

Evoked Response to Olfactory Stimulations in Anosmic Patients

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Abstract: In our study, we explored the influence of blast method introduction of odorant on evoked response. In normal patients, no detectable response was observed in the absence of an odor, and introduction of an odorant at the end of inspiration or during expiration did not result in any detectable positive response. In anosmic patients, glacial acetic acid, which is thought to be a strong trigeminal stimulating agent, evoked a negative response without detection of odor. Accordingly, the positively evoked response to odorant was thought to be elicited mainly by the odorant, not by the trigeminal stimulations or the auditory stimulations (or both).

Key Words: chemosensory event-related potential; olfactory evoked response; trigeminal excitation

Several reports about olfactory evoked potentials have pointed out that, although stable, constant responses were not easily elicited owing to problems associated with control of stimulus [1-3]. We introduced our technique of synchronizing olfactory stimulation with a patient's inspiration for the study of event-related potentials [4-7]. Here, we discuss the influence of extraneous stimuli associated with its introduction, such as nasal trigeminal afferent stimulations, auditory stimulations, or both.

SUBJECTS AND METHODS

Each patient was instructed to lie supine on a bed [4-7]. An electroencephalogram was recorded as upper negative from the central midline by an active electrode using a monopolar recording. Other electrodes were attached to one ear auricle (indifferent electrode) and the forehead (earth electrode), according to the International 10-20 system (bandpass, 1-30 Hz; impedance, 2-6 k Ω). Odorant pulses were introduced by our odorant stimulator at a flow rate of 1 liter/min (Fig. 1). Just prior to the onset of a patient's inspiration, the tip of the stimulator was atraumatically inserted 1 cm into the nostril.

After the odorant was introduced, the tip of the stimulator was removed gently from the nostril. The odorant pulse trigger was the patient's respiration. An electric valve was used to introduce the odorant stimulations and was activated for 300 msec by a trigger pulse generated by a hand-operated switch attached to the stimulator. Trigger pulses were generated just after the start of inspiration and were determined by visual inspection of the patient's abdominal movement at a rate of once in four slow, regular respirations. The analysis time was 1,000 msec. After eight responses to a given concentration of odorant had been recorded, the results were averaged by a Neuropack 4 computer (NIHON KOHDRN Co., Japan) [4-7].

The study population consisted of seven male, anosmic Japanese nonsmokers, 37-48 years old. Their olfactory abilities were determined to be anosmic by testing them with an olfactometer that was adopted by the Japanese Society of Otorhinolaryngology as a standard olfactory acuity test [8]. Each patient was tested using odorant E5 (the highest concentration [9.75%] of skatole) and glacial acetic acid, which is thought to be a trigeminal stimulating agent. New odorant was introduced at 15-minute intervals. The environmental temperature of the test room was maintained at between 21° and 24°C.

RESULTS

First, we introduced evoked response in healthy young patients. We observed no detectable response in the

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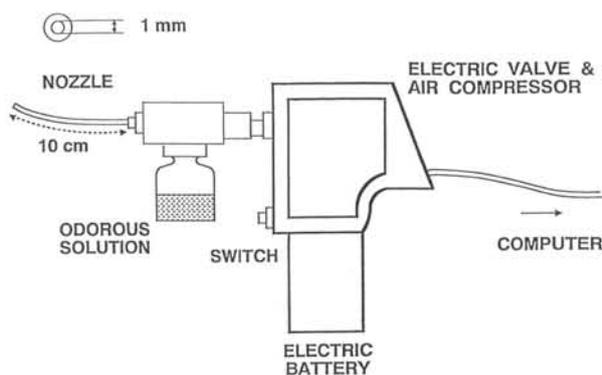


Figure 1. Schematic diagram of the stimulator. (Nozzle length, 10 cm; inside diameter, 1 mm).

absence of the odor, as shown in Fig. 2. When the odorous stimulant was introduced at the end of inspiration or during expiration, no positive evoked response was detectable. A typical pattern of an evoked response to skatole E5 in a healthy young patient before averaging is shown in Figure 3. Positive responses were distinguishable as the evoked response at a certain peak latency by using the technique of superimposition before averaging (see Fig. 3), and the positive response became obvious after averaging (Fig. 4). In this graph, wave 8 represents eight times the total, forming the basis for the following remarks. The largest amplitude of "main positive response" is recognized by averaging four or five responses, and clearest wave may tend to be shown by averaging of seven to eight responses. That is, the saturation of evoked responses is considered to have been recognized by averaging four or five responses. Skatole E5 evoked a positive response with

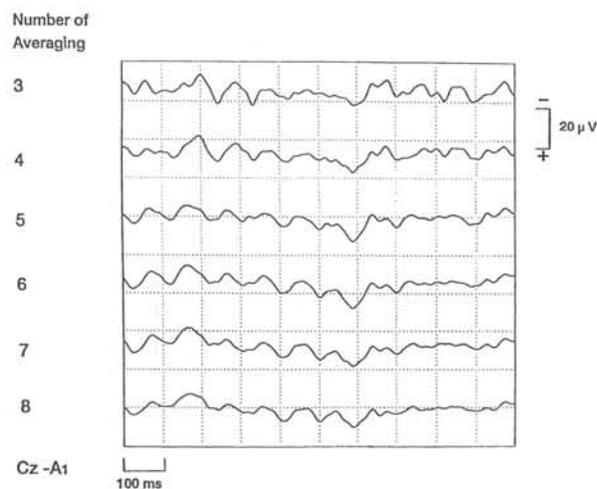


Figure 2. Responses to unscented air. Unscented air produced no positive response.

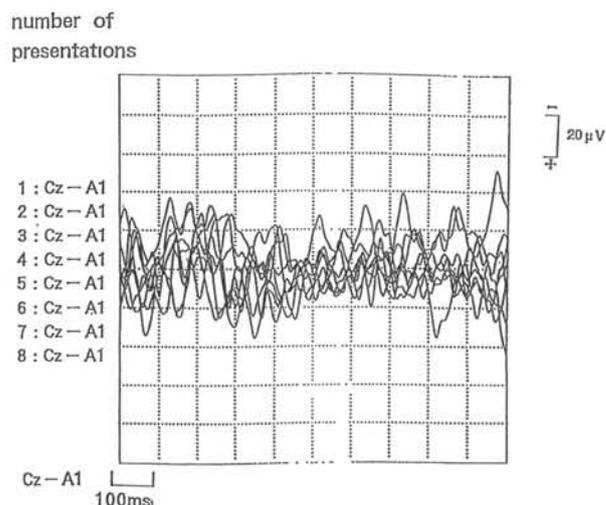


Figure 3. Evoked responses (before averaging) to E5 (9.75% skatole) in a normal young patient. The responses showed good reproducibility before averaging, and the positive responses were detectable at a certain peak latency by using a superimposition technique.

a peak latency of between 68 and 84 msec in eight normal young patients [4,5].

Next, we explored the response to the highest concentration of skatole E5 in anosmic patients. Skatole E5 did not result in any detectable positive response in anosmic patients (Fig. 5). Furthermore, glacial acetic acid evoked a negative deflection without detection of odor (Fig. 6).

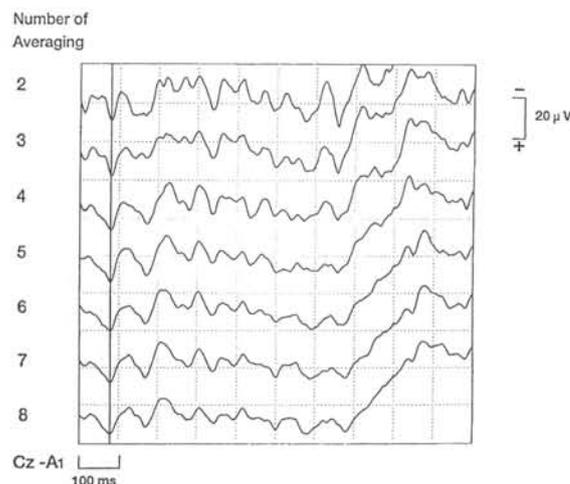


Figure 4. The averaged evoked responses to E5. The positive responses became obvious with averaging technique. The number 8 wave represents eight times the total. Waves 4 to 5 show the largest amplitude. E5 evoked a positive response with a peak latency of between 68 and 84 msec in eight normal young patients.

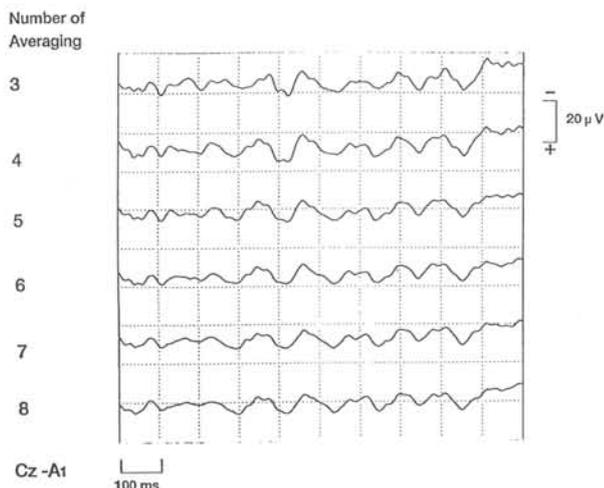


Figure 5. Response to skatole E5 in anosmic patients, in whom the highest concentration of skatole E5 did not result in any detectable positive response.

DISCUSSION

Olfaction must be stimulated precisely at a certain time so as to calculate accurately the origin of olfactory evoked responses, which may not yet be confirmed. Nonetheless, according to our data, in many cases at least, the peripheral system of the olfactory nerve path appears to be important, and adaptation may be influenced by peripheral and central factors. For this reason, we opted to deliver the aerosol odorant to the olfactory fissure via pressurized air synchronized with a patient's inspiration [4,5]. That a reproducible and stable re-

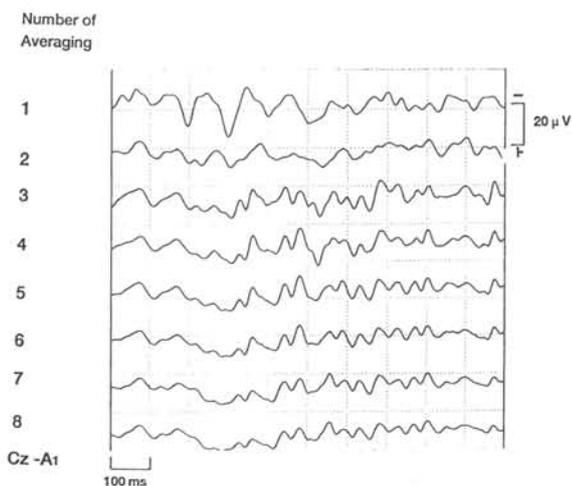


Figure 6. Response to glacial acetic acid in anosmic patients. Glacial acetic acid evoked a negative deflection without detection of odor.

sponse is recorded by our technique can be explained as follows: Respiration is constant in the same patient. If slow and regular respiration is achieved, respiration will be repeated at a constant speed and, consequently, odorous air will be delivered to the olfactory fissure at a certain time in the same patient.

Some discussion has centered around whether a response was evoked by the excitation of the trigeminal nerve or by the olfactory nerve [1,2]. However, we did not consider it necessary to distinguish one from the other, because both the trigeminal and olfactory nerves are usually affected by an odorant. To exclude specific influences, we tested the effect of inserting a nozzle and sudden blast of odorant (glacial acetic acid), thought to be a trigeminal stimulating agent, in anosmic patients. Glacial acetic acid evoked a negative response without detection of odor, whereas a blast of skatole E5 produced no effect. Also, introduction of an odorant at the end of inspiration or during expiration did not result in any detectable positive response; in other words, the pressurized odorous air itself did not result in any positive response when an odorant was introduced but not synchronized with patient's inspiration.

If the responses are elicited by nasal trigeminal afferent stimulation or sound of the stimulation, positive response should be recognized even if the odorant is not introduced synchronously with the subject's inspiration, such as by the introduction of odorant at the end of inspiration or during expiration or in anosmic patients. Furthermore, trigeminal stimulation or auditory stimulation must not show the saturation only by the averaging of four to five responses. Thus, we are certain that positive responses are evoked by the odorant and not by some extraneous stimuli associated with its introduction, such as a reaction to the insertion of the stimulator, presentation of pressurized air, respiration, or the sound of the stimulation.

Our findings suggest that the evoked potential technique and olfactory electroencephalographic response as measured by our method could be beneficial in a clinical setting for assessing abnormal olfaction.

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