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Original Article

Investigation of prognostic factors for post-traumatic olfactory dysfunction

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Abstract

Background: Post-traumatic olfactory dysfunction is common but has a poor prognosis. The purpose of this study was to analyze the effect of clinical features on improvements in post-traumatic olfactory dysfunction.
Methods: From 2007 to 2013, patients with post-traumatic olfactory dysfunction were enrolled. Olfactory function was assessed using the Sniffin' Sticks test at the first and final visits. Olfactory improvement was defined as a change in olfactory state to an improved level. Variables with a potential effect on improvements in olfactory dysfunction, including age, sex, time from trauma to first visit, initial olfactory function, observation time, and olfactory bulb integrity, were entered into logistic regression analysis.
Results: In total, 107 patients were included, with a mean age of 40 years. The mean follow-up period was 9.4 months. Eighteen patients (16.8%) had improvements with regard to olfactory function. No clinical factors were found to influence olfactory recovery in univariate and multivariate analyses (all $p > 0.05$). In addition, there were no differences in clinical features between the patients with and without olfactory recovery (all $p > 0.05$).
Conclusion: No significantly favorable prognostic factors for post-traumatic olfactory recovery were identified, reflecting, to some extent, the poor prognosis of post-traumatic olfactory damage. The results of this study provide useful information that clinical physicians can use when counseling patients with post-traumatic olfactory disorder regarding the prognosis, observation choice, and possible treatment strategy.

Keywords: head injuries; olfaction disorders; post-traumatic; smell

1. Introduction

Head trauma is a common cause of olfactory dysfunction. Although the rates of post-traumatic olfactory dysfunction have been reported to range between 4% and 60%, a few studies have reported the rate to be as high as 75–90%.[1] Such patients usually have irreversible dysfunction and a poor prognosis.[2] This can lead to anxiety in the patients, so the more information on the prognosis that can be given, the more their concerns will be allayed.[3] Therefore, clinicians need to explain the prognostic factors when counseling patients and when planning treatment. The identification of clinical prognostic features may thus facilitate the counseling of patients on the chances of olfactory improvement following head trauma.

As such, the aims of this study were to conduct a prognostic study using univariate and multivariate analyses on the predictive role of clinical features in improvements in post-traumatic olfactory dysfunction.

Conflicts of interest: The authors declare that there are no conflicts of interest related to the subject matter or materials discussed in this article.

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2. Methods

2.1. Ethical considerations

The Institutional Review Board of our hospital approved this descriptive, retrospective chart-review study. Written informed consent was obtained from all involved patients.

2.2. Patients

Patients with post-traumatic olfactory dysfunction between 2007 and 2013 were included in this retrospective study. The treatment principle was to try a 1-month tapering course of oral steroids, and then vitamin B_{12} and ginkgo (*Ginkgo biloba*) thereafter. The patients were followed up at the same doctor's outpatient department at our hospital, a tertiary referral center in Taiwan. Detailed history taking was performed to confirm subjective olfactory dysfunction after the head trauma. The patients with insufficient olfactory function data were excluded. Intranasal damage and scarring was ruled out by intranasal endoscopy.

2.3. Olfactory function assessment

Olfactory function was examined in every patient using the Sniffin' Sticks test, which includes olfactory threshold, discrimination, and identification tests.[4,5] These tests can be used together or separately.[6] The TDI (Threshold, discrimination and identification) score was the sum of these three tests. We defined normosmia as a TDI score $\geq$ 30, hyposmia as a TDI score between 16 and 29, and anosmia as a TDI score $\leq$ 15, according to previous studies. If the patient had only one of the three parameters (threshold, discrimination, or identification) available, we classified them by threshold score = 1, discrimination score $\leq$ 8, or identification $\leq$ 7 for anosmia, threshold score > 1 and $\leq$5.5, discrimination score > 8 and $\leq$ 11, or identification > 7 and $\leq$ 13 as hyposmia, and threshold score > 5.5, discrimination score > 11, or identification > 13 as normosmia.[5] Olfactory improvement (diagnosis scale improvement) was defined as a change in olfactory state to an improved level, such as from anosmia to hyposmia or hyposmia to normosmia. Data at the first visit and the final visit were collected. At the first visit, the patients were divided into three groups according to their olfactory function.

2.4. Outcome predictors

Based on data from the related literature and on clinical expertise, we selected the variables with a potential effect on the improvement of olfactory dysfunction, including (1) age, (2) sex, (3) time to diagnosis (time between head injury and first visit), (4) olfactory scale score at first visit, (5) observation time, and (6) olfactory bulb injury reviewed by magnetic resonance imaging (MRI). Each patient underwent MRI during their first visit, and the results were reviewed by the same radiologist.

2.5. Statistical methods

Univariate and multivariate logistic regression analyses were used to evaluate the factors affecting improvements in olfactory function. A comparison of clinical features between the patients with and without improvements in the diagnosis scale was carried out using Chi-square analysis. All of the statistical analyses were performed using a commercially available software package, SPSS, version 18.0 (SPSS, Inc., Chicago, IL, USA). Any p values < 0.05 were considered to be statistically significant.

3. Results

A total of 107 patients were included in this study, with a mean age of 39.45 ± 14.34 years (range 17–71 years). Therefore, we used 40 years of age as the cutoff age for logistic regression analysis. Of the 107 patients, 51 (47.7%) patients were male. Sixty patients (56.1%) presented to our outpatient department within 6 months of the occurrence of head trauma. Seventy-four patients (69.2%) were in the anosmia group, 32 (29.9%) patients in the hyposmia group, and 1 (0.9%) patient in the normosmia group. The median follow-up period was 7 months (range 1–52 months). Most of the patients had olfactory bulb injuries (70.1%). The demographic characteristics of the patients are shown in Table 1.

Univariate and multivariate analyses of the prognostic features in the patients with post-traumatic olfactory dysfunction (Table 2) showed that none of the factors (age, sex, time to diagnosis, diagnosis at first visit, observation period, olfactory bulb integrity) affected improvements in olfactory function (all p > 0.05). Eighteen of the 107 patients had an improvement in diagnosis scale, and 89 patients did not (Table 3). Of the patients with and without an improvement in the diagnosis scale, 12 (66.7%) and 48 (53.9%) patients came to our outpatient department within 6 months, respectively.

Table 1
Demographic characteristics of the patients (n = 107).

Variables	No. (%)
Sex	
Male	51 (47.7)
Female	56 (52.3)
Age (mean, y)	39.45 ± 14.34 (17–71)
Observation period (median, mo)	7 (1–52)
Time to diagnosis	
≤6 mo	60 (56.1)
7–12 mo	24 (22.4)
13–24 mo	12 (11.2)
>25 mo	11 (10.3)
Diagnosis on first visit	
Anosmia	74 (69.2)
Hyposmia	32 (29.9)
Normosmia	1 (0.9)
Olfactory bulb integrity	
Intact	32 (29.9)
Nonintact	75 (70.1)

Table 2
Logistic regression analysis of the prognostic features in the patients with post-traumatic olfactory dysfunction.

Factors	Cases (n = 107)	DS upgrade, n (%)	Univariate		Multivariate	
			Odds ratio (95% CI)	p	Odds ratio (95% CI)	p
Time to diagnosis				0.663		0.473
≤6 mo	60	12 (20.0%)	1.13 (0.21–5.90)	0.889	1.56 (0.26–9.42)	0.626
7–12 mo	24	2 (8.3%)	0.41 (0.05–3.37)	0.406	0.45 (0.05–4.18)	0.479
13–24 mo	12	2 (16.7%)	0.90 (0.10–7.78)	0.924	0.85 (0.09–8.41)	0.885
>25 mo	11	2 (18.2%)	1 (Ref)		1 (Ref)	
Diagnosis on first visit				0.408		0.394
Anosmia	74	15 (20.3%)	1 (Ref)		1 (Ref)	
Hyposmia	32	3 (9.4%)	0.41 (0.11–1.52)	0.181	0.38 (0.10–1.52)	0.172
Normosmia	1	0 (0%)	<0.001	> 0.99	<0.001	> 0.99
Age				0.900		0.939
≤40 y	58	10 (17.2%)	1.07 (0.39–2.96)		1.05 (0.33–3.33)	
>40 y	49	8 (16.3%)	1 (Ref)		1 (Ref)	
Observation period				0.466		0.513
≤7 mo	57	11 (19.3%)	1 (Ref)		1.49 (0.45–4.90)	
>7 mo	50	7 (14.0%)	0.68 (0.24–1.92)		1 (Ref)	
Sex				0.215		0.239
Male	51	11(21.6%)	1.93 (0.68–5.42)		1.96 (0.64–6.00)	
Female	56	7 (12.5%)	1 (Ref)		1 (Ref)	
Olfactory bulb integrity				0.438		0.362
Intact	32	4 (12.5%)	1 (Ref)		0.56 (0.16–1.97)	
Nonintact	75	14 (18.7%)	1.61 (0.49–5.32)		1 (Ref)	

CI = confidence interval; DS = diagnosis scale; Ref = reference category.

Fifteen (83.3%) patients with an improvement in the diagnosis scale and 59 (66.3%) patients with no improvement in the diagnosis scale had anosmia. There were no differences in clinical features between the patients with and without improvements in the diagnosis scale (all $p > 0.05$).

Table 3
Comparison of clinical features between the patients with and without improvements in the diagnosis scale.

Factors	No. of patients with DS improvement, n = 18 (%)	No. of patients without DS improvement, n = 89 (%)	p
Time to diagnosis			0.653
≤6 mo	12 (66.7)	48 (53.9)	
7–12 mo	2 (11.1)	22 (24.7)	
13–24 mo	2 (11.1)	10 (11.2)	
>25 mo	2 (11.1)	9 (10.1)	
Diagnosis on first visit			0.385
Anosmia	15 (83.3)	59 (66.3)	
Hyposmia	3 (16.7)	29 (32.6)	
Normosmia	0 (0)	1 (1.1)	
Age			0.900
≤40 y	10 (55.6)	48 (53.9)	
>40 y	8 (44.4)	41 (46.1)	
Observation period			0.465
≤7 mo	11 (61.1)	46 (51.7)	
>7 mo	7 (38.9)	43 (48.3)	
Sex			0.210
Male	11 (61.1)	40 (44.9)	
Female	7 (38.9)	49 (55.1)	
Olfactory bulb integrity			0.435
Intact	4 (22.2)	28 (31.5)	
Nonintact	14 (77.8)	61 (68.5)	

DS = diagnosis scale.

4. Discussion

Age did not affect post-traumatic olfactory outcomes in this study, which is consistent with many other studies. Doty et al[7] found that olfactory test scores were not meaningfully related to patient age at the time of trauma, an observation supported by Welge-Lüssen et al[8] in whose study age at the time of trauma did not influence the rate of TDI score improvement. However, more patients (55.6%) with an upgrade in olfactory test were in the younger group. In other words, there was a trend that younger patients had a higher olfactory improvement rate. This finding, although it did not reach statistical significance, was supported by Jiang et al,[9] who found that younger patients had better response to oral steroid treatment and had a better improvement of olfactory function. Younger patients were also found to have better proliferation of neurons in the olfactory epithelium, whereas older patients had greater sensitivity to the effects of inflammation.

This study had an almost equal number of males (n = 51) and females (n = 56). Univariate and multivariate analyses showed that sex had no significant effect on olfactory recovery (Table 2). We also found no significant difference in sex between the patients with and without olfactory recovery (Table 3). These findings are consistent with previous studies on post-traumatic olfactory dysfunction with long-term follow up.[8–10] Therefore, sex is conclusively not associated with better outcomes.

In order to determine whether a shorter time to diagnosis resulted in better olfactory outcomes, we divided our patients into four groups according to the time between the head injury and first visit (Table 2). We found that this time period was not

significantly associated with improvements in olfactory function, which is consistent with previous studies.[7,9]

In this study, the median observation period was 7 months, thus we used 7 months as the cutoff point. There was no significant association between observation time and olfactory improvement. In other words, the longer the patients were followed up, the likelihood that olfactory function would improve did not increase. According to the laws and regulation of payment from labor insurance in Taiwan, a patient must be followed up for at least 6 months before a diagnosis of anosmia without improvement can be made. After this period, most of our patients were lost to follow up. However, among the 18 patients who eventually had improved olfactory function, 7 (39%) saw improvements after 7 months, and 4 (22%) after 1 year. This reflects that there is still chance of olfactory recovery after the current 6 months of follow up. Our results are consistent with those of Welge-Lüssen et al,[8] who reported that 33% of their patients with head trauma had olfactory function improvements after an average follow-up time of 74 months.

Any obstruction or trauma to the olfactory pathway will cause olfactory disorder (Fig. 1).[8] We examined our patients with an endoscope to evaluate olfactory tract obstruction, and all of the patients also underwent MRI during their first visit to determine the integrity of the olfactory tract. Interestingly, there was no significant difference in the recovery of the olfactory function between the patients with intact and nonintact olfactory bulbs. One possible reason is that MRI is somewhat limited in the detection of injuries at the ciliary nerve or olfactory epithelium level.[11] However, although olfactory bulb volume is unlikely to recover,[12] olfactory function may improve by nerve regeneration and connection to the secondary neurons of the olfactory bulb. It is also possible that the small sample size and short-term follow up contributed to these results. Further studies with a larger sample size and a longer follow-up time may be required to determine whether olfactory bulb volume will change, and whether its integrity predicts future olfactory outcomes.

This study objectively evaluated the olfactory function of patients with post-traumatic olfactory disorder. This method is more suitable for disability certification than subjective evaluation, and is easier to validate in future studies.

There are some limitations to this study. First, olfactory improvement was defined as an improvement on the diagnosis scale, namely a change in olfactory state to an improved level, such as from anosmia to hyposmia, hyposmia to normosmia, or anosmia to normosmia. However, this is a form of measured olfactory improvement rather than patient self-rated olfactory improvement. In other words, a patient with improved measured olfaction may not experience improvement in olfactory function. Occasionally, patients may even experience a decline in olfactory function. Such disparity may limit the interpretation of our results. Second, selection bias was unavoidable. Because of the chapter authors' specialized smell disorder treatment center in Taiwan, our patients' conditions may be more severe than those in other clinics. This may thus explain the lower rate (16.8%) of improvements in our patients. This study was also limited by small patient group size and the inherent bias associated with a study that is retrospective in nature. In addition, the results from the Taiwanese patients in this study may not be directly applicable to other ethnic groups because other clinicians may use different treatments.[13] Moreover, some unknown confounding factors may not have been included in the logistic regression model, and these factors may actually be associated with clinical outcomes.[14] Finally, because a correlation may not necessarily

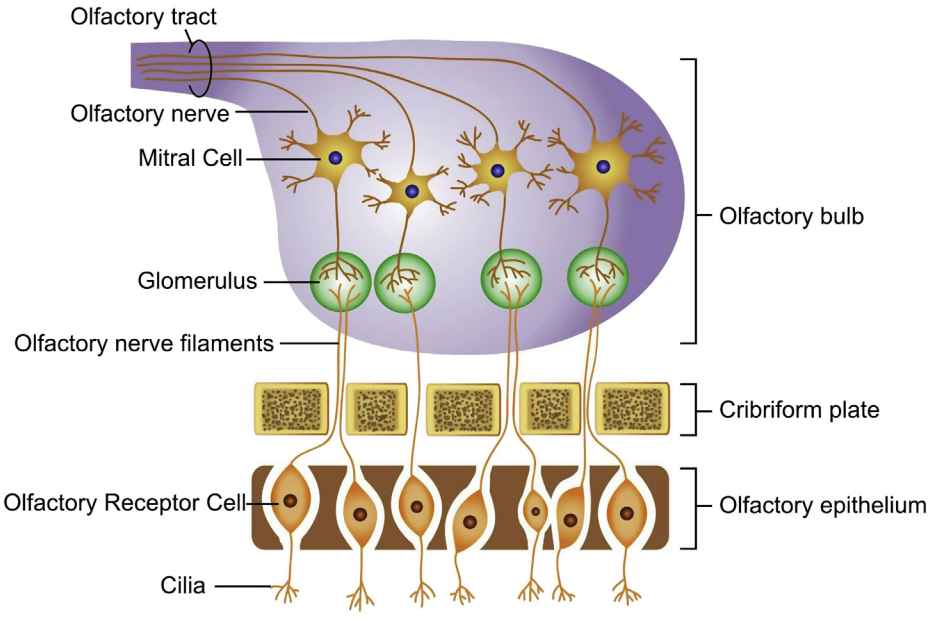

Fig. 1. Olfactory pathway. The olfactory tract passes olfactory information from the nose to the olfactory bulb of the brain, allowing it to interpret odors. Any obstruction or trauma to the olfactory pathway will cause olfactory disorder.

mean that a causal relationship exists, the regression analysis results must be interpreted with caution.

In conclusion, this study found no significant favorable prognostic factors for post-traumatic olfactory recovery. Although the prognosis of post-traumatic olfactory damage remains poor, the results of this study still provide useful information for clinical physicians when explaining prognosis, observation choice, and possible treatment strategies. Because the prognosis is so poor, doctors may consider early discussion of further occupational considerations, life modifications, and safety measures, such as gas leak alarms, in patients with post-traumatic olfactory disorder.

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