

Midline olfactory implantation: a cadaveric study of endoscopic transseptal transcribriform approach*

Hakim Benkhatar^{1,2}, Charlotte Loubieres^{1,2}, Anass Rahim Kada^{1,2},
Maxime De Malherbe³, Nicolas Meunier⁴

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¹ Centre Hospitalier de Versailles, Service d'ORL et chirurgie cervico-faciale, Le Chesnay-Rocquencourt, France

² Ecole de Chirurgie du Fer à Moulin, Paris, France

³ Centre Hospitalier de Versailles, Service de Radiologie, Le Chesnay-Rocquencourt, France

⁴ Université Paris-Saclay, INRAE, UVSQ, VIM, Jouy-en-Josas, France

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Dear Editor:

Along with stem cell transplantation and olfactory epithelium transplantation, olfactory implants could be one of the promising approaches to treat long-lasting anosmia⁽¹⁾. Although optimal area of electrical stimulation to induce odor percept is still debated, landmark animal studies showed direct stimulation of the deafferented olfactory bulb (OB) can reproduce spatial patterns of odorant induced neural activity^(2,3). Moreover, microstimulations of the OB in different locations has been successfully used to induce learning of specific task in rats⁽⁴⁾. In humans, both subdural and transthemoid electrical stimulation of the OB could induce perception of smell^(5,6). Consequently, a first device of olfactory implant has been recently described. Similarly to cochlear implants, it includes an external hardware -consisting of a sensor module called "electronic nose", a microprocessor and a transmitter- and an internal part, namely a receiver-stimulator prolonged by an electrode array to be placed under the OB⁽⁷⁾. However, the placement of this internal component would require a neurosurgical approach that would not be acceptable for the majority of anosmic patients and there is currently no described surgical technique for olfactory implantation in humans⁽⁸⁾. In order to avoid transcranial approach, we evaluate here the feasibility of midline olfactory implantation (MOI; Figure S1) using dummy Oticon cochlear implants (Neuro Zti model) through a combined endoscopic transseptal and external approach (with Fer à Moulin School of Surgery ethics approval). Seven fresh cadavers were dissected in a staged manner by the same surgeon (H.B.). Implant embedment required 3 steps: 1) hemitransfixion incision, transseptal dissection and removal of the perpendicular plate of the ethmoid, 2) nasion incision and nasal bone minitrephination, 3) scalp incision and dissection through the loose areolar layer over the pericranium up to the nasion to introduce the electrode array in the septal space and place the receiver-stimulator (which has a diameter of

30.5 mm) behind the hairline (Figure S2). Two types of electrode array placement were investigated: 1) extracranial placement under the cribriform plate (CP) next to the olfactory foramina and 2) extradural placement between the OB after transcribriform removal of the posterior two-third of the crista galli (CG) (Figures 1, 2, and S3). This additional step required specific bone resection tools including a high-speed drill with 1 mm diamond burr, a House curette and endonasal micro forceps. As a result, septal mucosa perforation occurred in five cases (71.4%), following septal mucosa dissection and/or midline drilling of the CP. The high rate of septal mucosa perforation was attributed to the marked thinness of both mucosa and perpendicular plate of the ethmoid under the CP. Therefore, in case of mucosal injury, a solution would be to cover the perforated area by autologous tissue (such as a pericranium graft harvested through the scalp incision) to promote proper healing and avoid subsequent implant infection or extrusion. For the last 3 cases, transfrontal subdural perfusion of fluorescein-dyed saline (1ml of fluorescein for 100 ml of saline, with unclamped tubing for maximum infusion rate) was implemented to simulate cerebrospinal fluid (CSF) flow and seek for leakage while performing midline fenestration of the skull base. We observed mild leakage in all three cases with CSF flow simulation (100%). These leaks did not occur from the beginning as part of the CG could be removed without leakage but happened next to the ethmoidal slits in two cases and next to the most posterior olfactory foramina in one case. This result demonstrates the high risk of CSF leak related to midline transcribriform approach (Figure 2). However, it might be possible to reduce this risk by performing a smaller midline skull base fenestration and by using an ultrasonic bone aspirator to avoid dural injury. In case of CSF leak, pericranium graft could be harvested through the scalp incision and used for skull base sealing. Two other adverse events occurred during the procedure: drilling through the nasal bones led to frontal sinus

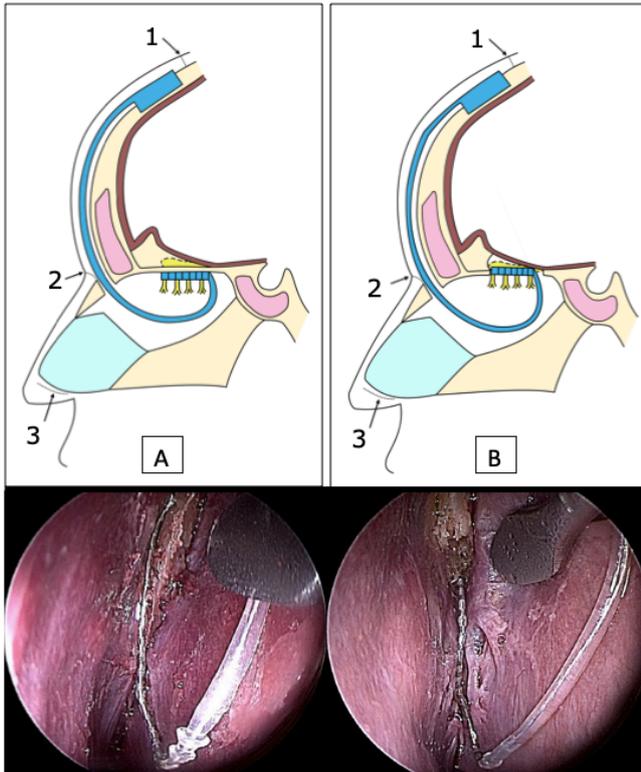


Figure 1. Midline olfactory implantation: (A) extracranial electrode placement with endoscopic view, (B) extradural electrode placement with endoscopic view. 1: scalp incision, 2: nasion incision, 3: hemitransfixion incision

floor penetration in one case (14.3%), and midline drilling of the CG lead to dural perforation in one case (14.3%). We acknowledge that this preliminary study had some limitations and several improvements could be implemented: 1) preoperative and postoperative anatomical study of the CP and the OB with CT scan and MRI would provide useful information for skull base fenestration planning and control of electrode array placement (Figure S4), 2) use of infusion pump to deliver the fluid in pulsating mode and CSF pressure monitoring would enable a more realistic CSF flow simulation⁽⁹⁾, 3) use of specifically designed electrode array in terms of length and diameter would enable better contact with the OB. At a later stage, animal models can be used to confirm the safety and efficacy of midline olfactory implants. Lastly, giving current experience with cochlear implants, the main long-term issue with olfactory implants would be device replacement in case of failure or extrusion and would require specific technical solutions.

To conclude, MOI with extracranial electrode array placement is a simple procedure that mainly carries a risk of septal mucosa perforation and would allow electrical stimulation of the OB

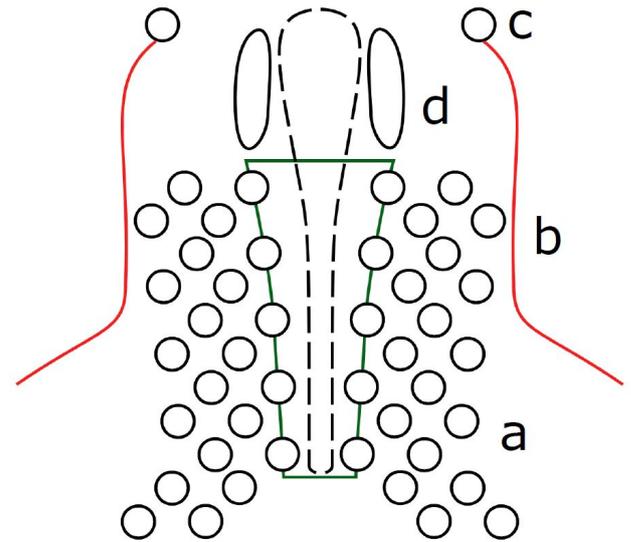


Figure 2. Midline transcribriform approach illustration with bone resection limits (green line) and crista galli area (dashed line). a: cribriform plate foramina, b: anterior ethmoidal artery, c: criboethmoidal foramen, d: ethmoidal slit.

through the CP. MOI with extradural electrode array placement would reduce the distance between the electrode array and the OB but carries an additional risk of CSF leak. Smaller skull base fenestration and use of ultrasonic bone aspirator might be helpful in this regard. We believe that the technical aspects of olfactory implantation deserve more research effort to find out the safest way to place an electrode array along the OB.

Abbreviations

MOI: midline olfactory implantation; OB: olfactory bulb; CP: cribriform plate; CG: crista galli; CSF: cerebrospinal fluid.

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Authorship contribution

HB: study design and conduct, data analysis, original draft writing, final approval; CL: data acquisition, editing, final approval; ARK: data acquisition, editing, final approval; MDM: data acquisition, editing, final approval; NM: data analysis, editing, final approval.

Conflict of interest

None

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Hakim Benkhatar, MD
ENT-Head and Neck surgery
Centre Hospitalier de Versailles
177 rue de Versailles
78150 Le Chesnay-Rocquencourt
France

Tél : 33-1 39 63 87 57

E-mail: hbenkhatar@ch-versailles.fr

SUPPLEMENTARY MATERIAL

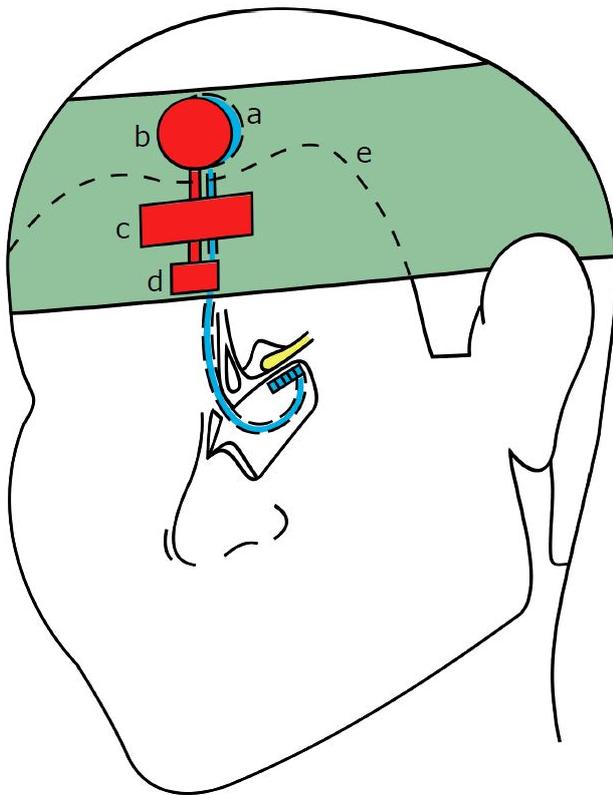


Figure S1. External (red) and internal (blue) components of the midline olfactory implant. The external component is held in place by a head-band.

a: receiver-stimulator, b: transmitter, c: microprocessor, d: biosensor (electronic nose), e: hairline

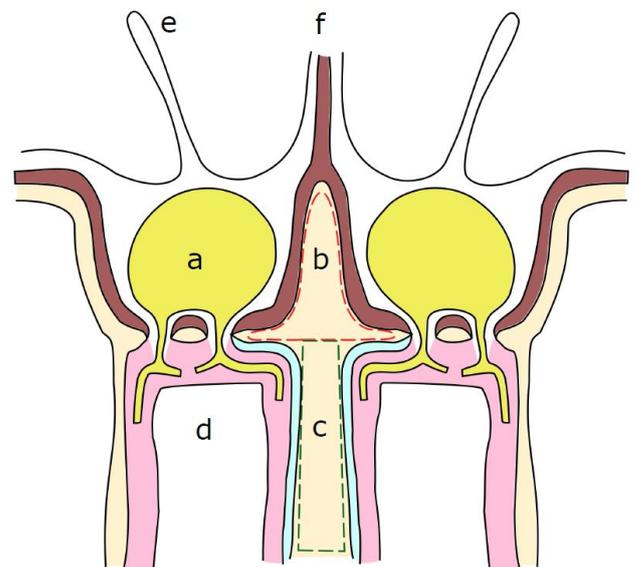


Figure S3. Coronal section showing extent of bone resection for extracranial implantation (dashed green line) and for extradural implantation (dashed redline).

a: olfactory bulb, b: crista galli, c: perpendicular plate of the ethmoid, d: olfactory cleft, e: olfactory sulcus, f: falx cerebri, pink layer: olfactory mucosa, light blue layer: perichondrium, brown layer: dura mater.



Figure S2. Implant embedment: (A) electrode carrier insertion through scalp incision and forehead tunnelization up to the nasion (B) placement of the receiver-stimulator.

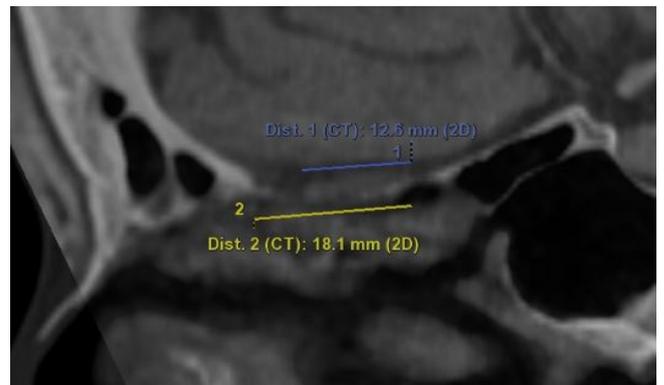


Figure S4. Olfactory bulb (blue line) and cribriform plate (yellow line) lengths measurement based on MRI/CT image fusion.