Original article

Discordance between olfactory psychophysical measurements and olfactory event related potentials in five patients with olfactory dysfunction following upper respiratory infection

GUAN Jing, NI Dao-feng, WANG Jian and GAO Zhi-qiang

Keywords: olfactory neuropathy; olfactory disorder; olfactory dysfunction; upper respiratory infection; olfactory event related potentials

Background  Subjective olfactory tests are easy to perform and popularly applied in the clinic, but using only these, it is difficult to diagnose all disorders of the olfactory system. The olfactory event related potentials technique offers further insight into the olfactory system and is an ideal objective test. This analysis was of subjective and objective data on the olfactory function of twelve patients with loss of smell associated with an upper respiratory infection (URI).

Methods  We tested the twelve patients with URI induced olfactory loss by medical history, physical examination of the head and neck, olfactory tests and medical imaging. Olfactory function was assessed by Toyota and Takagi olfactometry including olfactory detection and recognition thresholds and olfactory event-related potentials (OERPs) recorded with OEP-98C Olfactometer.

Results  An unusual phenomenon was observed in five patients in whom the subjective detection and recognition thresholds were normal, while the expected OERPs were not detectable.

Conclusions  We suggest that the discordance between olfactory psychophysical measurements and OERPs might be the results of abnormal electrophysiology related with olfactory neuropathy caused by viral URI. In addition, the measurement of OERPs might play a significant role in evaluating olfactory dysfunction.

Methods

Anterior rhinoscope examination
Each subject’s nasal mucous membrane was observed by anterior rhinoscope for colour, surface texture, swelling, inflammation, atrophy, exudates and ulceration.

CT scanning
Nine patients had a coronal and axial CT scanning of the nasal cavities and paranasal sinuses. Slice thicknesses were 5 mm.

Psychophysical measurement of olfactory function
Japanese T&T Olfactometer was used to evaluate each subject’s bilateral olfactory ability and the degree of smell impairment. T&T Olfactometer uses five odors and each odor is diluted into eight concentrations except Door B, which is diluted into seven concentrations. The sensitivity of sense of smell is classified into six levels according to mean T&T score of recognition threshold. The

Subjects
The clinical data of twelve patients (4 males, 8 females, aged 27 years to 59 years) with URI olfactory loss over several months or years with no other nasal complaints were analysed. Olfactory dysfunction was usually the primary complaint. Medical history, physical examination of the head and neck, olfactory tests and medical imaging were all completed at the Department of Otorhinolaryngology of Peking Union Medical College Hospital (Table).

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### Table. Data of twelve patients with post UPI related olfactory disorder

<table>
<thead>
<tr>
<th>Patient code</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Time of having UPI</th>
<th>T&amp;T Olfactometry assessment</th>
<th>OERPs</th>
<th>Result of CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Female</td>
<td>59</td>
<td>Six months ago</td>
<td>Anosmia</td>
<td>Absent</td>
<td>Normal</td>
</tr>
<tr>
<td>B</td>
<td>Female</td>
<td>58</td>
<td>One month ago</td>
<td>Anosmia</td>
<td>Absent</td>
<td>Normal</td>
</tr>
<tr>
<td>C</td>
<td>Female</td>
<td>56</td>
<td>One month ago</td>
<td>Anosmia</td>
<td>Absent</td>
<td>Normal</td>
</tr>
<tr>
<td>D</td>
<td>Female</td>
<td>50</td>
<td>Two months ago</td>
<td>Normal</td>
<td>Absent</td>
<td>—</td>
</tr>
<tr>
<td>E</td>
<td>Female</td>
<td>48</td>
<td>Two years ago</td>
<td>Normal</td>
<td>Normal</td>
<td>Sinusitis (without nasal polyps)</td>
</tr>
<tr>
<td>F</td>
<td>Female</td>
<td>44</td>
<td>Six weeks ago</td>
<td>Normal</td>
<td>Absent</td>
<td>Normal</td>
</tr>
<tr>
<td>G</td>
<td>Female</td>
<td>42</td>
<td>Three months ago</td>
<td>Anosmia</td>
<td>Absent</td>
<td>Normal</td>
</tr>
<tr>
<td>H</td>
<td>Male</td>
<td>33</td>
<td>One year ago</td>
<td>Anosmia</td>
<td>Absent</td>
<td>Sinusitis (without nasal polyps)</td>
</tr>
<tr>
<td>I</td>
<td>Male</td>
<td>33</td>
<td>Six months ago</td>
<td>Moderate hyposmia</td>
<td>Normal</td>
<td>Normal Sinusitis (without nasal polyps)</td>
</tr>
<tr>
<td>J</td>
<td>Male</td>
<td>32</td>
<td>One year ago</td>
<td>Normal</td>
<td>Absent</td>
<td>—</td>
</tr>
<tr>
<td>K</td>
<td>Female</td>
<td>29</td>
<td>Three months ago</td>
<td>Normal</td>
<td>Absent</td>
<td>Normal</td>
</tr>
<tr>
<td>L</td>
<td>Male</td>
<td>27</td>
<td>Six months ago</td>
<td>Normal</td>
<td>Absent</td>
<td>—</td>
</tr>
</tbody>
</table>

*Patients with normal smell recognition function tested by the subjective method of T&T olfactometer but no OERPs.*

The twelve patients were represented by different letters from “A” to “L” according to their ages from the oldest to the youngest (Table). Each subject had a free nasal passage. The CT scanning showed that three patients (E, H and I) had chronic sinusitis without polyps and the others were normal. The T&T olfactometer and OERPs measurements of olfactory testing revealed that five patients (A, B, C, G and H) were total anosmic with no OERPs responses, one (I) was moderate hyposmia with OERPs response and a normal latency of P2 peak (Figure 1) and one (E) had a normal sense of smell with OERPs response and a normal latency of P2 peak (Figure 1). However the other five patients (D, F, J, K and L) had also normal olfactory recognition ability by the T&T Olfactometer, but no OERPs responses could be recorded (Figure 2). Two patients (F and K) had normal CT results in these five patients (Figure 3).

**Electrophysiological measurement of olfactory function**

OERPs evoked by 3-methylbutyl ethanoate were recorded using OEP 98C Olfactometer, which was developed by Peking Union Medical College Hospital. Each subject was sitting and tested in an electrically shielded and well ventilated room. The door stimulus at high concentration (<1648 ppm) to the nostril was presented ten times at inter-stimulus interval of approximately 30 seconds. At this level, 3-methylbutyl ethanoate can be easily detected and assumed to be far below the threshold for activation of the trigeminal nerve system. Silver chloride cup electrodes were attached to the scalp using a water soluble conductance paste. The recording electrode was placed at Cz using the International 10/20 System of electrode placement and the reference electrode was at the left ear lobe and an earth electrode was placed on the forehead. The sound produced by the magnetic valves is masked by broadband noise delivered via earphones at 60 dB SPL to confound the auditory evoked response. Bandpass was 0.1 Hz to 30 Hz and electrode impedance <5 kΩ–10 kΩ. The OERPs’ late major P2 peak was analyzed.

**RESULTS**

The sense of smell requires normal anatomical and physiological functions of olfactory pathway. Usually, assessment of the sense of smell can rely on the report of the patient and psychophysical evaluation such as the Japanese T&T olfactometer test or the University of Pennsylvania Smell Identification Test. Although the psychophysical tests are easy to perform and thus have been popularly applied in the clinic, it is difficult to discover all disorders of the olfactory system only using the subjective olfactory tests. Objective tests are thus indispensable for investigating the functioning of sensory systems. OERPs offer a deeper insight into the olfactory system and are an ideal supplementary tool to olfactometry. We tested twelve patients with URI induced olfactory loss. The objective OERPs results were in

**DISCUSSION**

The twelve patients were represented by different letters from “A” to “L” according to their ages from the oldest to the youngest (Table). Each subject had a free nasal passage. The CT scanning showed that three patients (E, H and I) had chronic sinusitis without polyps and the others were normal. The T&T olfactometer and OERPs measurements of olfactory testing revealed that five patients (A, B, C, G and H) were total anosmic with no OERPs responses, one (I) was moderate hyposmia with OERPs response and a normal latency of P2 peak (Figure 1) and one (E) had a normal sense of smell with OERPs response and a normal latency of P2 peak (Figure 1). However the other five patients (D, F, J, K and L) had also normal olfactory recognition ability by the T&T Olfactometer, but no OERPs responses could be recorded (Figure 2). Two patients (F and K) had normal CT results in these five patients (Figure 3).
Figure 2. OERPs records in five patients D, F, J, K, L. Two curves were recorded in each patient, the above was a control result stimulated by air and the other was OERPs evoked by 3-methylbutyl ethanoate. The expected changes potentials could not be induced by 3-methylbutyl ethanoate in the five patients. All had normal olfactory recognition ability tested by T&T Olfactometer, and the images of patients F and K receiving nasal CT scanning revealed normal nasal cavities and paranasal sinuses. These results illustrate discordance between the subjective and objective olfactory tests.

Figure 3. The normal coronal CT result of patient F. The red arrow illustrates olfactory cleft.

accord with patients’ self reports of olfactory loss and subjective T&T tests in seven patients. However, five patients had normal detection thresholds and recognition thresholds, but the OERPs were absent. In our laboratory, we had previously tested the olfactory function by T&T Olfactometer and OERPs test with OEP 98C olfactometer of 55 young volunteers with normal olfactory function and ranging in age from 18 to 33 years. Normal T&T results and OERPs were obtained from all these volunteers. However, notably five cases of our experimental group of 12 patients had normal T&T Olfactory function, but no OERPs responses were elicited.

URI is likely to be virally induced. Direct injury to the olfactory neuroepithelium is probably the cause of the problem by URIs. Some animal studies demonstrate that many viruses have an adverse influence not only on the olfactory neuroepithelium but also on the olfactory bulb, olfactory tracts and higher cortical regions. Generally, even after seemingly complete destruction of all receptor neurons, the olfactory epithelium is able to reconstitute itself and restore behavioural function within a month or two. The five special cases in this group had complained of olfactory loss over months or years: long enough for the olfactory epithelium to have regenerated. Anterior rhinoscopy and CT scanning ought to show that the nasal passage is free, odorous air can reach the olfactory epithelium and sense data can be conducted upward when evaluated by T&T and OERPs measurements: normal T&T result could be thus explained. OERPs reflect synchronous electrophysiological activities elicited by odorous stimuli. OERPs reflect generation, conduction and integration of odour elicited signals. The absence of OERPs response might represent certain abnormalities in olfactory conduction circuit, at least the nonsynchronization of olfactory nerves activities. Recent studies indicate that the components of the positive peak P2 are largely aroused by exogenous olfactory sensation. Therefore, we suggest that this type of olfactory impairment is due to olfactory nerve dysfunction. When considering the auditory system, an auditory neuropathy is characterized by absence or severe abnormality of auditory brainstem potentials and mild to moderate deterioration of hearing assessed by subjective audiometric testing. Analogously, the special clinical characters of olfactory impairment could be termed olfactory neuropathy.

In this article, we describe the discordance between subjective olfactory threshold measurements and objective OERPs in patients with defective sense of smell subsequent to a URI. Such data improve our knowledge of olfactory neuropathy and show that the objective measurement of OERPs may be indispensable in diagnosing olfactory disorders.

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REFERENCES


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