Case Report

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Olfactory event-related potentials in a functionally anosmic patient with arrested hydrocephalus

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Abstract

Hydrocephalus is one of the lesser known causes of central olfactory loss. The pathogenesis of hydrocephalus involves the olfactory bulbs or tracts, and more rarely, other frontotemporal cortical regions. We describe a case of olfactory dysfunction in a macrocephalic 63-year-old female patient with arrested hydrocephalus. Her olfactory function was assessed by using the Sniffin' Sticks test, olfactory event-related potentials (OERPs), and 3-Tesla magnetic resonance imaging (MRI). An OERP examination suggested partial impairment of the central olfactory pathways and central parietal regions where OERP amplitude is maximal. Indeed, we found an evident olfactory potential trace with an increased latency only on Pz derivation. However, structural MRI showed important cortical brain thinning and large expansion of the third ventricle, with evident damage of the olfactory frontotemporal areas. The Sniffin' Sticks test and MRI supported the diagnosis of anosmia, while OERP findings indicated partial preservation of olfactory function, likely due to an adaptation of the central olfactory system. These findings highlight the importance of a multi-integrated approach to detect olfactory impairment.

Keywords

Fronto-temporal area, hydrocephalus, hyposmia, magnetic resonance imaging, olfactometer, olfactory bulb, olfactory dysfunction, olfactory event-related potentials, neuroplasticity, rostral-medial temporal area

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Introduction

Hydrocephalus is a pathological condition that is characterized by an excessive quantity of liquid in the ventricles and/or in subarachnoid spaces because of an imbalance in production, circulation, and absorption. Hydrocephalus is one of the lesser known causes of central olfactory loss. The pathophysiological mechanism of hydrocephalus involves the olfactory bulbs or tracts, and more rarely, frontotemporal cortical regions. To the best of our knowledge, few studies[1,2] have assessed olfactory function in patients with hydrocephalus. A previous study[1] showed that patients with idiopathic normal pressure hydrocephalus had a significantly smaller olfactory bulb volume compared with healthy controls, as detected by magnetic resonance imaging (MRI). Furthermore, these patients had impaired smell function, as detected by the Sniffin' Sticks test (SST).

Numerous psychophysical tests are available for clinical evaluation of olfaction, such as the SST.[3,4] Olfactory event-related potentials (OERPs) and MRI allow objective assessment of integrity of the olfactory system. OERPs are an electrophysiological method that allows objective assessment of olfactory function. OERPs show activation of olfactory brain areas that involve the olfactory bulbs and tracts, the orbitofrontal and insular cortices, and temporal areas.[5] The OERP components are similar to ones of other event-related potentials as follows: P1, N1, P2, N2, and P3. The main OERP complex consists of a large negative and positive component, called N1-P2. The presence of this component is a good indicator of normal olfactory function. In contrast, absence of the N1-P2 complex indicates loss of smell. Latency of P2 is observed from 530 to 800 ms after onset of a stimulus. The amplitude of N1-P2 is recorded between 4 and 20 μV.[6,7]

We present a case of arrested hydrocephalus in which olfactory function, as assessed by SST and OERPs, was correlated with MRI findings. To the best of our knowledge, this is the first case where an electrophysiological technique, such as OERPs, was used to assess olfactory impairment in a patient who was affected by arrested hydrocephalus.

Case report

We describe a case of a macrocephalic 63-year-old female patient with severe congenital triventricular hydrocephalus. She is the fourth of five children and was born from a normal pregnancy. She had a natural childbirth. With regard to the anamnestic record, two other cases of congenital hydrocephalus are present in her family on the maternal side (data not shown). The patient has always refused surgical treatment for hydrocephalus. All procedures complied with clinical practice and thus ethical approval was not required. The patient provided written informed consent.

The patient came to our attention because she reported a loss of smell. She had some of the typical symptoms of arrested hydrocephalus, such as dizziness, difficulty in walking, urinary urgency, and a deficit of visual acuity. At a neurological examination, she had spastic quadriplegia that was prevalent in the left side and a gait with small steps. An otorhinolaryngological examination excluded nasal and paranasal cavity pathologies, which could cause impairment of smell. Additionally, the patient did not take any therapy that could influence smell function. A computed tomography examination (data not shown) and upper airway rhinoscopy confirmed the integrity of the nasal and paranasal cavities.

Neuropsychological assessment showed cognitive performance within normal limits (Mini-Mental State Examination score: 27/30) and a moderate state of

anxiety and depression (Hamilton Rating Scale for Depression score: 17; Hamilton Rating Scale for Anxiety score: 14).

A preliminary evaluation of olfactory dysfunction was conducted by using the SST (Burghart Messtechnik GmbH, Wedel, Germany, www.burghart-mt.de). The following scores were obtained. The normal value was 9.5 ± 0.9 for the threshold sub-test "0", 12.6 ± 1.6 for the discrimination sub-test "0", and 14.9 ± 1.2 for the identification sub-test "4". The final TDI score was 4, which was confirmed as functional anosmia.

Consequently, we studied the patient's olfactory function by using OERPs. Five age and sex-matched healthy subjects were used as controls. OERPs of healthy controls were recorded in the same experimental conditions as those of the patient (Figure 1a). We elicited OERPs by using a computer-controlled olfactometer (Olfactometer OM2S; Burghart, Medical Instruments, Wedel, Germany) associated with an electroencephalograph (Micromed Brain Quick 32 Ch) (Olfaktologie). During the OERP recording, we presented two odorants of phenyl ethyl alcohol (40% v/v; Labochem Science S.r.l., Catania, Italy) and H2S/N2 (4 ppm; Rivoira, Milan, Italy). The flow of air (8 L/min) that carried the odorants had a constant temperature (36.5°C) and humidity (80%) level. The patient was alert and cooperative. A Teflon outlet nose (4-mm lumen tube) piece was placed in the nasal vestibulum. We presented a succession of 40 randomized olfactory stimuli in two blocks of 20 stimuli, alternating between the right and left nostrils. The duration of each stimulus was 200 ms and the time between stimuli (interstimulus interval) was 40 seconds.

We performed an OERP examination in five control subjects (mean [standard deviation] age: 61 ± 2.24 years), which showed the presence of olfactory potentials in derivations Fz, Cz, and Pz (Table 1). OERP findings showed an unclear olfactory response on derivations Fz and Cz. An evident olfactory potential trace was present

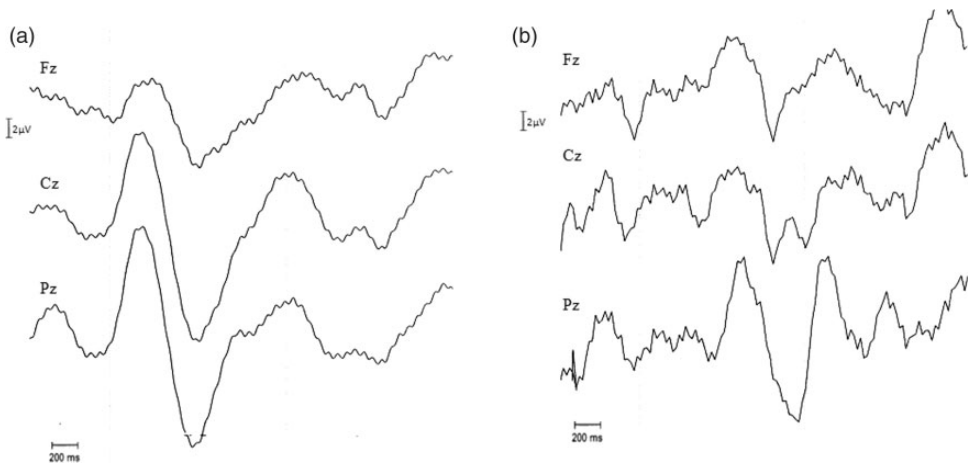

Figure 1. Filter band-pass of 0.01 to 30 Hz. Electroencephalographic averaging from a 500-ms pre-stimulus to 2000-ms post-stimulus was performed. (a) OERPs of a 63-year-old healthy female subject showed normal morphology and component parameters in Fz, Cz, and Pz positions. (b) OERPs of the patient show an absence of a clear response derived from Fz and Cz and the presence of a response derived from Pz. N1 latency was 722 ms, P2 latency was 890 ms, and the amplitude was 4.5 μv.
OERPs: olfactory event-related potentials

Table 1. Olfactory event-related potential components

	Fz		Cz		Pz	
	Patient	Controls Mean ± SD	Patient	Controls Mean ± SD	Patient	Controls Mean ± SD
N1 latency (ms)	NA	635 ± 16.58	NA	632.6 ± 12.88	722	627.6 ± 15.17
P2 latency (ms)	NA	708.8 ± 9.73	NA	709 ± 11.87	890	712.4 ± 13.24
N1-P2 amplitude (μV)	NA	6.71 ± 1.19	NA	10.57 ± 3.01	4.5	8.89 ± 3.88

Five healthy control subjects were studied. NA: not applicable; SD: standard deviation

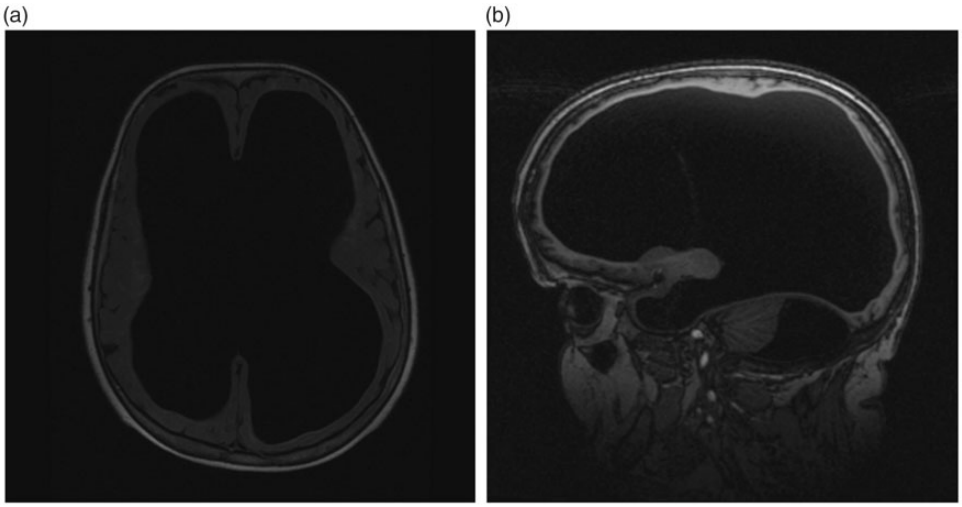

Figure 2. (a) An axial fluid-attenuated inversion recovery image and b) sagittal T1-weighted image show marked ventricular expansion and brain cortical thinning

only in the derivation Pz, where the N1 component latency was 722 ms, the P2 component latency was 890 ms, and the N1-P2 amplitude was 4.5 μv (Figure 1b and Table 1).

An MRI examination was performed on a system operating at 3.0 Tesla (Philips Achieva, Best, The Netherlands). T1-weighted, T2-weighted, and fluid-attenuated inversion recovery axial and sagittal sequences were acquired. MRI showed the presence of triventricular hydrocephalus with severe volume loss. In particular, large expansion of the third ventricle showed diastasis of the interpeduncular cistern, with marked structural alterations of the optic chiasm, and frontal and temporal areas. These are the elective areas of the sense of smell (Figure 2a, 2b).

Discussion

Smell disorders have been described in several neurological diseases,[5–10] but they are often underestimated and rarely assessed in clinical practice. Few studies have reported assessment of smell function in patients with hydrocephalus.[1,2] Recently, Passler et al.[2] reported that patients with

normal-pressure hydrocephalus had better olfactory performance compared with patients with Alzheimer disease. This finding suggests the usefulness of an olfactory examination in differential diagnosis. Additionally, Podlesek et al.[1] combined olfactory testing with MRI to evaluate the possible relationship between olfactory deficit and hydrocephalus-induced structural damage of cerebral areas involved in smell.

We report a case of a patient with arrested hydrocephalus and olfactory dysfunction that was evaluated by combined approach. The SST showed a severe deficit in detection, identification, and discrimination of odors. These results are consistent with previous studies.[1,2] However, an OERP examination confirmed moderate olfactory dysfunction. Additionally, the patient's event-related responses were unclear in Fz and Cz derivations and were present only in Pz derivation compared with healthy subjects. This finding suggested partial preservation of central olfactory system function.

An MRI examination showed severe expansion of the third ventricle with diastasis of the interpeduncular cistern and thinning of primary olfactory areas, such as fronto-basal structures (olfactory bulbs and tracts, and orbitofrontal cortex) and rostral-medial temporal areas.

In this case of arrested hydrocephalus, the mechanism for the etiology of olfactory deficit is not easy to interpret. Although our patient had considerable cerebral atrophy, cognitive performance was surprisingly normal, which resulted in reliable psychophysical SST results. Although the patient had an important reduction in volume of the frontal and temporal cerebral areas, there was only a partial OERP response. This result suggested that the olfactory deficit was independent from cerebral atrophy. However, absence of an olfactory response in derivations Fz and Cz and the functional anosmia detected by the SST suggest that olfactory impairment could be particularly related to damage of the frontal areas (central substrate for odor processing). However, the presence of an olfactory response in the Pz derivation could be due to an adaption condition of the central olfactory system to progression of structural brain damage.

In conclusion, a combined approach for assessing functional and structural olfactory pathways (psychophysical test, and OERP and MRI examinations) could be useful for obtaining some indications on the possible etiopathogenesis of anosmia associated with arrested hydrocephalus. In particular, a psychophysical test allows identification of the degree of impairment of smell abilities, while OERPs and MRI measure functional and structural damage of central olfactory pathways. Longitudinal studies and pre- and post-surgery comparisons are required to determine if OERPs and the SST can have a prognostic role and help clinicians in decision making.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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