A Marker for Consciousness State Following Brain Injury

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Overview

Improvements in emergency medicine have increased survival rates after brain injury but, paradoxically, have resulted in an increasing number of survivors living with disorders of consciousness. The limitations of current consciousness assessment tools result in a high rate of misdiagnosis, which has numerous therapeutic, economic, and ethical implications. The current technology enables discrimination between minimally conscious patients and patients in a vegetative state based on their sniff responses to pleasant and malodorous odorants. Moreover, responses in patients in a vegetative state were a concrete indication of future regaining of consciousness. Therefore, sniff responses can serve as a diagnostic and prognostic biomarker of states of consciousness and direct clinical decision-making processes.

The Need

Disorders of consciousness (DOC) resulting from a severe brain injury can range from no signs of awareness in a vegetative state (VS, also known as unresponsive wakefulness syndrome (UWS)) to inconsistent reproducible evidence of conscious awareness in a minimally conscious state (MCS). DOC is primarily diagnosed via behavioral assessment based on voluntary responses. However, due to motor impairments, communication difficulties, and fluctuations of vigilance state, reported rates of misdiagnosis are as high as 40%. Misdiagnosis between VS and MCS has significant therapeutic, ethical, and financial implications and can misdirect end-of-life decisions. Recent electrophysiological and neuroimaging developments addressing the challenge of consciousness detection in DOC were able to uncover awareness in DOC patients who appeared completely unresponsive. However, these techniques have substantial practical limitations. fMRI based-methods are costly, highly sensitive to motion, and require patient portability and a metal-free environment. EEG-based methods can be used at the bedside but are not available at all hospitals and care homes and require expertise. Thus, there remains a need for accurate and accessible awareness detection methods in DOC patients.

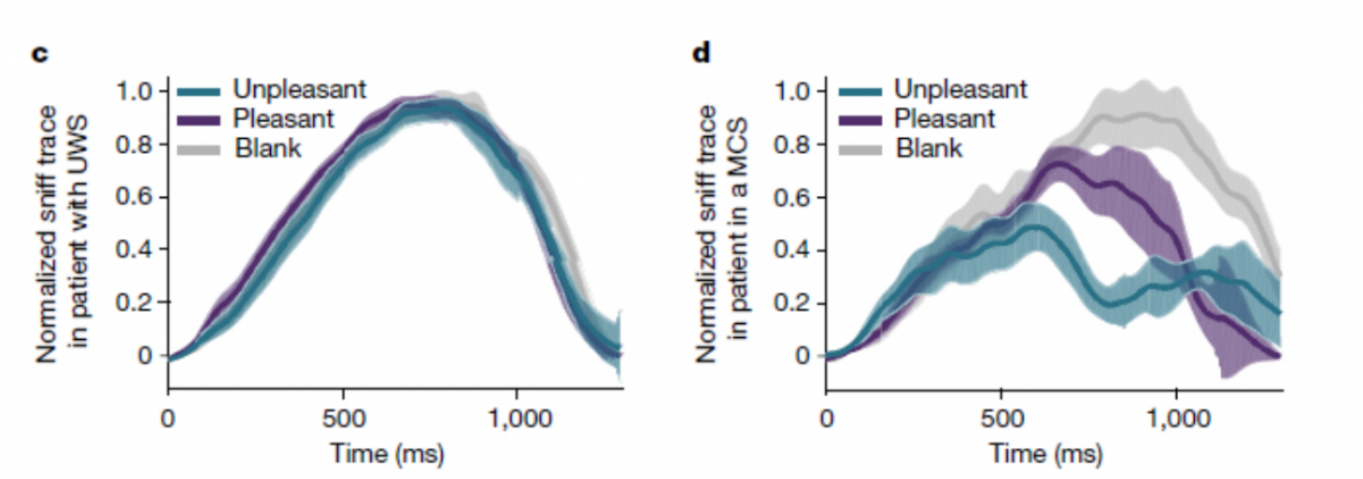
The Solution

In the proposed technology, the olfactory sniff response, an involuntary sensory process requiring cortical and sub-cortical structure integrity, is exploited to inform on state of consciousness.Â Â

Technology essence

This technology is founded on the reliance of olfaction on brain structures involved in the basic mechanisms of arousal. More specifically, while olfactory sniff response is an involuntary physiological process that can persist without conscious awareness, it still requires intact olfactory neuroanatomical structures. In a longitudinal, proof-of-concept study, 31 patients with MCS and 24 patients with VS were repeatedly exposed, over multiple independent sessions, to pleasant and unpleasant odors. Cognitive sniff responses were assessed by measuring nasal

inhalation volumes and comparing them to baseline volumes measured in the absence of an odorous agent; state of consciousness was assessed using standard clinical tools. Nasal airflow was reduced by approximately 10% in the group of MCS patients presented with either a pleasant or malodorous agent (Figure 1A), while no significant changes were measured in the VS patient group (Figure 1B). On the single-patient level, sniff responses in VS patients were a concrete indication (100% specificity) of future regaining of consciousness, and in some patients, preceded any other sign of consciousness recovery by days to months. Such responses also predicted 3.5-year survival rates at 92% accuracy.



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Applications & Advantages

Applications

- Patient triage
- Diagnosis of DOC
- Prognosis of DOC
- Guide medical decision-making processes
- Improved level of care

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Advantages

- Independent of verbal- and task-focused responsiveness
- Portable
- Cost-effective
- Simple to use
- Rapid

Development Status

A longitudinal, observational, comparative study demonstrated the feasibility of the technology in discriminating between MCS and VS patients. Future works will involve the definition of thresholds indicative of distinct DOC subclasses and the construction of algorithms for automated bedside measure and interpretation of sniff responses.

References

Arzi A, Rozenkrantz L, Gorodisky L, et al. Olfactory sniffing signals consciousness in unresponsive patients with brain injuries. *Nature* (2020) 581(7809):428-33.