Expanding the olfactory implant paradigm through recent advances in brain-computer interface technology

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Dear Editor:

The international opinion paper by Whitcroft et al. provides invaluable guidance for the emerging field of olfactory implants [(1)]. While the authors thoroughly address clinical considerations and current technological approaches, we would like to expand upon Statements 9.1 and 9.3 regarding electrode technology limitations and highlight recent advances in brain-computer interface (BCI) technology that could address key technological challenges around electrode longevity and biocompatibility.

Contemporary high-density microelectrode arrays (HDMEAs) now achieve electrode densities exceeding 4,000 channels with inter-electrode spacing approaching the 30-200 µm diameter range of mammalian glomeruli [(2)]. For surgeons considering transcribriform approaches, this represents a significant advancement over traditional Utah arrays, potentially enabling selective stimulation of individual glomerular units essential for odour-specific neural activation patterns during olfactory implantation.

Recent developments in electrode biocompatibility focus on enhancing long-term stability through improved compliance and surface modification strategies including stiffness modification, altering conductive properties and immunomodulatory coatings to reduce glial scarring and maintain neuronal viability [(3)]. Ultra-thin, flexible neural probes incorporating biocompatible polymeric substrates with tissue-matched mechanical properties show promising results for long-term implant stability [(4)], particularly important for olfactory implants where long-term stability near the olfactory bulb is required. Carbon nanotube-enhanced conductive coatings provide improved electrochemical properties while promoting neural integration [(5)] - essential characteristics for maintaining effective olfactory stimulation over extended periods.

Smart responsive materials that actively modulate the local environment to reduce inflammation represent an emerging approach to chronic implant stability [(6)], directly addressing the biocompatibility challenges specific to olfactory implant applications. The advent of 'bio-hybrid' regenerative bioelectric neural interfaces potentially addresses electrophysiological integration challenges through a layer of living cells at the brain-device interface, enhancing biomechanical compatibility with olfactory bulb tissue and functioning as a scaffold to facilitate tissue integration - crucial for maintaining intimate contact with glomerular structures [(7)].

Recent innovations in magnetically actuated liquid-metal (LM) multi-electrode arrays [(8)] represent potential for post-implantation geometric optimization to conform to individual variations in olfactory bulb morphology. This technology maximises biomechanical compatibility whilst enabling efficient utilization of a single electrode array - particularly valuable given the complex three-dimensional architecture of the olfactory bulb. The high-resolution cellular-scale 3D printing technique involved in electrode production enables customizability to individual variations in olfactory bulb morphology as well as structural and mechanical similarity to interfacing neurons.

Experimental BCI research in olfactory neurofeedback systems has demonstrated successful integration of respiratory monitoring with neural stimulation protocols that synchronize electrical stimulation with natural breathing patterns [(9)]. This approach is particularly relevant for olfactory implants, as it could enhance the ecological validity of artificially induced olfactory percepts by aligning stimulation timing with natural physiological rhythms. Additionally, insights from olfactory neurofeedback research could inform adaptive stimulation protocols that improve the reproducibility and validity of downstream neurocognitive and emotional responses associated with olfactory stimulation. This could be particularly relevant for patients undergoing post-implantation olfactory rehabilitation, enabling personalized stimulation parameters that optimize perceptual outcomes based on individual neural response patterns.

Conclusion

The convergence of recent advances in BCI technology with olfactory neuroscience presents unprecedented opportunities to address some of the technological limitations identified by Whitcroft et al. [1]. We encourage the olfactory implant community to incorporate these rapidly maturing BCI technologies in future translational research - potentially offering enhanced precision for glomerular-scale stimulation, improved long-term biocompatibility through bio-hybrid interfaces, and naturalistic stimulation paradigms synchronized with respiratory patterns – in a bid to accelerate progress towards clinically viable devices that provide meaningful individualized sensory restoration for patients with olfactory dysfunction.

Authorship contribution

EB has made significant contributions to conception and design of the work and drafting the work. MA has made significant contributions to design of the work and critically reviewing the work. Both authors have approved the final version submitted for publishing.

Conflict of interest

No conflict of interest to declare.

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