

A new clinical olfactory test to quantify olfactory deficiencies*†

Corinne Eloit¹, Didier Trotier²

¹ ENT Clinic, Hôpital Lariboisière, Paris, France

² Laboratoire Neurobiologie Sensorielle, CNRS/EPHE, Massy, France.



SUMMARY

We have recently developed a computer-assisted olfactory test to measure detection thresholds for five pure odorants. The reference group consisted of 30 subjects without olfactory complaints. Statistical analysis was carried out to identify a statistical criterion for determining olfactory deficiencies. This criterion was applied to 54 subjects suspected to have an olfactory deficiency, either on the basis of their subjective complaints or on clinical examinations (e.g. scanner radiography, endoscopic investigations, rhinomanometric measurements). Nine aetiological groups were screened: trauma, nasal polyposis, nasal obstruction, allergic rhinitis, post-influenza, post-anaesthesia, endocrine dysfunction, hereditary hyposmia, and subjective olfactory loss without a clear aetiology. In each group, this method allowed us to discriminate between deficient and non-deficient patients, and the olfactory deficit could be quantified. This rapid procedure was well-accepted by all subjects and gave reproducible quantitative results. It can provide useful information about the relationship between olfactory acuity and a given aetiological category.

Key words: olfactory testing, olfactory acuity, odour identification, olfactory deficiencies

INTRODUCTION

Various olfactory tests have already been proposed in order to clinically assess the olfactory function. The most popular procedures are those that use odour quality identification. The most widely used "scratch-and-sniff" UPSIT test (Doty et al., 1984) explores the ability of subjects to identify, from sets of descriptors, 40 odorants presented at one concentration. The limitations of this procedure are those of any identification task. For example, the link between olfactory perception and semantics is known to be somewhat sketchy with unexperienced patients; moreover, as only one supra-threshold concentration is proposed for each odorant, a partial loss of the olfactory acuity can not be clearly quantified. Other procedures use a set of concentrations of one or a few pure odorants, throughout the whole perception scale from no detection to unambiguous recognition. Such procedures allow for an approximate measurement of both detection and recognition thresholds. The most popular procedure, already tested on a large number of subjects, is the T&T Olfactometer (Takagi, 1989). It quantifies an olfactory deficiency in terms of differences in recognition thresholds. Starting with published data from this procedure, we have

attempted to improve it in the following ways. We rigged a computer to interact with the subject and monitor the experiment; the subject could therefore do the test without the constant physical presence of the investigator. We changed the stimulation protocol. We added two initial phases in the session, before the threshold measurements, in order to make the subject familiar with the odorants and the detection task. We analysed data in terms of detection thresholds, not in terms of recognition thresholds. Lastly, we defined a statistical criterion for classifying olfactory-deficient patients. In this paper we describe the method and present data on 84 subjects.

METHODS

Chemicals

For each subject, threshold measurements were successively done with five odorants: β -phenylethyl alcohol (PEA), γ -undecalactone (UND), isovaleric acid (IVA), skatole (SRA; 3-methyl-1H-indole) and cyclotene (CYC; methylcyclopentenolone). All chemicals were of a purity higher than 99% and were purchased from Janssen Chimica (France), except for CYC from Laserson & Sabenay (France). Each one has a characteris-

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tic smell, either pleasant or unpleasant, which is familiar to the general public (Table 1). They were dissolved in pure and odourless propylene glycol (Janssen Chimica; see Table 2). Twenty milliliters of each diluted solution were introduced into a brown glass bottle (45 ml) and completely adsorbed by a piece of odourless cotton. The purpose of this procedure is to increase the odorant-air interface and to bring quickly to equilibrium the odorant concentration in air. When kept at room temperature, solutions were chemically stable and we did not detect any obvious degradation or change in the odour quality after periods of more than one year.

Table 1. Odour qualities of odorants.

name of odorant	odour quality
β -phenylethyl alcohol (PEA)	rose, jasmine, flower
γ -undecalactone (UND)	apricot, peach, fruit
isovaleric acid (IVA)	sweat, goat cheese
skatole (SRA)	dander, cabbage
cyclotene (CYC)	caramel, cake

Table 2. Concentrations of odorants.

Level	PEA	UND	IVA	SKA	CYC
-1	6.2	6.1	7	7.1	6.6
0	5.2	5.1	6	6.1	5.6
1	4.2	4.1	5	5.1	4.6
2	3.2	3.1	4	4.1	3.6
3	2.2	2.1	3	3.1	2.6
4	1.2	1.1	2	2.1	1.6
5	0.2	0.1	1	-	-

Seven steps were prepared for each odorant. The indicated *number* corresponded to a dilution (w/w) of 10^{number} of the pure chemical in propylene glycol. The scale in the left column was used to measure individual thresholds. Level "0" corresponded to the mean detection threshold measured from a large population of subjects with a similar method (Takagi, 1989). Concentrations at level "4" were 10^4 -times as concentrated as those at level "0".

General presentation of the experimental set-up

All bottles were presented in a 6×8 matrix of circular holes in a wooden container. The order of presentation was random for the subjects, but recorded by the computer. The computer indicated which concentration of odorant to test by switching on a light-emitting diode located near the corresponding bottle. The subjects were asked a sequence of precise questions, which they answered by pressing the corresponding button on a specifically designed keyboard. The light-emitting diodes and the keyboard were connected to an IBM-compatible computer through a Logic 20 R16 TTL and relays interface (Nautil, France). The software was home-made in Quick-Basic. Special consideration was given to the clarity of the instructions.

Olfactory stimulation

For each sample, subjects removed the bottle cap, advanced the opening (2.5 cm^2) of the bottle to their nostrils and sniffed at

their convenience. The bottle was kept closed for a minimum of 15 min before testing to insure an equilibrated odorant concentration in the vapour phase. Precautions were taken to prevent contamination of the outside of the test bottles by the subject's hands. Only one subject worked at a time, in a well-ventilated and quiet room.

General organization of a session

At first, the five odorants were presented in sequence at a high concentration and the subjects tried to identify each of them. If the subject misidentified an odorant, the computer flashed a message informing him of his mistake, and the sample was sniffed again for learning. Afterwards, the same odorants were presented again in a different sequence. The aim of this initial phase was to make the subject familiar with the odorants. In a second phase, each odorant was presented starting from the highest concentration (level 4 or 5 in Table 2) to the lowest one (level -1). For each concentration, the computer first asked: "Did you smell an odour in this bottle?" If yes, it asked: "What was the odour?" The only possible answers to the first question were: "Yes" or "No". Possible answers to the second question were: "I detected the presence of an odorant, but I can not identify it"; or "I detected an odorant and I recognize it as..." followed by the corresponding odour descriptors used during the initial training phase of the session (see Table 1). The aim of this second phase was to train the subject with an olfactory detection task. The interstimulus time interval was of at least 15 s in the case of no detection, and at least 30 s when the odorant was detected, to prevent olfactory adaptation. Finally, in the third phase, odorant concentrations were presented as before, but from the lowest level to the highest one. Only data obtained with this detection task are presented here.

Finally, 6 pure odorants with a characteristic smell were presented at the end of the session to assess the general olfactory perception of the subject: (1) isoamyl acetate (banana); (2) vanillin (vanilla); (3) acetic acid (vinegar); (4) carvone (minty); (5) cyclohexanone (almond); and (6) exaltolide (musc).

Calculation of individual scores

For each odorant and each subject, the best estimate threshold was measured, following the ASTM E679 procedure (Meilgaard et al., 1987), as the geometric mean of the highest concentration not perceived and the next higher concentration. Detection scores for each subject were calculated as the mean of the thresholds for the 5 odorants.

RESULTS

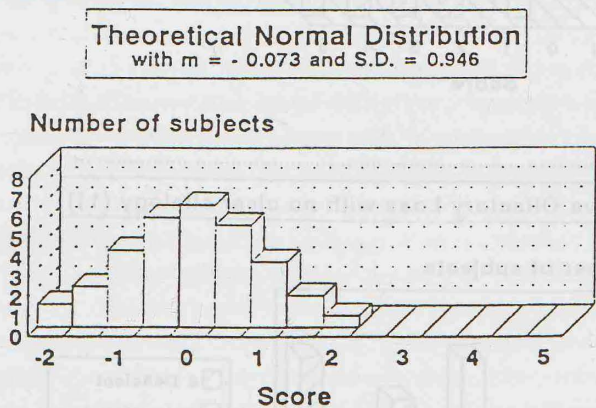
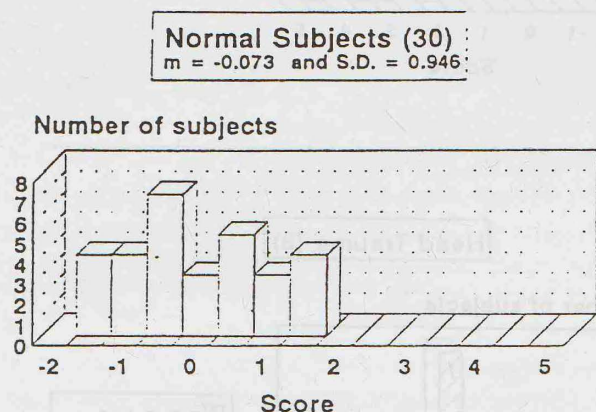
Statistical criterion for determining an olfactory deficiency

Thirty adults participated in this study to define a control group. They did not have specific complaints regarding olfactory problems, were normal breathers, and appeared to be in good health on the day of the test. Their olfactory scores ranged from -1.5 to 1.5. The mean score (m) was -0.073 with a standard deviation (SD) of 0.946 ($n=30$). The histogram repartition (Figure 1) was homogeneous. This distribution was not statistically different from the calculated theoretical Normal

Distribution (Figure 1). As only about 3% of the normal subjects could have a score higher than 1.75, we have taken this limit as a statistical criterion to determine an olfactory deficiency.

Screening of different groups of subjects

Nine aetiological groups of subjects were screened (Figure 2). For each group, subjects could be classified as non-deficient or olfactory-deficient. All subjects exhibiting either an allergic rhinitis or a nasal obstruction or an endocrine dysfunction were classified not-deficient. All subjects complaining about olfactory dysfunction after an influenza infection were considered olfactory-deficient. Half of patients suffering from nasal polyposis were deficient, with deficiencies ranging from moderate to strong. Seven out of 8 patients with a history of cranial trauma were also deficient. Only 1 out of 4 patients complaining about a change in their olfactory perception after anaesthesia (either local, for dental extraction, or general) was strongly deficient. For the final group, without a clear aetiology, only 6 out of 11 patients were classified as deficient. In addition, one subject having an hereditary hyposmia presented a selective anosmia



Chi Square = 9.16 ; no statistical difference

Only about 3 % of normal subjects have a score > 1.75

Figure 1. Statistical analysis of the reference group. The upper histogram shows the score values for the 30 normal subjects. The mean was -0.073 ± 0.946 . The theoretical Normal Distribution (lower histogram) was calculated with these parameters. Both repartitions were compared using Chi-square test and no statistical difference was found.

for SKA and UND, and a normal threshold for CYC (data not shown).

Reproducibility of score measurements

The test was repeated for 13 subjects after a time lag of 3-6 months. The graph in Figure 3 illustrates the relationship between the first and the second score values. Measurements can be considered as reproducible for almost all subjects, except for two subjects who exhibited a real recovery of their olfactory performance.

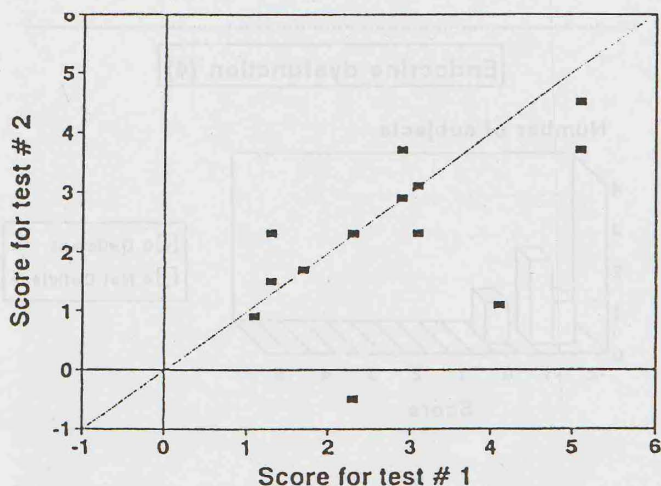


Figure 3. Reproducibility of score values. The test was repeated for 13 subjects after a time lag of 3-6 months. The score values for the second test are plotted against the score value for the first test.

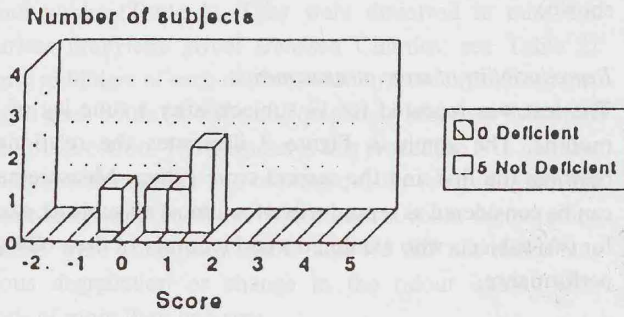
DISCUSSION

This test seems to be very convenient to assess the olfactory sensitivity. As a rule, it was very attractive for the subjects. It apparently gives a reproducible and quantitative measurement of the global detection ability.

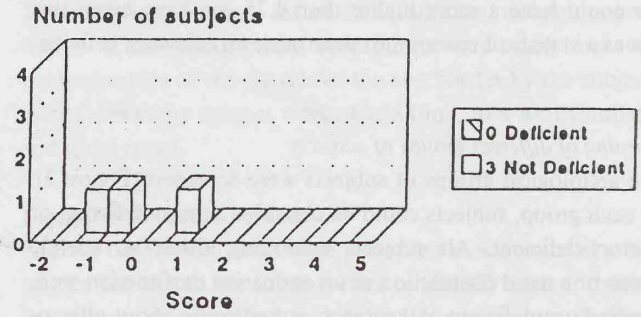
Our reference group shows a mean detection threshold which is identical to the mean detection threshold already measured on a large number of Japanese subjects (Takagi, 1989), validating the size of our sample. The screening of different aetiological groups, using a statistical criterion to distinguish between deficient and non-deficient patients, gave interesting observations. For instance, nasal polyposis is thought to always induce a strong hyposmia by obstructing nasal ducts. However, in our study, all corresponding patients had normal nasal resistance (rhinomanometric measures). Subjects having a normal olfactory score had polyps located in the middle meatus, whereas deficient patients had polyps all over the olfactory clefts.

One particularly interesting sub-group in this experiment is that composed of patients with endocrine dysfunction (delayed pubertary development). None were olfactory-deficient, thus they could not be considered as having a Kallmann's syndrome. In conclusion, this olfactory test could be included into every rhinologic clinical investigation, in complement to rhinomanometric and endoscopic examinations.

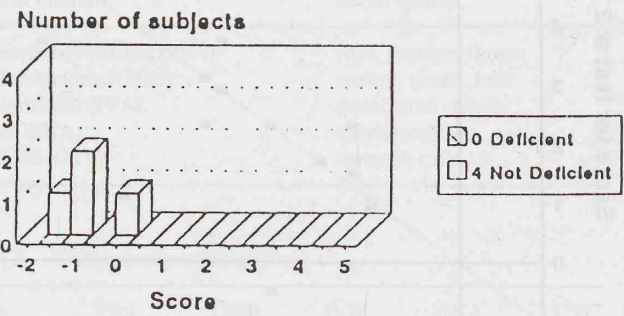
Allergic Rhinitis (5)



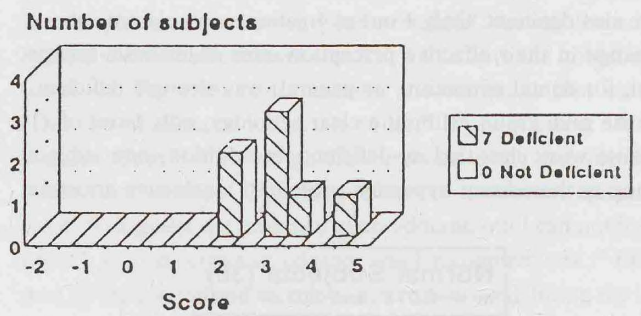
Nasal Obstruction (3)



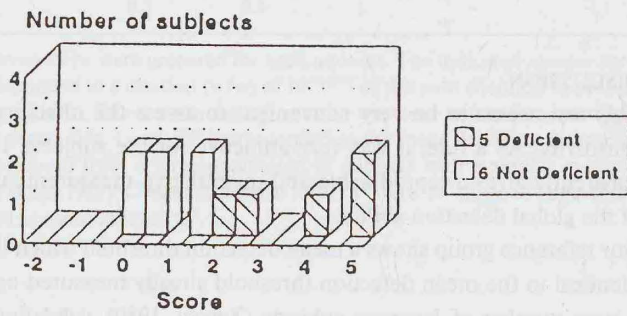
Endocrine dysfunction (4)



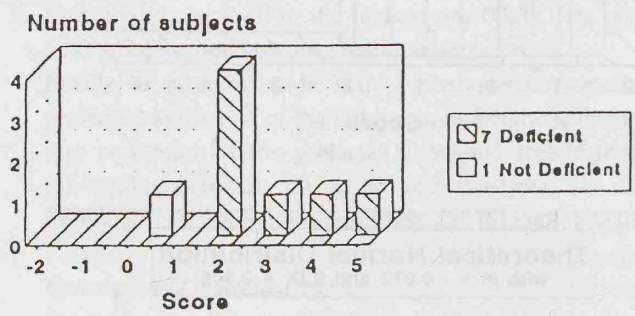
Post Influenza (n=7)



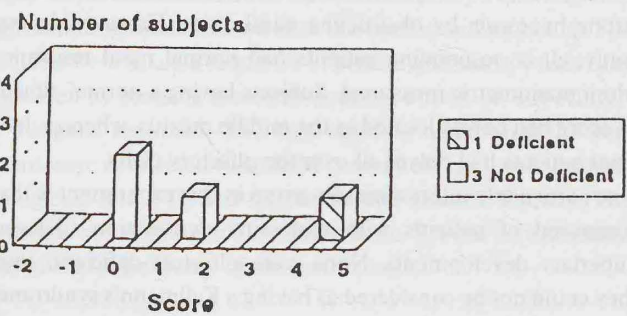
Nasal polyposis (11)



Head Trauma (8)



Post Anesthesia (4)



Subjective Olfactory Loss with no clear etiology (11)

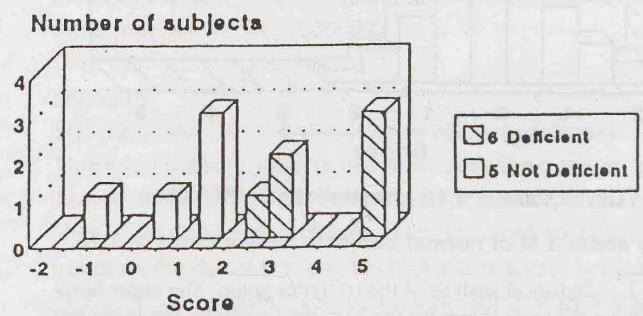


Figure 2. Analysis of aetiological groups. Patients were classified as deficient or non-deficient using a statistical criterion as defined in the text.

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Dr. C. Eloit
 Dept. of Otorhinolaryngology
 Hôpital Lariboisière
 2 rue Ambroise Paré
 F-75010 Paris
 France