evoked potential in response to stimulation of coffee smell (excitation of olfactory nerve).

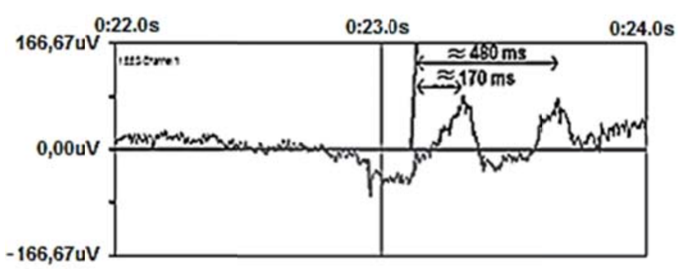


Fig. 6. Reconstruction of olfactory evoked potential in response to stimulation of peppermint oil smell (excitation of olfactory and trigeminal nerves).

response was 170 ms and 480 ms for trigeminal nerve and olfactory nerve respectively. In both cases there is no sign of neurodegenerative disease. The main idea of the project was to find a meaningful correlation between evoked potentials and disorders of the central nervous system, observed usually in the case of Alzheimer and epilepsy diseases. However, studies have been conducted on a small group of patients and only test on the bigger group could lead to far-reaching conclusions.

Example results obtained for patient no 1 are presented in Table III. It contains statistical results for all odours used during the test.

TABLE III
EXAMPLE RESULTS FOR PATIENT NO 1

| | | Coffee | Aniseed oil | Peppermint oil | Lemon oil |
|---|---|---|---|---|---|
| Latency of olfactory nerve response | Average | 466 | 473 | 477 | 475 |
| | Median | 470 | 460 | 480 | 470 |
| | Min | 440 | 450 | 460 | 460 |
| | Max | 490 | 510 | 490 | 495 |
| | Standard deviation | 20.74 | 24.39 | 10.95 | 13.23 |
| Latency of trigeminal nerve response | Average | - | - | 179 | 182 |
| | Median | - | - | 180 | 180 |
| | Min | - | - | 140 | 170 |
| | Max | - | - | 205 | 205 |
| | Standard deviation | - | - | 26.08 | 14.40 |

## VIII. CONCLUSION

Difficulties in precise registration and result's recurrence of olfactory event-related potentials are the main drawback in nowadays attempts to apply them in diagnosis systems. The author's main goal was to find a meaningful correlation between evoked potentials and disorders of the central nervous system, observed usually in the case of Alzheimer and epilepsy diseases [7]. Statistical elaboration of the results will be useful for final conclusions - how wide the ERP characteristics can be applied for diagnoses and treatment progress of brain diseases [8].

Therefore, the proposed measurement system permits to open quite new possibilities in early diagnoses of different disorders of the central nervous system. To realize this, the project addresses problems in several research domains and brings the following innovation beyond the state of the art in the following areas:

- new structure of the system for olfactory brain reaction is presented including new hardware and new software dedicated uniquely to olfactory ERP registration;
- detailed influence of smell sense disturbances for diagnosis of disorders of the central nervous system was investigated.

Obtained results allow prove that developed prototype enables the evaluation of the olfactory system disorders in the context of neurodegenerative disorders. However it is necessary to establish a standardization procedures, before a wide implementation in a clinical practice.

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