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Previews

Heart-brain connection: How can heartbeats shape our minds?

Shumao Xu,[1] Kamryn Scott,[1] Farid Manshaii,[1] and Jun Chen[1,*]

Recent neuroscience reveals the heart's impact on brain activity through blood pulsations, affecting mitral cells in the olfactory bulb. This connection, involving mechanosensitive ion channels like Piezo2, links cardiovascular dynamics to neuronal function, offering new treatments for neurological disorders, advancing closed-loop brain-computer interfaces, and emphasizing the body-mind interconnectivity.

The human body operates through a complex network of systems, with the dialogue between the heart and brain being one of its most fascinating interactions.[1,2] This connection has captivated both scientists and philosophers for centuries, emphasizing the significant impact of the interplay between the cardiovascular and nervous systems on our health, emotions, and behaviors.[3] The heart and brain interact closely, with the heart's pulsations through the brain's blood vessels directly influencing neuronal activity. This interaction is bidirectional: the central nervous system governs heart function, while heart activity in turn impacts brain function.[4] Furthermore, the rhythm of the heart significantly affects our emotions and cognitive state. Some previous studies observing behavior and personality changes following heart transplants suggest that the autonomic nervous system plays a key role in integrating cardiovascular and cognitive functions. However, this research area is still evolving, and the findings are not yet definitive. The role of the cardiovascular system extends beyond circulation; through its influence on the nervous system, it remains vital to cognitive and emotional processes. With each heartbeat, blood is disseminated into major arteries, supplying the brain with oxygen and nutrients and influencing neuronal activity through changes in blood pressure. This underscores the heart's regulatory effects on the brain and indicates a complex, reciprocal relationship between our cardiovascular and nervous systems.

Recent advances in neuroscience have significantly improved our understanding of the heart-brain connection. It is now understood that heartbeat-induced pulsations within cerebral blood vessels play a significant role in influencing brain activity.[5,6] A recent landmark study published in *Science* was instrumental in broadening our knowledge of the physiological communication underlying this connection.[7] This research discovered that blood pressure pulsations could impact neuronal activity in the brain through mechanosensitive ion channels. Specifically, mitral cells in the olfactory bulb (OB) detect rhythmic movements of blood vessels caused by the heartbeat and convert this mechanical energy into electrical signals. Furthermore, by mimicking the heart's rhythmic pumping, laboratory simulations have illustrated how brain tissue responds to such pulsations. The identification of fast-acting mechanosensitive ion channels in mitral cells that respond to changes in blood vessel pressure demonstrates a direct mechanism in which each heartbeat affects the brain's electrical signals. This is achieved using a 16-channel probe for OB recordings (Figure 1A). Additionally, research has highlighted the synchronization between neuronal firing patterns and heartbeats (Figure 1B), showing a degree of synchronicity beyond what is typically observed through traditional visceral sensory pathways. This synchronization is evident from spikes in neural activity that coincide with each heartbeat and has been further investigated through local field potential (LFP) recordings during inhalation (Figure 1C). These recordings illustrate that rhythmic pressure changes can modulate slow LFP oscillations in the OB, thus suggesting that the electrical activity of the brain, especially within the olfactory system, can be modulated by heart pulsations.

An integral component of this mechanism is Piezo2, a mechanosensitive ion channel recognized for its responsiveness to mechanical forces, including those generated by the heartbeat. This channel is especially sensitive at the peak of blood vessel pulsations, contributing to the rhythmic depolarization of neurons in harmony with the heartbeat. Its transmembrane domains and propeller-like structure, which includes an ion-conducting pore, play a crucial role in converting mechanical forces into electrical signals, enabling the precise translation of pressure fluctuations into neural signals (Figure 1D).

Precise control of the perfusion rate is crucial when working with OB tissues maintained in a live state through an artificial supply of nutrients and oxygen, a technique known as *in situ* perfusion. Proper regulation of this flow is necessary to preserve tissue viability and enable precise measurement of the OB's spontaneous electrical activity, including the filtered LFP and phrenic nerve activity

[1]Department of Bioengineering, University of California, Los Angeles, Los Angeles, CA 90095, USA

*Correspondence: jun.chen@ucla.edu

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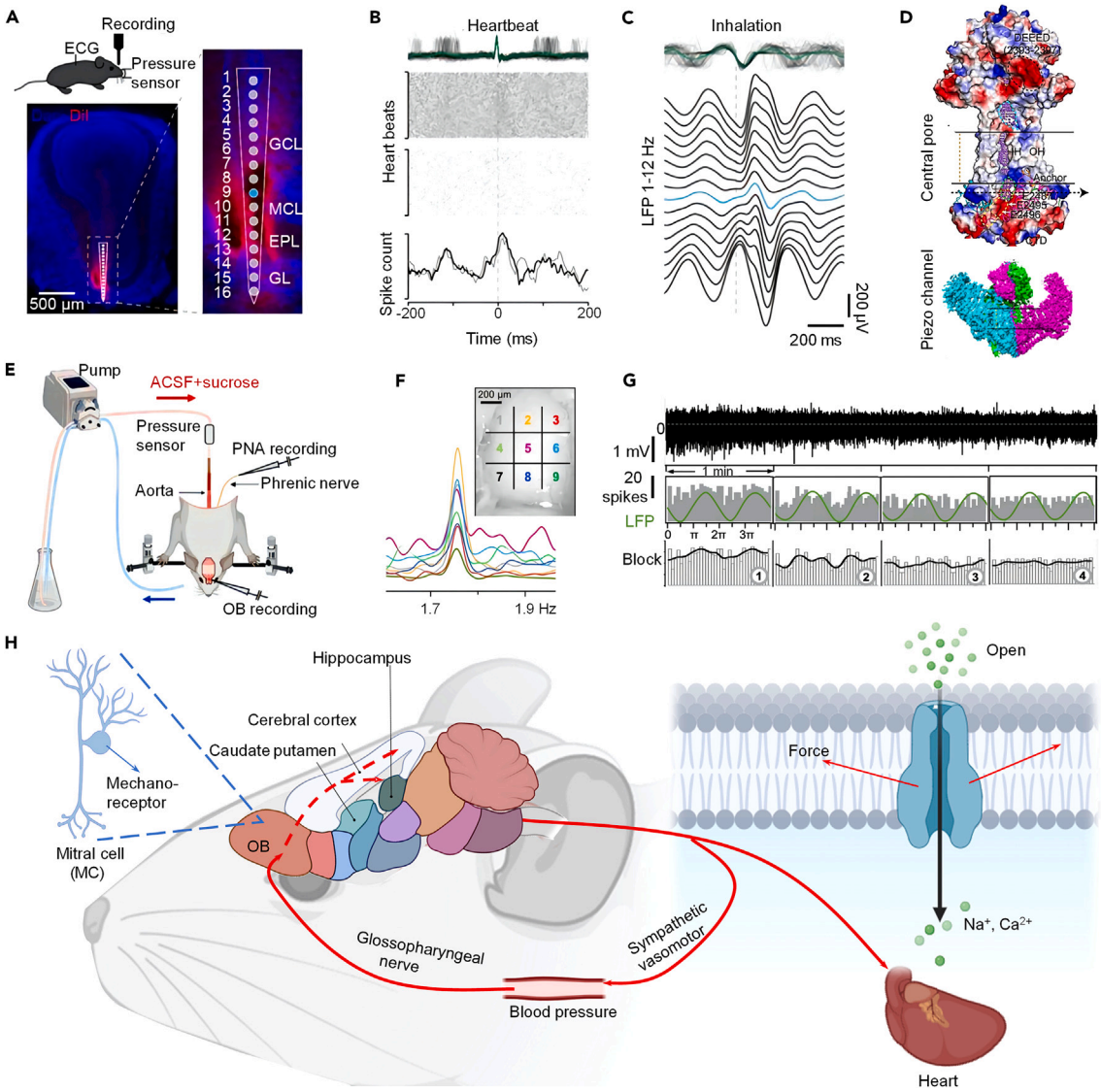

Figure 1. Heartbeat's influence on olfactory bulb function and neuronal activity

(A) *In vivo* recording setup with a silicon probe track in the olfactory bulb (OB). DiI, 1,1′-dioctadecyl-3,3,3′,3′-tetramethylindocarbocyanine perchlorate (a fluorescent dye for neuron tracing); GCL, granule cell layer (containing inhibitory neurons in the OB); MCL, mitral cell layer (the principal projecting neurons in the OB); EPL, external plexiform layer (where mitral cell dendrites intersect with axons of olfactory receptors); GL, glomerular layer (the initial synaptic contact point in the OB).

(B) Unit responses to heartbeat with raster plots.

(C) LFPs aligned and averaged over 1,000 inhalations with a respiration pressure signal displayed above.

(D) Central pore module with surface electrostatic potentials (negative, red; positive, blue) and Cryo-EM of the Piezo channel. From Zhao et al.[1]; copyright, the Nature Publishing Group.

(E) Illustration of the nasal-cerebral setup. Phrenic nerve activity (PNA) and OB-LFPs are monitored simultaneously.

(F) Recordings from different OB surface locations.

(G) LFP recordings with spike phase histograms.

(H) Mechanotransduction pathway from the cardiovascular system to the brain. The mitral cell, acting as a mechanoreceptor in the OB, detects mechanical forces transmitted through blood pressure changes. These signals are then conveyed via the glossopharyngeal nerve to various brain regions, including the hippocampus and cerebral cortex. The opening of ion channels in response to force facilitates the influx of ions such as Na^+ and Ca^{2+}, linking cardiac activity to neural function. The sympathetic vasomotor control loop back to the heart completes the feedback loop of the heart-brain connection. Partially created from Biorender.com.

(PNA). Figure 1E depicts a semi-intact rat olfactory system perfused with artificial cerebrospinal fluid (ACSF) and sucrose by a peristaltic pump, designed to imitate physiological heart-induced pressure pulsations. In-depth electrophysiological studies conducted at various points on the OB's surface within the same nose-to-brain tissue sample (Figure 1F) revealed a diverse pattern of oscillations triggered by the pulsations associated with heartbeats in the dorsal OB. These patterns vary across different areas, indicating a region-specific response to the pulsatile pressure. Additionally, assigning phase values to neural spikes in relation to the primary slow oscillation (Figure 1G) provides insights into how neural activity is synchronized with pulsation-pressure-induced LFP oscillations. This synchronization, observed when respiratory feedback is not present, underscores the profound influence of cardiovascular dynamics on the neural circuits of the OB, establishing a direct link between the rhythmic heartbeat and brain activity.

The research explores the role of mitral cells in the OB, which are notably large in mice, making them ideal for detailed study. It examines how arterial pulsations affect the activity of these cells, focusing on mechanosensitive ion channels that respond to changes in blood pressure. When activated by vascular pulsations, these channels modulate the activity of mitral cells, which in turn may influence associated neurons, potentially impacting the central nervous system and olfactory processing. This insight into mechanosensitive ion channels, especially Piezo2, has illuminated their potential role in disorders characterized by disrupted sensory processing, such as autism and schizophrenia.[8] These disorders are often marked by difficulties in sensory integration and cognitive function, which may in turn be linked to altered perception of the body's internal signals. Mitral cells in the OB are activated by mechanical forces generated by heartbeat-induced blood pressure changes. The structural domains of Piezo2 channels on these cells respond to such forces, leading to the influx of ions such as Na^+ and Ca^{2+} (Figure 1H), which converts mechanical pulsations into interpretable electrical signals. Exploring how these channels respond to cardiovascular pulsations may provide new insights into neural dysfunctions, subsequently informing the development of targeted treatments for conditions such as autism and schizophrenia, which are characterized by disrupted pathways within specific brain regions, including the hippocampus and cerebral cortex. Moreover, the ability of mitral cells to directly transduce mechanical stimuli into neural signals has potentially profound implications for advancing brain-computer interfaces (BCIs).[9] Incorporating these mechanosensitive pathways could enable invasive BCIs to emulate the body's natural signaling processes, offering more intuitive controls for users while delivering therapeutic outcomes for individuals with neural disorders.

However, the complex interplay between rhythmic heartbeat pulsations and their influence on different brain regions, alongside the subsequent effects on behavior and cognition, presents a significant challenge that remains partially unsolved. Tackling this issue could involve delving into several key areas:

(1) Mechanosensing across the brain: Current hypotheses suggest that the distribution of mechanosensitive ion channels along blood vessel walls, which might interact with various brain cells, including astroglia,[7] could significantly influence brain regulation. Therefore, evaluating the distribution of these channels through advanced imaging and neurophysiological methods is crucial for evaluating their functional impact on the brain.

(2) Connection to neurological disorders: The potential link between changes in mechanosensing and neurological conditions such as autism and schizophrenia requires in-depth exploration. Investigating how variations in the sensitivity or expression of mechanosensitive channels could contribute to the pathology of these disorders may reveal molecular-level targeted treatment pathways. This involves examining the molecular and cellular mechanisms by which heartbeat pulsations affect neuronal function and identifying any dysregulation in these pathways due to neurological disorders.

(3) Improvement of invasive neural interfaces: Leveraging cardiovascular dynamics to modulate brain activity through mechanosensitive pathways could enhance closed-loop neural interfaces.[10] This would entail real-time monitoring and modulation of neural activity with the potential to decode emotional or physiological states at the level of individual neurons.

The heart-brain connection represents a fundamental aspect of our physiology, with the heart's rhythm playing a pivotal role in shaping brain function. This connection not only influences our emotional and cognitive experiences but also opens new avenues for understanding how different bodily systems interact. Furthermore, ongoing research into this connection is expected to advance our knowledge of human health and disease, enabling innovative therapeutic approaches that leverage this dynamic interplay.

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DECLARATION OF INTERESTS

The authors declare no competing interests.

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Mechanics-informed ultrafast assembly of semiconductor optoelectronic fibers

Yonggang Huang[1,*]

Semiconductor optoelectronic fibers integrate semiconductor and metal materials and protective shields into a single fiber with ultrahigh aspect ratio, thus paving the way for versatile applications such as intelligent fabrics and highly efficient energy storage. However, scalable fabrication approaches to obtain long fibers in an endurable time in the industry are lacking. Recently, Wang et al. proposed an innovative drawing-based assembly strategy that can hopefully resolve these problems by utilizing mechanical analyses on the assembly processes in extremely high-temperature environments. With proper treatment for the capillary instability and strain mismatch problems, optoelectronic fibers of over hundreds of meters long can be fabricated at the speed of a few tens of meters per minute.

Semiconductor optoelectronic devices, facilitating the transmission of optical signals to electrical signals or vice versa, have garnered extensive applications in diverse fields such as telecommunications, light sensing, medical procedures, and beyond.[1] In contrast to the traditional multi-dimensional optoelectronic devices, the fiber counterparts integrate all optoelectronic components into a confined geometry of large aspect ratios and can be regarded as one-dimensional. The slender geometries bring outstanding benefits to the application of optoelectronic fibers in such scenarios as flexible electronics[2] and optogenetics[3] due to their high structural compliance and durability. The cladding layer of the fiber protects the interior components from severe damage and fracture when the fiber experiences significant tension, bending, and torsion.

At present, the approaches to fabricating semiconductor optoelectronic fibers include the growth-based and drawing-

[1]Departments of Mechanical Engineering, Civil and Environmental Engineering, and Materials Science and Engineering, Northwestern University, Evanston, IL 60208, USA

*Correspondence: y-huang@northwestern.edu

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