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Short communication

Kallmann's syndrome and chemosensory evoked potentials

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Summary. Kallmann's syndrome is generally assessed by history and subjective tests of olfactory function. In this study three patients suffering from Kallmann's syndrome were investigated with more objective techniques, including the recording of chemosensory evoked potentials (CSEPs). After testing olfactory function by means of a simple odor identification test, anosmia was confirmed in only one patient, since the other two patients were able to distinguish between several odorants. However, investigations in which CSEPs were employed indicated that all three patients had complete loss of their olfaction as well as hypersensitivity of the trigeminal nerve. These findings prove the usefulness of CSEPs in clinical investigations of the sense of smell.

Key words: Kallmann's syndrome – Chemosensory evoked potentials

Introduction

Kallmann's syndrome is the combined occurrence of hypogonadal hypogonadism and anosmia, and has been reported in a number of cases during the last century [5]. The syndrome is caused by abnormal development in the hypothalamic area with lack of secretion of gonadotropin-releasing hormones in combination with aplasia or hypoplasia of the olfactory bulb. It is generally assumed that the syndrome is recessively transmitted X-linked [1], but recent findings also suggest an autosomal dominant inheritance [6]. The frequency of Kallmann's syndrome in patients with hypogonadism is estimated to be 1:40, with the mean age of diagnosis at 25 years [7].

In general, the degree of the loss of the sense of smell is established by history and subjective tests [6, 7]. Lately, the introduction of chemosensory evoked potentials (CSEPs) into clinical routine has made it possible to objectively establish olfactory deficits in patients [2, 3]. Olfactory sensations caused by stimulation with, for example, vanillin or hydrogen sulfide (H_2S) are exclusively mediated by the olfactory nerve, whereas painful sensations, occurring after stimulation with such substances as carbon dioxide (CO_2), are mediated exclusively by the trigeminal nerve [4]. If menthol or a mixture of CO_2 and vanillin are used as stimulants, both nerves are affected. Characteristically, latencies of CSEPs decrease and amplitudes increase after stimulation with the mixture of vanillin and CO_2 when compared to latencies and amplitudes of CSEPs obtained after stimulation with CO_2 or vanillin alone. Stimulus intensity of the mixture is subjectively perceived to be higher than that of the single compounds [3]. Investigating interactions between these sensory systems is helpful in tracing deficits in one or the other, e.g., the olfactory system.

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Materials and methods

In our laboratory three male patients (ages 18, 19 and 34 years), suffering from Kallmann's syndrome, were investigated. In their histories and review of systems, all three patients had stated that they were able to perceive strong smells, such as the smell of flowers or the stench of feces. The olfactory sense was tested by separately presenting sniff bottles to both nostrils. Bottles contained 12 different odorants. In order to compare psychophysical findings with electrophysiological data, the technique of evoked potentials was employed and CSEPs to CO_2 (52% v/v), menthol (21.07 ppm), H_2S (2.06 ppm), and vanillin (0.78 ppm) stimuli were recorded.

Results

Anosmia was established in one case using the sniff bottles, since the patient could only perceive acetic acid, which he described to be causing an unpleasant painful sensation. The other two patients to a certain degree were able to distinguish between several odorants (e.g., eugenol vs acetic acid). They even perceived odorants like anethol and isoamyl acetate, although they were unable to correctly name or describe their olfactory sensa-

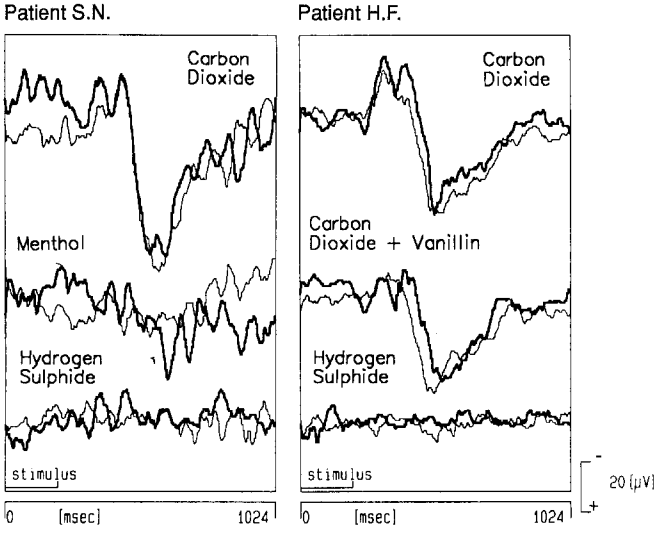

Fig. 1. Chemosensory evoked potentials after stimulation with different odorants (*bold lines*, stimulation of left nostril; *thin lines*, stimulation of right nostril; recording position Cz/A1+A2; *left*, patient 1; *right*, patient 2).

Table 1. Chemosensory evoked potentials after stimulation with carbon dioxide (52% v/v)

	Patients			Control ($n = 20$)	
	1	2	3	Mean	SD
Amplitude N1/P2 (μV)	65.7	55.0	67.6	27.7	9.9
Latency N1 (ms)	400	272	416	316	54
Latency P2 (ms)	572	476	780	492	70

– Recording position Cz
– Stimulus left nostril

tions. In one patient, the presentation of phenylethyl alcohol, commonly considered to be a pure olfactory stimulant, resulted in a diffuse olfactory sensation. In all three patients, CO_2 and menthol both evoked CSEPs (Fig. 1). The amplitudes of these CSEPs were extremely large (Table 1), indicating a hypersensitivity of the trigeminal nerve. In one case (patient 2), the mixture of CO_2 and vanillin was used as a stimulant. The corresponding CSEP (amplitude N1/P2, 42.0 μV; latency N1, 360 ms; latency P2, 496 ms) showed no decrease in latency when compared to that obtained after stimulation with CO_2 alone (Table 1). Additionally, stimulation with H_2S and vanillin evoked no CSEPs.

Comment

The CSEP results obtained when using CO_2 and vanillin as a stimulant when compared to CO_2 stimulation alone indicated a missing interaction between the olfactory and the trigeminal senses. In addition, CSEPs could not be recorded after stimulation with pure olfactory stimulants. On the basis of these findings, "anosmia" was diagnosed in all three patients. However, the investigations reveal the difficulties in diagnosing disorders of the olfactory system by just having recourse to historical information and subjective olfactory tests. The method of recording chemosensory evoked potentials described allows more detailed investigations of the olfactory system and consequently helps to determine more precisely the degree of any olfactory deficits present.

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