*Sensors and Materials*, Vol. 17, No. 7 (2005) 391–395
MYU Tokyo

S & M 0616

# Gamma Band Oscillations and Real-Time Breath Gas Monitoring Using Artificial Noses in An Intravenous Olfaction Test

Tadashi Ishimaru*

Department of Otorhinolaryngology, Nanto General Hospital,
2007-5 Umeno, Nanto, Toyama 939-1724, Japan

(Received December 1, 2004; accepted May 9, 2005)

***Key words:*** olfaction, gamma band, artificial nose, Alinamin, intravenous olfaction test

Most clinical olfactometry is a psychological test, and electrophysiological tests are rare. To develop clinically objective olfactometry, the applicability of intravenous olfactory-elicited gamma band oscillation (GBO) was investigated. The GBO was elicited by intravenous olfactory activation by thiamine propyldisulphide (Alinamin, Takeda Pharmaceutical Company, Osaka, Japan). Intravenous olfaction occurred because of odorous breath gas caused by an intravenously administrated odorant. The breath gas was monitored by an odor meter using artificial noses (FPO-II, Futaba Electric, Yokohama, Japan). Odorant intensity in the breath gas was increased after the administration of Alinamin. GBO was also observed after the administration of alinamin. The change in GBO amplitude was similar to the change in odorant intensity until the first peak of odorant intensity after the administration of Alinamin. After the first peak, GBO amplitude still increased in one subject but decreased in another. Although GBO was thought to correlate to the intensity of an odorant in breath gas (IOBG), the difference in olfactory fatigue among subjects seemed to affect the difference in GBO. Measuring GBO combined with IOBG monitoring provides a method to analyze the relationship between olfactory response and for real-time odorant intensity in the nasal cavity. This seems a useful method not only for basic but also for clinical research and even suggests ways to improve the artificial nose.

## 1. Introduction

Most clinical olfactometry is conducted using psychological tests, and electrophysiological tests are rarely performed. When electrophysiological olfactometry has been performed, odorant concentration or intensity in the nasal cavity has generally remained

*Corresponding author, e-mail address: taishimaru-alg@umin.ac.jp

unknown. In the study of human olfaction, it has been difficult to record an electrophysiological response combined with odorant concentration in the nasal cavity until the invention of the artificial nose. Olfaction is composed of front and retro nasal olfaction. It is possible to record the intensity of an odorant in the expired air, which simulates retro nasal olfaction, using the artificial nose.

A unique method of clinical olfactometry, the intravenous olfaction test (IVO-test), which is also called the "Alinamin test," is a test of retro nasal olfaction that is widely used in Japan. One of the weak points of the IVO-test is the unclear odorous intensity in the nasal cavity. Therefore, Nakashima[1,2] attempted to measure the intra nasal intensity of an odorant breathed from the lungs using the artificial nose during IVO-testing. In this study, the electrophysiological response combined with the response of artificial noses was recorded during the IVO-test. The aim of this study is to provide a method for investigating whether the electrophysiological response was linked to the odorant concentration in the nasal cavity in the IVO-test.

## 2. Subjects and methods

### 2.1 *Subjects*

Two male volunteers, 58 and 37 years old, who have normal olfaction participated in this study. The subjects gave their informed consent. The subjects were instructed to respond using a hand switch when odor was detected and this was labeled subjective response (SR).

### 2.2 *Stimulation*

The IVO-tests were conducted according to the standard clinical protocol; thiamine propyldisulphide (Alinamin, Takeda Pharmaceutical Company, Osaka, Japan) was intravenously administrated for 20 s.[3] The duration of Alinamin administration was marked by the experimenter by stepping on a pedal switch.

### 2.3 *Electrophysiological recordings*

Olfactory elicited gamma band oscillation (GBO) recorded from the human frontal scalp was amplified and filtered over a range from 28 to 200 Hz. This technique is same as in our previous report.[4]

### 2.4 *Artificial noses*

The breath in the nasal cavity was monitored by an odor meter with artificial noses (F PO-II, Futaba Electric, Yokohama, Japan). Odorous air was aspirated by an air pump and lead to two artificial noses in an odor meter. The aspiration tube was located in the nasal cavity 1 cm from the nostril. The odor meter was constructed of two different types of artificial nose and their data were analyzed by a built-in microprocessor. These raw data were translated to odorant intensity and character and saved on memory chips.[5]

### *2.5 Capture and analysis of data*

GBO data, SR, and the pedal switch signal for Alinamin administration were captured using a personal computer with a 12-bit A/D converter. The odorant intensity saved on the

FPO-II was read using a personal computer via an RC232C port and was merged with the data captured via the A/D converter (Fig. 1). GBO was rectified and sent through a band pass filter to generate a pseudo-DC-response (GBO-DC, Fig. 2).

## 3. Results

Odorant intensity in the breath gas increased after administration of Alinamin. GBO was also observed after administration of Alinamin. Changes in GBO-DC were similar to the changes in odorant intensity during Alinamin administration. In one subject, odorant intensity and GBO-DC decreased post administration of Alinamin but increased again after a 120 s interval (Fig. 3(a)). In the other subject, odorant intensity increased following the administration of Alinamin but GBO-DC decreased after the peak during Alinamin administration (Fig. 3(b)).

## 4. Discussion

GBO was thought to correspond to the intensity of odorant in the breath gas (IOBG). Therefore, measuring GBO combined with IOBG monitoring provides a method to distinguish real olfactory response and is a breakthrough in clinical electrophysiological olfaction testing. When Alinamin is mixed with blood, propyl mercaptan is generated. The odorized breath produced by intravenous administration of Alinamin was proven as the

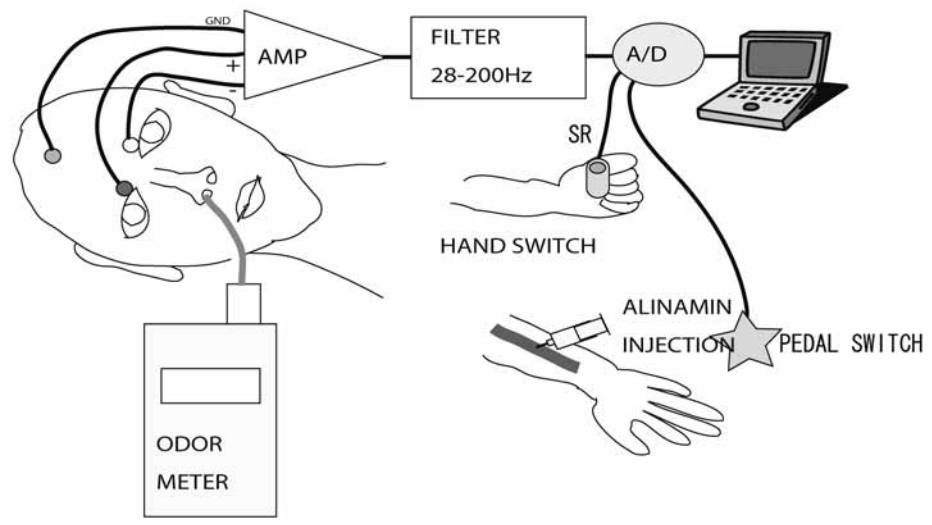


Fig. 1. Block diagram of the system for this study. The amplified gamma band oscillation and switch responses for SR and Alinamin administration were captured by a personal computer.

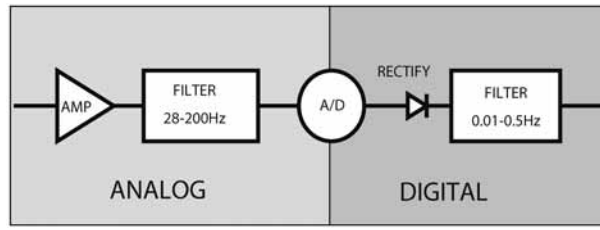


Fig. 2. Procedure for generating GBO-DC. The gamma band oscillation is amplified (G = 100), filtered (28–200 Hz), and digitalized. A post A/D converter process was performed by a personal computer. The absolute value of the digitalized gamma band oscillation was filtered (0.01–0.5 Hz) to eliminate DC drift and noise.

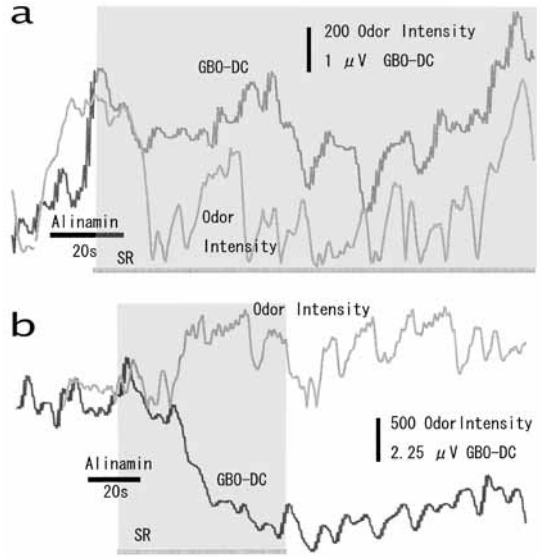


Fig. 3. GBO-DC and artificial nasal responses. Data from (a) a 58 years old man and (b) a 37years old man are shown. Black and gray traces indicate GBO-DC and odor intensity (IOBG), respectively, measured by the artificial nose; an upper deflection is positive. Black and gray horizontal bars indicate the periods of Alinamin administration, 20 s, and SR.

propyl mercaptan generated was measured using a gas chromatograph.[6] In this study, changes in IOBG were sometimes very similar to changes in GBO, but at other times they were not. The human sense of smell often decreases when an odorant is delivered continually and this phenomenon is known as olfactory fatigue. Until the first peak of

IOBG, GBO-DC of the two subjects showed similar increases, but after the peak, changes in IOBG and GBO-DC differed between the two subjects. Individual differences exist among subjects regarding odorous intensity and the tendency toward the occurrence of olfactory fatigue. When a subject experiences olfactory fatigue easily despite sustained or increased odorant intensity, the sense of smell decreases. Hatanaka[7] *et al.* investigated GBO induced by intravenous administration of Alinamin on 179 subjects and reported typical cases as follows. In one typical case, the GBO amplitude elicited by intravenous olfactory stimulation was suppressed before the end of odordetection was reported. Another typical case showing the GBO amplitude suppressed below the base line after administration of Alinamin was also reported. Multiple increases in GBO amplitude despite the administration of Alinamin was also reported once. Nakashima measured changes in IOGB using the artificial nose and surmised that multiple increases in IOGB were possibly produced because of the stimulation of generally circulated Alinamin by blood[2]. This may be an explanation for the differences between the response curves of GBO-DC and IOBG. Olfactory fatigue is also called olfactory desensitization and it occurs within the olfactory receptor neuron.[8] Pseudo-human olfaction modeled by the artificial nose may need to simulate the olfactory desensitization phenomenon. In other words, in order for the artificial nose to more close by approximate the human nose, the following developments are necessary. 1) The time-series response of the artificial nose should simulate the human nose. 2) The intensity response of the artificial nose should correspond to physiological responses such as those described by the Weber-Fechner law. Because a computer simulation model of typical responses of the olfactory receptor neuron was proposed,[9] it is possible that post-processing of information from the artificial nose emulates the computer model of the olfactory receptor neuron. When a more human-like artificial nose is developed, differences between changes in GBO-DC and IOBG showed become smaller.

In this way, acquisition of electrophysiological responses combined with the artificial nose response many improve not only the clinical appreciation, but also may assist the development of a more human-like artificial nose.

## References

1 T. Nakashima, J. Miyazaki, K. Kidera and A. Inokuchi: Jpn. J. Rhinol. **41** (2002) 251. (in Japanese)
2 T. Ishimaru: Aroma Research **5** (2004) 106. (in Japanese)
3 S. F. Takagi: Olfactory Tests, Human Olfaction (University of Tokyo Press, Tokyo, 1989) p. 35.
4 T. Ishimaru, S. Hatanaka, T. Yata, I. Horikawa, T. Tsukatani, T. Nishimura, T. Miwa and M. Furukawa: Chem. Senses **29** (2004) 247.
5 T. Okano: Keiso **43** (2000) 85. (in Japanese)
6 R. Kazama and H. Zusho: Nippon Jibiinnkouka Gakkai Kaiho **84** (1981) 400. (in Japanese)
7 S. Hatanaka, T. Ishimaru, T. Yata, T. Miwa and M. Furukawa: Acta Otolaryngol. Suppl. **553** (2004) 65.
8 T. Kurahashi and A. Menini: Nature **385** (1997) 725.
9 N. Suzuki, M. Takahata and K. Sato: Chem. Senses **27** (2002) 789.