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Chemosensory-Event-Related Potentials to Olfactory Stimulations

Byung Chan Min*, Se Jin Park*, Chul Jung Kim* and Masashi Wada**

Abstract A new device introducing brief pulses of odorozed air synchronized with subject's respiration to human subjects creating a positive response was developed. By the using superimposition technique of an evoked potential the positive responses to skatole in normal subjcets were distinguishable. The odorant pulse trigger was the subject's respiration. Responses to aerosolized skatole consisted mainly of a positive wave with a peak latency of approximately 150 ms. In our cases, saturation of responses was found after 4-5 averagings with the responses becoming most clear after 7-8 averagings. And in cases of Alzheimer disease very quick adaptation was recognized.

Key words : Chemosensory event related potentials, Odorous stimulation, Objective measurement, Averaging and Superimposing technique , Alzheimer disease

1. Introduction

The sense of smell has long been played an important role in the course of human life. Smell initially served mankind in a protective role to warn of approaching dangers and identify harmful substances. Yet, the utility of smell has expanded beyond these basic practical concerns into various facets of everyday life, and even to the esoteric. For instance, certain odiferous (e.g., perfume) scents are currently commercially exploited for their unique capacity to make one feel noble. Consequently, smell has become an indispensable component of our cultural life. Even so, studies of human olfactory functionality, like those of taste, lag far behind similar research endeavors of the other senses, namely, the somatosensory, visual, and auditory. In these latter cases, research efforts are generally conducted by affecting the target sensory organs with a physical input stimulation, and recording the clear output response. Subsequently, functionality studies of the target sensory organs are made by studying the relationship between these input and output responses. With respect to the olfactory sense, there are a number of similarly patterned research efforts which are worthy of note.

Recording the human auditory and visual evoked potentials from the scalp has been commonly performed since the advent of the response averaging technique. In order to quantify alterations in the sense of smell, it is of interest to apply the technique of olfactory event related potentials(OERP) which help to overcome subjective interpretations (Kobal et

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al.,1992). In addition,OERPs can also be used to investigate lateralisation phenomena (Kobal et al.,1992) within the olfactory system which are characterized by an initially ipsilateral pathway. Since a relative specialization of the hemispheres for pleasant (left) and unpleasant (right) emotions has already been reported (Davidson,1984), it may be possible to establish such a relationship between hedonic estimates of a given stimulus and the lateralization of the OERP. A new device introducing brief pulses of odorized air synchronized with subject's respiration for creating positive waveforms was developed, and stable response was obtained.

2. Materials and methods

Subjects

The subjects were 18 healthy men aged 22 to 39 years with normal olfactory sensens. All subject were non-smokers and were instructed to restrain from drinking or eating for at least one hour prior to the measurement.

Odorant

Each was tested using several odors, including skatole and vanillin. Their olfactory abilities were determined to be normal by testing them with a T&T olfactometer (Zusho 1990), which has been adopted as a standard by the Japanese Society of Otorhinolaryngology. Skatole is one of the standard odorants supplied with the T&T olfactometer (Zusho 1990).

Testing procedure

The subject was instructed to lie flat on his back on a bed. All subjects were explicitly instructed not to blink after an odorant had been perceived. Due to a specially devised stimulation technique the presentation of the chemical stimuli did not activate mechano or thermosensors in the nasal mucosa. This monomodal chemical stimulants provides a constant flowing air stream with controlled temperature and humidity (36.5C: 80% relative humidity). The air stream was introduced into the nasal cavities by way of a

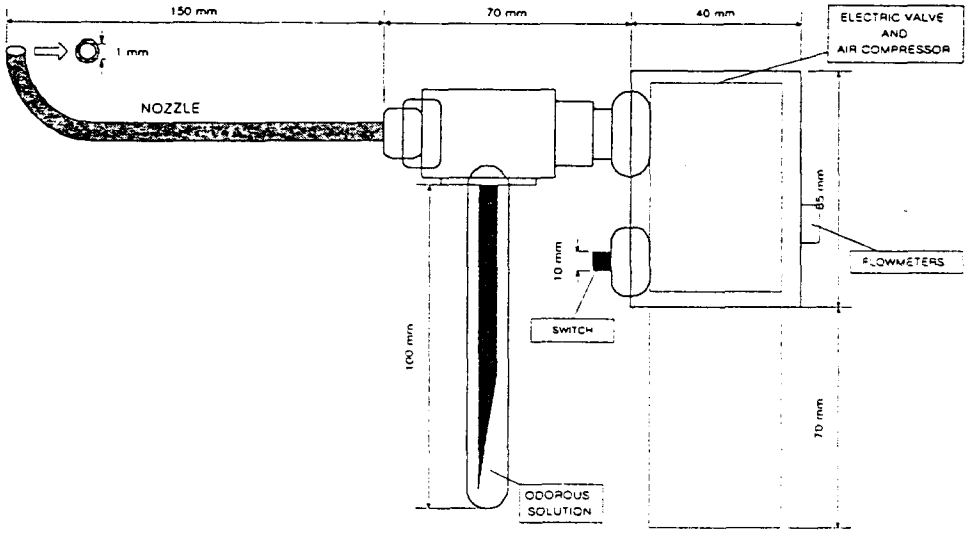

Fig. 1. The device used for introducing the odors. The odorant pulses were intorduced synchronizing with subject's respiration.

teflon tubing (15Cm lenth, 1mm inter diameter), the tip of which was inserted into either the left or the right nostril. The odorant pulses were intorduced by the pressurized stimulater at a flow rate of 1l / min (Fig.1). Stimulus duration was 200ms with a rise time below 20ms (for further details see Kobal and Hummel,1991).

Just prior to the onset of the subject's inspiration, the tip of a stimulater was inserted 1cm into his nostril as automatically as possible. After introducing the odorant, the nozzle was .gently removed from his nostril. Stimulation was given without giving any special attention to the occurrence of eyeblinks during the prestimulus interval. White noise of approx. 60dB SPL(ERA stimulator, Nihon-Koden Co., Japan) prevented the subjects from hearing the switching process.

Olfactory event-related potentials(OERP)

EEG was measured in a quiet electrically shielded chamber with good air circulation. A one minute rest time between the tests was taken, so that the results were not affected by fatigue of olfactory sense or adaptation. The temperature of the measurement chamber was kept at 21-24C and the time for the measurement was from 2:00 to 5:00 in the afternoon. In the measurement of evoked potential, the monopolar leading between Cz (10/20 international system) A1(the left lobe) was taken, and ground was set on Fpz. The silver-silver chloride electrodes of 7mm in diameter (Nohon Kohden,NE-121B) were used. Electrode impedances were adjusted to be less than 6k. The band pass of the recording system was between 1 and 30Hz. Trigger pulses were generated by hand switch just after the start of inspiration and were determined by visual inspection of the subject's abdominal movement at a rate of once in four slow, regular respirations. After eight responses have been recorded, the results were averaged by a Neuropack Eight Computer. An electric valve introducing the odorous stimulation was activated for 300ms by a trigger pulse. The analysis time was 1000ms. In these late nearfield potentials the peak-to-peak amplitudes P1N1 and N1P2, and the latencies of P1, N1 and P2 (in relation to stimulus onset) were measured.

3. Results

When the odorous stimulation was introduced at the end of inspiration or during the expiration, the evoked response was undetectable. Also, there was no detectable response in the absence of the odor (Fig.2).

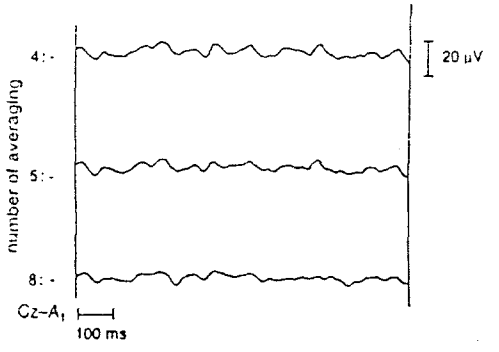

Fig. 2. Absent responses to uncented air in a test subject using distilled water as the control.

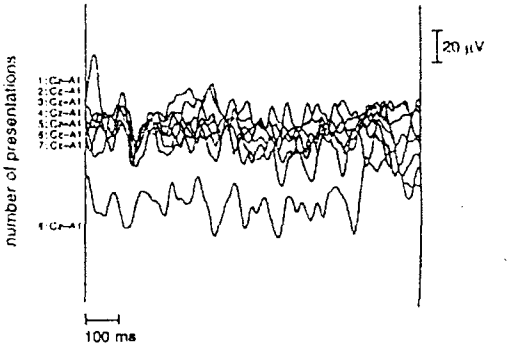

Fig. 3. Typical pattern of evoked potentials to odorant sitmulations demonstrating evoked responses to skatole before averaging. As seen here, the responses showed good reproducibility.
Before the averaging, the positive responses were detectable at a certain peak latency by the superimposition technique.

using distilled water as the control.

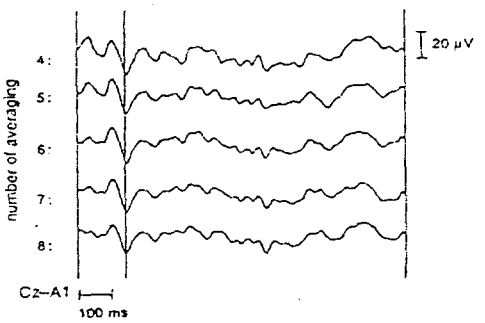

Fig. 4. Averaged evoked potentials to skatole. The positive wave evoked by the odorant was obvious with averaging, with the number 8 wave representing eight times the total. Waves 4-5 show the largest amplitudes, which waves 7-8 are the clearest.

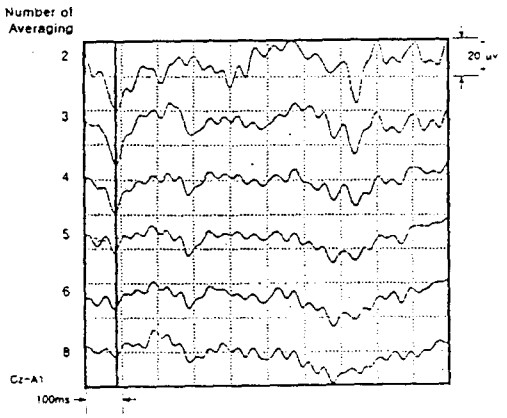

Fig. 5. Response in cases of Alzheimer disease. Quick adaptation was recorded.

A typical pattern of an evoked response to skatole before averaging is shown in Fig.3. Positive responses were detectable at a certain peak latency by using the superimposition technique before and after the averaging(Fig.4). In the graph shown, the number 8 wave represents 8 times the total; thus wave 4 or 5 shows the largest amplitude and wave 7 or 8 represented the clearest wave. With the total number of stimulations exceeding 8, peak amplitude decreased and waveforms decayed. Similar results were obtained from all 18 subjects tested.

Saturation of responses was found after 4-5 averagings, and the response became most clear after 7-8 averagings. Accordingly, the saturation was determined with 4-5 averagings, and the peak latency was measured with 8 averaging. In general, it took approximately 20 min to obtain a good response with different odorant stimulations. If the interval was insufficient(less than 20 min), the evoked response was unclear in the following test. After a sufficient interval(greater than 20 min) the next odorant was introduced and the different concentrations evaluated for their olfactory evoked responses. Responses to skatole evoked positive waves had a peak latency of 147.115.3ms in the 18 normal subjects tested.

In order to evaluate the influence of the presentation of odorant stimulation with blast method, glacial acetic acid was introduced to anosmic patient and evoked a negative deflection. This negative response was thought to be elicited by the trigeminal nerve excitation. Also, in all 6 cases of Alzheimer disease tested quick decrease of amplitude in averaged waves were recognized, and after eight averagings positive response was undetectable(Fig 5).

4. Discussion

A major problem in this study was the method used to synchronize the odorant stimulations with respiration to record a stable evoked response. For this reason the initiation of respiration has been checked by a thermistor placed beside the nostril or by an abdominal band for detecting abdominal movements (Tonoike and Kurioka 1982). According to our previous study, regulation of stimulation using these methods is unstable. In another words, it was impossible to stimulate olfaction precisely

at a specific time after the start of respiration. When the start of respiration was determined by observing abdominal movements in a slow, regular respiration pattern, introduction of an odorant stimulation at the end of inspiration or during expiration resulted in an evoked response being undetectable. In other words, a slow and regular inspiration is necessary to deliver an aerosolized odorant to the olfactory fissure at a certain period.

The reason that a reproducible and stable response was produced in our research is as follows: respiration is constant in the same subject. If the slow and regular respiration is achieved, respiration will be repeated at a constant speed and consequently the odorant air will be delivered to the olfactory fissure in a certain period. The present study showed that positive waves were distinguishable as the evoked response by using the technique of superimposition before averaging. The positive wave evoked by the odorant was made clearer by averaging. The saturation phenomenon was related to the amplitude of the evoked potentials for repeated pulse sitmuli and was found to be related to olfactory fatigue(Koster and Wijk 1991). Previous studies have also shown that a clear response was obtained by the total of 20-30 waves. However, Tonoike and Kurioka (1982) found that saturation occurred and the amplitude of the main positive response decreased after more than 10 averagings. In our cases, a saturation of responses was found after 4-5 averagings and the response became most clear after 7-8 averagings. Accordingly, peak latency was measured with 8 averaging. Other reports have shown a difference in peak latency (Kobal and Hummel 1991). This is believed to be due to variations in the length of the odorant transmission system used and the correlation with inspiration. Our measurements began when the oscilloscope sweep started on which the electric valve was activated. We, then, calculated that a few milliseconds were required for the odorant pulse to travel the final 22cm length of the tubing of our stimulator system. Some discussion has involved whether a response was evoked by excitation of the trigeminal nerve or olfactory nerve(Smith, Allison, Goff and Principato 1971). However,it has not been considered necessary to distinguish one from the other,since both the trigeminal and olfactory nerves are usually affected by an odorant if a pure trigeminal nerve exciting odor is not used for stimulation. In the study,glacial acetic acid was used as a trigeminal nerve sensitive substance and evoked a response without perception of smell in anosmic patients showing no response to skatole. This was recorded as a negative deflection at almost the same latency as a main positive response to skatole in normal subjects. Accordingly, the evoked response to skatole reported in this paper was thought to be mainly elicited by odorant stimulation to the olfactory nerve. The data suggest that the odorant response is evoked primarily by olfactory stimulation, but there is still a possibility of nasal trigeminal afferent stimulation.

Kobal and Hummel (1991) reported that the changes in peak latency were depended on the concentration of the odorant used. In their study, the shortening of peak latency was recorded for the more concentrated odorant. However, the averaged evoked response technique may offer a more sensitive and specific measure of olfactory function. Our findings suggest that the evoked potential technique and olfactory EEG response could be beneficial in a clinical setting for the assessment of abnormal olfaction.

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