Olfactory outcomes after resection of tuberculum sella and planum sphenoidale meningiomas via a transcranial approach

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Abstract

Objectives

Controversy exists surrounding the optimal approaches to tuberculum sella meningioma (TSM) and planum meningioma (PM). Olfaction is infrequently considered within this context but is nonetheless an important quality of life measure. The evolution of olfactory outcomes following contemporary transcranial surgery remains unclear. This study reviews olfactory outcomes after supraorbital craniotomy for TSM or PM and defines temporal trends in its recovery.

Design and setting

A prospective study of a patients who underwent a minimally invasive supraorbital craniotomy for TSM or PM, was conducted at a single neurosurgical center.

Participants & main outcome measures

All patients were questioned about olfaction at presentation, 3 months post-operatively, 12 months post-operatively, and annually thereafter (median follow-up 37 months). The olfactory status of patients was categorised as: normosmia; anosmia; hyposmia; parosmia, (altered perception of odours) or phantosmia, (olfactory hallucinations).

Results

Twenty-two patients were included in the study analysis, (range 27-76). Three months after surgery seven patients had normal olfaction (32%). Six patients were anosmic, (27%) four hyposmic, (18%), three

parosmic, (14%) and two were phantosmic (9%). At one year follow-up, almost half of patients (10; 48%) were normosmic, whilst two patients (9.5%) were anosmic. There were no further improvements in olfaction between one year and long term follow-up.

Conclusions

Subfrontal transcranial approaches for TSM or PM appear to be associated with changes in olfaction that can improve with time; these improvements occur within the first year after surgery. Impacts upon olfaction should be considered when selecting a surgical approach and patients counselled appropriately.

Keywords: olfaction; tuberculum sella meningioma; supraorbital craniotomy

Introduction

Resection of anterior skull base meningiomas, specifically tuberculum sella (TSM) and planum meningiomas (PM) is surgically challenging due to their anatomically complex location and sensitive surrounding structures.[8,43] The goal of surgery is traditionally decompression of vital structures, optimising the chance of visual improvement, and tumour control. There has been much controversy regarding optimal surgical approaches to achieve these goals.[6,29] However, olfaction is rarely considered as part of pre-operative planning discussion between clinicians and with patients prior to surgery.[31] Furthermore, the evolution of olfaction following surgery for TSM and PM is not well reported.[12,16] Notwithstanding this, loss of olfaction is known to be associated with significant patient morbidity, as it impairs patients' abilities to detect harmful fumes and food spoilage, and reduces satisfaction derived from pleasant aromas.[1,24,32] Olfactory dysfunction is also associated with the development of psychiatric morbidity such as debilitating depression.[4,41,45] Therefore, protection of olfaction should always be considered when planning surgery for TSM and PM.

Established surgical treatment options include transcranial approaches such as pterional, bicoronal, and more recently supraorbital craniotomies, along with endoscopic endonasal approaches (EEAs). The effects of endoscopic endonasal surgery upon olfaction have been reported, with significant risk of olfactory dysfunction when extended endoscopic endonasal surgery is performed for anterior skull base lesions.[12,31,48] Rates of anosmia or hyposmia after EEAs are variable within the literature, with long-term rates of olfactory morbidity reported between 24-36% after EEAs for TSM and PM.[7,9,31,50] Olfactory dysfunction is also reported after established transcranial approaches to TSM and PM, after which 10-65% of patients can suffer with olfactory dysfunction.[10,37] However, descriptions of the evolution of olfaction following contemporary transcranial techniques are lacking within the current literature. This study evaluates temporal trends in olfactory outcomes in patients following minimally invasive unilateral subfrontal transcranial resection of TSM or PM.

Methods

A single-center, prospective study was performed over an eight year period (2011-2018) at a single neurosurgical center. All adult patients admitted within the study period with a diagnosis of a primary anterior skull base meningioma involving the tuberculum sella or planum sphenoidale, with normal olfaction prior to surgery, were recruited. Olfactory groove meningiomas were excluded due to their high rates of anosmia at presentation.[12,16,31] Demographic data collected for each patient included: tumour location, age, sex, presenting symptoms, comorbidities, smoking history, preoperative tumour diameter, surgical approach, and operative complications. Evaluation of maximal tumour diameter was determined on pre-operative MRI. Within the cohort, twenty patients had tuberculum sella meningiomas and two had planum sphenoidale tumours. Twenty-one patients underwent surgical resection of their tumour via a minimally invasive subfrontal approach. One patient underwent a mini-pterional craniotomy due to an additional sphenoid wing meningioma. Details of these surgical techniques have been described previously.[10,28,30,31,35,50] At surgery, the olfactory tract was identified early, and its macroscopic anatomical integrity preserved in all cases. Gross total resection (GTR) was defined by an absence of residual enhancing tumour on 3-month post-operative imaging.

Olfaction was assessed via qualitative patient telephone screening. All patients were canvassed about olfaction at presentation, 3 months post-operatively, 12 months post-operatively, and annual follow-up thereafter (median follow-up 37 months). All patients had a minimum of 12 months follow-up. Olfactory function was categorised as: anosmia; hyposmia; phantosmia, (olfactory hallucinations); parosmia, (altered perception of some odours), and normosmia. For some analyses, patients were subcategorized as normosmic, anosmic or dysosmic, (any of hyposmia, parosmia or phantosmia) because anosmia is more debilitating than the dysomias, wherein patients can often still taste food and detect significant dangerous odors. Statistical analyses, (Fischer's exact tests and Kruskal-Wallis Tests) were carried out using Graphpad Prism Software V8™ , with p values <0.05 being considered statistically significant. This study

was carried out in accordance with the ethical standards of the Cardiff and Vale University Health Board Neurosciences directorate research and audit department, and with the 1964 Helsinki Declaration and its later amendments.

Results

Twenty- three patients were screened for recruitment to the study (Table 1). This cohort comprised 2 males and 21 females. The mean age was 52yrs (range 27-76). Nine (39%) of the patients had a smoking history. Twenty-two patients (96%) presented with visual deterioration, and 22 (96%) were normosmic prior to surgical resection. The mean pre-operative tumour diameter was 24mm (range 16-36mm).

Table 1 Summary of study cohort demographics (n=23). GTR = Gross Total Resection; NTR = Near total resection.

Twenty-one patients (91%) experienced improvement or stabilisation of vision post-operatively. Gross total resection (GTR) was achieved in 19 patients (83%; Table 1). Post-operative complications developed in four patients. One patient developed a pseudomeningocele, two developed transient SIADH, and one suffered a CSF leak (4.3%). There were no cases of hypopituitarism, focal neurological deficits, or new seizures after surgery. There were no post-operative mortalities, and no patients experienced recurrence of disease requiring further surgery at most recent follow-up (median 37 months).

Table Two summarises the evolution of individual patient olfactory outcomes after surgery. The pre-operative hyposmic patient (Patient 16) was excluded from further analysis, as it is known that pre-operative olfactory dysfunction is unlikely to recover after surgery for anterior skull base lesions.[10,12,40] Therefore, at 3 months post-operatively, (Figure 1a, n=22) seven patients had normal olfaction (32%) whilst 15 had some degree of olfactory dysfunction. Of these fifteen patients, six were anosmic (27%) and four (18%) were hyposmic. Two patients were phantosmic, (9%) whilst three reported parosmias (13%).

At one year post-surgery, four patients were anosmic, one of whom was patient 16 who was already excluded from analyses due to pre-existing hyposmia before surgery. Moreover, one further anosmic patient, (Patient 1, Table 2) was both a heavy smoker and diagnosed with Alzheimer's disease in the first year after surgery. Considering that she was normosmic 3 months post-operatively, the self-reported development of 'anosmia' by this patient may not be reliable, nor be related to her surgery. The patient's next-of-kin were interviewed for clarification but did not confirm whether she was truly anosmic. This patient was therefore excluded from subsequent analyses (Figure 1b, n=21). This leaves two patients

confirmed as anosmic one year post surgery (9.5%). Ten patients (48%) were normosmic, five were hyposmic, (24%) one was phantosmic, (5%) and three (14%) had parosmias.

Out of the fifteen patients who had some degree of olfactory dysfunction 3 months after surgery, eight (53%) reported improvement in olfaction over the first year after surgery. Of the six patients who were anosmic at 3-month review, four (67%) reported improvement in symptoms over the first year after surgery. No further patients stated that olfaction improved significantly between 12 months post-operatively and their most recent follow-ups (Median 37 months). Therefore, at most recent follow-up post-surgery, 48% of patients were normosmic, 42% had retained olfaction with a degree of dysosmia, and 9.5% were anosmic (Figure 2).

Smoking history, extent of tumour resection, and tumour location (TSM Vs PM) were not statistically associated with post-operative olfactory dysfunction at one year follow-up, ($p = 0.390$; $p = 0.59$; $p = 0.99$). Tumour size in this series was also not associated with a greater risk of olfactory dysfunction at long term review after surgery ($p = 0.72$). Sub-cohort analysis of the patients who had olfactory dysfunction three months post-operatively revealed that smoking did not demonstrate an association with early post-operative anosmia either ($p = 0.99$).

Table 2 Summary of study cohort peri-operative features and olfactory outcomes. Patient 16 was hyposmic prior to surgery, and thus is excluded from further analyses. Patient 1 developed anosmia at long term follow-up, but this was deemed unlikely to be a consequence of her surgery (see text). TSM = Tuberculum Sella Meningioma; PM = Planum meningioma; GTR = Gross Total Resection; NTR = Near total resection.

Fig. 1

Fig. 2

Discussion

The optimal surgical approaches to achieve tumour clearance whilst also protecting olfaction and vision for TSM and PM lesions remain hotly debated.[14,23,24,36,38,43] Whilst early post-operative changes in olfaction are described within the current published literature,[16,51] the evolution of olfaction long-term post-operatively must also be defined. Unfortunately, few studies to date on contemporary transcranial approaches for TSM/PM assess temporal trends in recovery of olfaction after surgery. The present study reviews these trends after supraorbital transcranial surgery. It demonstrates that just under a third of patients were normosmic three months after surgery, after which patients may experience ongoing recovery of olfaction over the subsequent year; almost half of the study cohort reported normosmia one-year post-surgery, with no change in this proportion at longer-term follow-up. The rate of long-term complete anosmia in this series was 9.5%, improving from 27% in the early post-operative period. These rates are comparable or superior to rates of anosmia following both similar and alternative approaches to

resection of TSM and PM in the literature.[7,10,12,28,30,31,37] The supraorbital approach utilised in the current study, with early identification of the olfactory apparatus and meticulous dissection around and preservation of these structures, may reduce the risk of olfactory rootlet or olfactory tract injury when compared to traditional large craniotomies and approaches to this region from below (EAA). However, it is vital to also review other advantages and disadvantages of the various surgical options to approach TSM and PM, and the relevance of olfactory preservation or recovery to patient quality-of-life. These considerations could then aid neurosurgeons in making evidence-based clinical decisions, and in appropriately counselling their patients prior to surgery.

The importance of olfaction upon patient quality-of-life

Knowledge of the evolution of olfaction after TSM or PM surgery is vital for pre-operative patient counselling; patients may have occupations, (e.g. chefs, perfumer) or enjoy leisure activities, (e.g. wine tasting) which rely upon olfaction, and so loss of this sense is known to have a significant negative impact upon quality of life.[5,32] Olfaction is also vital for detection of spoiled foods and dangerous odours (e.g. gas leaks); patients with anosmia are three times more likely to be at risk of experiencing a hazardous event than normosmics,[4] and between 25% and 50% of anosmic patients report becoming unwell from eating spoiled food because they could not detect its malodour.[39,46] Other health and quality of life issues can plague anosmic patients, such as unhealthy weight loss due to reduced desire to eat.[1,4,5] It is therefore unsurprising that anosmia is associated with psychiatric sequalae, with significant correlations between the degree of olfactory dysfunction with the presence and severity of depressive symptoms.[4,5,15,22,46] Whilst dysosmias, such as hyposmia and phantosmias are known to be troubling for some patients, the retention of some degree of olfaction in these cases means that patients are still able to detect some significant pleasurable and harmful odours, and they may thus be less troubled by their symptomatology than wholly anosmic patients.[4] Complete anosmia is therefore an olfactory outcome clinicians should strive to avoid, where possible.

Surgical options for resection of TSM and PM

Visual outcomes (>90% preservation of vision), extent of resections (83% GTR), and complications such as CSF leak (4.3%) in the present study cohort are comparable to rates for traditional craniotomies for anterior skull base lesions, (visual improvement 70-95%; GTR 60-90%; CSF leak 2-10%[6,10,14,26,38] and to other published series of supraorbital craniotomies.[28-31]

Traditional transcranial approaches to the anterior cranial fossa, such as bicoronal, orbitozygomatic, and pterional routes, come with significant risks such as venous sinus injury, optic and olfactory nerve and frontal lobe retraction injuries, cosmetic issues, and lengthy hospital stays post-operatively.[8,49] They can be associated with delayed recovery and major post-operative complications; meta-analysis has identified that approximately a quarter of patients may require readmission to hospital after traditional craniotomies due to perioperative complications such as infection, seizures, and cardiovascular-respiratory issues.[11] They may also be associated with long term psychological and cognitive morbidity after being utilised for meningioma resection, including impaired memory, psychomotor speed, and poor attention.[27,44,49] This stimulated the development of alternative approaches, such EEAs and minimally invasive supraorbital craniotomies, to provide focussed yet adequate surgical access to tumours.[29,43,49] Endonasal endoscopic strategies provide theoretical advantages such as: reduced brain and nerve retraction; early decompression of the optic canal; better visualization and preservation of the superior hypophyseal artery supplying the chiasma; the absence of a cranial scar, and more rapid patient recovery when compared to traditional craniotomies.[13,31,40,44,51] Likewise, theoretical advantages of contemporary transcranial approaches include lower incidence of endocrine dysfunction, lower rates of arterial injury, and reduced risk of CSF leak.[13,29,31]

Only a handful of comparisons of contemporary transcranial approaches for TSM and PM and EEAs have been performed.[13,24,26,29,31] Furthermore, very few of these comparative studies have focussed upon identifying differences in impact upon olfaction, instead being designed to compare factors such as visual outcomes, CSF leaks, extent of resection, and recurrence.[6,13,29,51] The chances of achieving GTR after EEAs and transcranial approaches for TSM are similar in the existing literature, (80-95% for both

techniques).[6,12,26,29] CSF leaks after EEAs to anterior skull base lesions are generally more commonly reported (11-40%)[13,26,29] than after contemporary craniotomies for TSM (2-10%).[28,29,50]

Olfactory outcomes after transcranial or EEAs for TSM and PM

It is accepted that olfactory function may be affected by both traditional transcranial surgery and EEAs to the floor of the anterior cranial fossa.[43] Impaired olfaction after established transcranial resections of anterior skull base lesions occurs in 10%-66% of cases.[10,31,37,47] Olfactory outcomes after contemporary supraorbital craniotomy for TSM or PM are sparsely published, with small series reporting post-operative anosmia rates between 8-40%.[28,30,31,33] The rate of olfactory anosmia at early stages after surgery in the present study was 27%. However, less than 10% of patients were anosmic at 12-months post-surgery and beyond. Furthermore, over half of the patients (8/15) who had early post-operative olfactory dysfunction reported improvement in olfaction over the first year after surgery. Therefore, the rate of anosmia following craniotomy for TSM or PM in the present series is lower or comparable to the rates currently published in the literature[10,28,30,31,37,47] and olfactory dysfunction in the early phases post-surgery can improve over the subsequent year.

It is known that extended endonasal endoscopic surgeries for anterior skull base meningiomas may be associated loss of olfaction,[12,34,42,45,48] due to cribriform plate resection which may be necessary to eradicate disease in the anterior skull base.[8,13] This puts the olfactory fibres passing downwards through the cribriform plate at high risk of injury both pre-operatively due to tumour growth, and during a surgical approach from below.[13,31] In contrast to transcranial supraorbital approaches, the evolution of olfaction after EEAs has been evaluated[7,15,34]; during the initial months following EEAs, rates of olfactory dysfunction can be high, (60-88%)[12,16,19,20,51] followed by gradual improvement; lower rates of anosmia are reported at follow-up of 12-18 months (24-36%).[7,15,31] The rates of anosmia following supraorbital craniotomy for TSM or PM in the present series are therefore lower at both early stages, (27%) and at

twelve months and beyond post-operatively, (9.5%) than the current published rates of olfactory dysfunction after EAA.[7,12,15,16,19,20,31]

Furthermore, many of the studies which have assessed olfactory outcomes after endoscopic surgery do so on pooled analyses of anterior skull base meningioma resections along with endoscopic pituitary operations.[7,20-24,45] Endonasal operations for purely pituitary tumours represent a lower risk to olfaction than extended EEAs required to access more anteriorly based lesions,[12,45] and thus the reduced olfactory risk in this sub-cohort may dilute the true olfactory morbidity rate after EEAs specifically for TSM or PM in these studies. The significant variation in rates of olfactory dysfunction following EEAs may thus partly be explained by the variable pooling of sellar, parasellar, and anterior skull base lesions within analyses, post-operative nasal mucosal changes, and evolving equipment, techniques and operator experience with endoscopic neurosurgery.[14-16,19,20,22,34,51] A focussed analysis of the evolution of olfactory outcomes after EEAs specifically for TSM and PM is required. Such a study could attempt to validate the suggestion that, based on the present study data and literature review, there may be a lower risk of anosmia, and a greater potential for the recovery of olfaction over time, following supraorbital craniotomy compared to EEAs for TSM or PM.

Study limitations

Smoking is purported as a risk factor for sensitivity to injury of olfactory epithelium.[32] Despite this, neither our analysis nor that of others[34] identified smoking as a statistically significant risk factor for post-operative olfactory morbidity. The current study did not identify any risk factors which predicted the chance of olfactory morbidity post-operatively at 3-months, nor at one-year post-surgery. However, it must be noted that both our study and others may be underpowered to detect the effect of smoking history and other factors upon olfaction after surgery. This therefore warrants investigation in a larger study cohort. Indeed, whilst not statistically significant in the present study, it has been established that tumour

size is associated with increased risk anosmia after surgery for skull base meningiomas in both EEAs and transcranial surgery.[16,28,31,47]

Another limitation of the present study is its use of a qualitative data for assessing olfaction. Validated scores of olfactory function such as the University of Pennsylvania Smell Identification Test (UPSIT) or Sniffin Sticks® (Burghadt,Wedel, Germany), can be utilised to assess olfaction objectively.[22,23,34,41,42] However, these scales do not necessarily reflect individual patients' experiences of the inherently subjective nature of olfaction. For instance, a patient with a low score on an objective olfaction scale may not report significant change in sense of smell if their personal circumstances do not require significant olfaction for their day-to-day life. Since the aim of this study was to begin to highlight the evolution of olfaction after supraorbital craniotomy for individual TSM or PM patients, a qualitative assessment of olfaction was appropriate, as it enabled the study to identify whether individual patient-relevant olfaction can improve over time following these operations; this reflects the main quality-of-life parameters for patients. Future studies could attempt to verify this finding using quantitative measures of olfaction. These could include the UPSIT or Sniffin sticks® as described above, or utilise olfaction-related quality of life scores, to objectively study the impact of olfactory disturbance upon patients' lives. The Questionnaire of Olfactory Disorders (QOD-NS™) has been used to assess olfactory quality of life after ENT surgery,[41] and could be utilised to provide holistic assessments of clinically relevant temporal changes in olfaction following EEAs and transcranial resections of TSM and PM.

Olfaction and the choice of surgical approach for TSM or PM

The choice of surgical approach for TSM and PM requires evaluation of several factors, including tumour size, extent of lateral extension, and vascular encasement and optic canal invasion.[6,26,29] These features were used to develop the Sekhar-Mortazavi classification system, and another by Magill and colleagues, to aid surgical decision making for these patients.[26,28] However, these classification systems do not take the risks to olfaction, nor the consequences of olfactory morbidity, into account. More recently devised algorithms by Ottenhausen and colleagues and Ung and colleagues have developed algorithms to aid in

this decision-making process which do take olfaction into account.[31,47] In brief, for lesions which have >50% of their mass anterior to the sphenoid sinus, or that are larger than 4cm, the authors only advocate EEAs for patients who are already anosmic prior to surgery; the algorithms advocate supraorbital craniotomies for patients who have retained olfaction pre-operatively. Whilst these are without doubt helpful paradigms, they are based on reviews of disparate case series within the literature, rather than data from comparative studies designed to assess the evolution of olfactory outcomes after these procedures.

Notwithstanding the lack of an existing high-quality evidence base, these algorithms[28,31,47] are supported by our data, which highlights that olfaction can be preserved or potentially improve within approximately one year after contemporary transcranial procedures for TSM and PM. Given the significant risks of physical and psychological harm with long-term anosmia,[4,5,32,33] this data highlights the potential for improving clinical outcomes and patient satisfaction through judicious patient selection and patient counselling regarding surgical approaches when attempting resection of a TSM or PM.

Conclusion

Olfactory morbidity is an understudied yet important complication of anterior skull base surgery, contributing to impaired quality of life. Minimally invasive transcranial approaches are an option in the management of TSM and PM, and although just under a third of patients were anosmic three months after surgery, this improved over subsequent months such that less than 10% of patients were anosmic by one year post-operatively. Patients must be adequately counselled regarding the potential impact of olfactory morbidity prior to surgery, and olfaction should always be considered when planning the surgical approach. A strong evidence base to guide surgical decision-making for these patients is currently lacking. A large, comparative study of objective olfaction and olfactory quality of life, following contemporary transcranial surgery and EEAs for anterior skull base meningiomas, is needed.

Declarations

Ethics approval

This study was carried out in accordance with the ethical standards of the Cardiff and Vale University Health Board Neurosciences directorate research and audit department, and with the 1964 Helsinki Declaration and its later amendments.

Consent to participate

Informed consent was obtained from all individual participants included in the study.

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Conflicts of interest

All authors certify that they have no conflicts of interest to declare. The authors have no affiliations with or involvement in any organization or entity with any financial interest, or non-financial interest in the subject matter or materials discussed in this manuscript.

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Figure Legends

Fig. 1 Olfactory outcomes for patients after contemporary transcranial resection of TSM or PM at 3 months (Fig. 1a) and 12 months (Fig. 1b). There were no changes in outcomes between 12 months and most recent follow-up (Table 2). There were three more normosmic patients at one-year follow-up compared to 3-month review. There were four fewer anosmic patients at one-year follow-up compared to early post-operative assessments

Long term Follow-up = 12-57 months (Median 37 months)

Fig. 2 Changes in olfaction following supraorbital surgery for TSM or PM. Parosmic, phantosmic and hyposmic patients are combined within the 'normal olfaction with dysosmia' cohort. Between 3 months and 12 months post-operatively a significant proportion of anosmic patients reported return of some or all olfaction (4/6; 67%). No patients reported any further improvement in olfaction between 12 months and longer-term follow-up

Tables

Table 1 Summary of study cohort demographics (n=23). GTR = Gross Total Resection; NTR = Near total resection.

Table 1: Demographics of study cohort (n=23)

Age range (years)		27-76
Gender		
	Female	21 (91%)
	Male	2 (9%)
Smoking history	Yes	9 (39%)
	No	14 (61%)
Presenting symptoms	Visual deterioration	22 (96%)
	Seizures	1 (4%)
Pre-operative tumour diameter	10-20mm (small)	6 (26%)
	20-30mm (medium)	9 (39%)
	30-40mm (large)	7 (30%)
Pre-operative olfactory function	Normosmia	22 (96%)
	Hyposmia	1 (4%)
Operative approach	Eyebrow craniotomy	11 (48%)
	Lateral Supraorbital craniotomy	11 (48%)
	Mini-pterional craniotomy	1 (4%)
Resection	GTR	19 (83%)
	NTR	4 (17%)
WHO Grade	1	22 (96%)
	2	1 (4%)

Table 2 Summary of study cohort peri-operative features and olfactory outcomes. Patient 16 was hyposmic prior to surgery, and thus is excluded from further analyses. Patient 1 developed anosmia at long term follow-up, but this was deemed unlikely to be a consequence of her surgery (see text). TSM = Tuberculum Sella Meningioma; PM = Planum meningioma; GTR = Gross Total Resection; NTR = Near total resection

Table 2: Olfactory outcomes for patients undergoing subfrontal craniotomy for TSM or PM

Patient	Sex	Tumour location & diameter (mm)	Smoking status	Pre-op olfaction	Operation	Post-op olfac. (3 months)	Post-op olfac. (12 months)	Post-op olfac. (Months follow-up)
1	F	TSM; 31	Smoker	Normosmia	Eyebrow craniotomy; GTR	Normosmia	Anosmia	Anosmia (47)
2	F	TSM; 19	Smoker	Normosmia	Eyebrow craniotomy; GTR	Normosmia	Normosmia	Normosmia (56)
3	F	TSM; 17	Smoker	Normosmia	Eyebrow craniotomy; GTR	Hyposmia	Hyposmia	Hyposmia (46)
4	F	TSM; 17	Smoker	Normosmia	Eyebrow craniotomy; GTR	Anosmia	Hyposmia	Hyposmia (19)
5	F	TSM; 30	Ex-smoker	Normosmia	Eyebrow craniotomy; NTR	Normosmia	Normosmia	Normosmia (45)
6	F	TSM; 29	Smoker	Normosmia	Eyebrow craniotomy; GTR	Anosmia	Anosmia	Anosmia (37)
7	F	TSM; 24	Ex-smoker	Normosmia	Eyebrow craniotomy; GTR	Parosmia	Parosmia	Parosmia (33)
8	F	TSM; 30	Non-smoker	Normosmia	Eyebrow craniotomy; GTR	Normosmia	Normosmia	Normosmia (44)
9	F	PM; 28	Smoker	Normosmia	Eyebrow craniotomy; GTR	Parosmia	Parosmia	Parosmia (47)
10	M	TSM; 36	Non-smoker	Normosmia	Eyebrow craniotomy; GTR	Parosmia	Normosmia	Normosmia (43)
11	F	TSM; 31	Non-smoker	Normosmia	Supraorbital craniotomy; NTR	Phantosmia	Hyposmia	Hyposmia (40)
12	F	TSM; 38	Smoker	Normosmia	Supraorbital craniotomy; NTR	Anosmia	Anosmia	Anosmia (37)
13	F	TSM; 20	Non-smoker	Normosmia	Supraorbital craniotomy; GTR	Hyposmia	Parosmia	Hyposmia (57)
14	F	TSM; 26	Non-smoker	Normosmia	Supraorbital craniotomy; GTR	Hyposmia	Normosmia	Normosmia (30)
15	F	PM; 36	Non-smoker	Normosmia	Supraorbital craniotomy; GTR	Hyposmia	Normosmia	Normosmia (31)
16	F	TSM; 16	Smoker	Hyposmia	Supraorbital craniotomy; NTR	Anosmia	Anosmia	Anosmia (18)

17	M	TSM; 23	Non-smoker	Normosmia	Supraorbital craniotomy; GTR	Anosmia	Hyposmia	Hyposmia (23)
18	F	TSM; 16	Non-smoker	Normosmia	Eyebrow craniotomy; GTR	Normosmia	Normosmia	Normosmia (45)
19	F	TSM; 22	Non-smoker	Normosmia	Mini-pterional craniotomy; GTR	Normosmia	Normosmia	Normosmia (16)
20	F	TSM; 16	Non-smoker	Normosmia	Supraorbital craniotomy; GTR	Anosmia	Parosmia	Parosmia (16)
21	F	TSM; 16	Ex-smoker	Normosmia	Supraorbital craniotomy; GTR	Phantosmia	Normosmia	Normosmia (13)
22	F	TSM; 20	Non-smoker	Normosmia	Supraorbital craniotomy; GTR	Anosmia	Phantosmia	Phantosmia (12)
23	F	TSM; 25	Non-smoker	Normosmia	Supraorbital craniotomy; GTR	Normosmia	Normosmia	Normosmia (13)