Invasive Brain-Computer Interface Applications: Memory Decoding and Modulation

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Abstract

The treatment of diseases characterized by memory impairment as typical symptoms, such as Alzheimer' s disease and post-traumatic stress disorder (PTSD), represents a key direction in brain-computer interface research. This article focuses on the application of invasive brain-computer interfaces in the processing of spatial and emotional information within episodic memory, with emphasis on elucidating how precise decoding of multi-dimensional memory information —including motor states, environmental boundaries, spatial location, and emotional valence—can be achieved based on local field potential signals from deep brain regions of the human brain combined with machine learning algorithms. Regulation techniques founded upon these neural features enable targeted intervention of memory and emotion. Current technical bottlenecks encompass individual differences, insufficient electrode stability, and limitations of adaptive algorithms. Future development necessitates the integration of dynamic network models and flexible electrode technology to propel the advancement of clinical personalized closed-loop intervention paradigms.

Full Text

Preamble

Invasive Brain-Computer Interface Applications: Decoding and Modulation of Memory

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Abstract

Brain-computer interface (BCI) research is increasingly focused on treating memory disorders characteristic of Alzheimer's disease (AD) and post-traumatic stress disorder (PTSD). This review examines invasive BCI applications in processing spatial and emotional information within episodic memory, emphasizing how local field potentials (LFPs) from deep brain structures, combined with machine learning algorithms, enable precise decoding of multidimensional memory information including movement states, environmental boundaries, spatial locations, and emotional valence. Neuromodulation techniques based on these neural signatures can achieve targeted intervention for memory and emotion. Current technical bottlenecks include individual variability, insufficient electrode stability, and limitations of adaptive algorithms. Future development must integrate dynamic network models with flexible electrode technologies to advance clinical personalized closed-loop intervention paradigms.

Keywords: brain-computer interface, invasive electrodes, neuromodulation, closed-loop stimulation

Humans have long sought to transcend physiological limitations, interacting directly with the world through thought alone: controlling robotic arms with intention, reading minds, or even selectively enhancing pleasant memories while erasing painful ones—scenes once confined to science fiction are gradually becoming reality through brain-computer interfaces (BCIs). Traditional BCI technology has primarily achieved external device control through sensory feedback and motor decoding \cite{Gao_{{{etal}}}*{{2021}}}, *Lebedev*{{{Nicolelis}}}*{{2017}}*, *Wolpaw*{{{Wolpaw}}}*{{2012}}}. *Clinically, it has enabled individuals with motor disabilities to approach normal mobility and allowed those with language impairments to express their needs \cite{Anumanchipalli*{{{etal}}}{{2019}}}, *Bhaya-Grossman*{{{Chang}}}*{{2022}}}, *Chang*{{{etal}}}*{{2015}}}}. *Beyond motor function, humans suffer profoundly from memory and emotional deficits that severely impact daily life, most notably in Alzheimer' s disease (AD) and post-traumatic stress disorder (PTSD) \cite{Cisler{{{etal}}}{{2024}}}, *Coughlan*{{{etal}}}*{{2018}}}, *Fenster*{{{etal}}}*{{2018}}}, *Kim*{{{etal}}}*{{2025}}}, *Mary*{{{etal}}}*{{2020}}}}. *AD, a neurodegenerative disease, progressively erodes the spatiotemporal fabric of memory—from forgetting loved ones' faces to losing the way home—ultimately destroying temporal and spatial cognition and self-identity \cite{Coughlan{{{etal}}}{{2018}}}}. *PTSD manifests memory' s destructive power differently: traumatic episodic memories become pathologically over-consolidated, forcing patients to repeatedly re-experience fear and blurring the boundary between reality and recollection \cite{Fenster{{{etal}}}{{2018}}}}. *Both disorders represent dysregulation of the episodic memory system: patients cannot organize spatiotemporal experiences into coherent cognitive maps or update existing ones \cite{Behrens{{{etal}}}{{2018}}}, *Cisler*{{{etal}}}*{{2024}}}, *Coughlan*{{{etal}}}*{{2018}}}, *Whittington*{{{etal}}}*{{2022}}}}. *BCI technology offers new hope for treating these conditions. The envisioned future of BCI lies in decoding advanced cognitive functions such as emotion, memory, and*

consciousness, while restoring or enhancing brain function through closed-loop interaction and adaptive adjustment \cite{Shanechi{2019}}. This review focuses on memory, particularly episodic memory with spatiotemporal context. We first briefly introduce BCI technology and clinical memory intervention needs, then emphasize current progress in decoding spatial and emotional information in episodic memory, followed by recent work leveraging these neural mechanisms for open-loop and closed-loop neuromodulation to enhance memory and achieve clinical applications. Finally, we discuss future visions for the field.

2.1 Evolution of Brain-Computer Interface Technology

A brain-computer interface is fundamentally a brain-external device (e.g., computer, robotic arm) communication system that decodes users' mental states or intentions to enable direct interaction with the environment \cite{Gao_{{{etal}}{{2021}}}, Lebedev{{{Nicolelis}}{{2017}}}, Wolpaw{{{Wolpaw}}{{2012}}}}. *It can both "read" brain intentions to control external devices and "write" stimulation signals to regulate neural activity* \cite{Xiao{{{etal}}{{2024}}}}. *A complete BCI system generally comprises five components [Figure 1: see original paper]. (1)* ***Signal acquisition****: Electrodes capture neural activity evoked by cognitive behaviors, including action potentials from single neurons (spikes) or local field potentials (LFPs) generated by synchronized neural ensemble activity. (2)* ***Signal processing****: Raw electrode recordings undergo preprocessing such as signal enhancement and noise reduction, followed by feature extraction to obtain critical information. (3)* ***Signal decoding****: Machine learning algorithms construct mapping models between neural activity patterns and user commands (e.g., robotic arm control), converting neural features into control commands. (4)* ***Command execution****: Decoded signals drive terminal devices like prosthetics or robotic arms; alternatively, external devices "write" instructions to the brain (typically via neuromodulation), establishing brain-machine communication. (5)* ***Feedback****: Users observe external device responses and adjust their thoughts or intentions to control brain signals more effectively* \cite{Edelman{{{etal}}{{2025}}}, Oganesian{{{Shanechi}}_{{2024}}}}.

Electrodes are central hardware components as they acquire neural signals or deliver electrical stimulation. Based on implantation approach, BCIs are classified as non-invasive or invasive (including semi-invasive). Non-invasive electrodes (e.g., scalp EEG) have significant limitations: low spatial resolution (recording signals from millions of neurons), inability to precisely localize deep brain regions (e.g., amygdala, hippocampus), poor signal quality (attenuation by scalp, skull, CSF, and brain tissue), substantial high-frequency activity attenuation, and susceptibility of low-frequency signals to physiological noise. Additionally, their modulation capacity is limited, as conventional transcranial electrical stimulation can only non-specifically affect superficial cortical layers. Semi-invasive electrodes, implanted beneath the skull but outside the cortex, primarily use

electrocorticography (ECoG) for signal acquisition and analysis. While offering significantly improved signal quality compared to non-invasive methods, they still cannot precisely target deep brain structures. These technical limitations severely constrain precise analysis and modulation of advanced cognitive functions like emotion and memory.

Invasive electrodes fall into two functional categories: microelectrodes that acquire single-neuron action potentials (spike signals) and macroelectrodes that record LFPs. Surgically implanted in cortical or deep brain regions, these electrodes enable millisecond-level temporal resolution, support precise microcurrent modulation, and offer high spatiotemporal resolution and rapid information transmission, providing critical technical support for precise neural circuit analysis and intervention \cite{Kirkby_{{{etal}}*{{2018}}}, *Sani*{{{etal}}_{{2018}}}}.

Invasive BCI technology has achieved remarkable progress in motor function restoration. At the 2014 Brazil World Cup opening ceremony, Duke University' s brain-controlled exoskeleton system, using electrode arrays implanted in the motor cortex, successfully helped a paralyzed teenager perform the kickoff by converting neural signals into robotic leg movement commands within 300 milliseconds \cite{Nicolelis_{2014}}. In 2024, Neuralink' s human trials achieved new breakthroughs, enabling patients to control robotic arms for fine movements like drinking water and typing, marking a new stage in motor function reconstruction \cite{Kumar_{{{etal}}*{{2025}}}, *Vindhya*{{{etal}}*{{2024}}}}. *Currently, the technology is expanding from motor control to cognitive functions. Through neural encoding/decoding algorithms and closed-loop feedback systems, researchers aim to achieve bidirectional interaction: decoding memory-related mental activity while adaptively stimulating specific neural circuits \cite{Shanechi*{2019}}*. This development offers new avenues for personalized treatment of PTSD and AD and may extend to frontier domains like consciousness regulation and cognitive enhancement. Notably, relevant human studies primarily rely on patients with refractory epilepsy who require intracranial electrode implantation (e.g., subdural or stereoelectroencephalography) for seizure focus localization, providing researchers with unique opportunities to simultaneously record high-spatiotemporal-resolution neural signals (mainly LFPs) that offer a window into the mechanisms of memory and emotion.

2.2 Memory Intervention Needs

AD has become one of the world' s most severe health crises. Due to its irreversible progression and unclear etiology, treatment becomes extremely limited in middle-to-late stages, making early screening and intervention the current research focus \cite{Coughlan_{{{etal}}*{{2018}}}, *Coughlan*{{{etal}}*{{2019}}}, *Igarashi*{2023}}. The disease typically manifests as progressive loss of episodic memory, particularly significant deficits in spatial navigation and memory function \cite{Coughlan_{{{etal}}*{{2018}}},

Lester{{{etal}}_{{2017}}}}. These deficits often lead to social isolation and trigger anxiety and depression. Existing treatments can only temporarily alleviate symptoms without reversing the neurodegenerative process, highlighting the clinical value and social significance of studying spatial memory decoding and modulation.

In stark contrast to AD' s memory loss, PTSD' s core problem lies in the over-consolidation of negative memories \cite{Cisler_{{{etal}}*{{2024}}}, *Fenster*{{{etal}}*{{2018}}}}. *Functional imbalance between the hippocampus and amygdala severely disrupts the relationship between memory and emotion regulation systems, leading to abnormal strengthening of traumatic memories \cite{Anderson*{{{etal}}*{{2025}}}, Mary*{{{etal}}*{{2020}}}}. This pathological state manifests as patients' inability to distinguish traumatic experiences from normal events, resulting in persistent excessive anxiety in daily environments, which in turn further strengthens traumatic memories, creating a vicious cycle \cite{Brewin*{{{etal}}*{{2025}}}}. This situation urgently demands rapid and effective treatments to address the growing patient population \cite{Cantor*{{{etal}}_{{2023}}}}.*

The interaction mechanism between emotion and memory has been well-validated in neuroscience research. Studies show that emotional valence critically regulates episodic memory encoding and retrieval processes \cite{Akiki_{{{etal}}*{{2025}}}, *Bicanski*{{{Burgess}}*{{2020}}}, *Dolan*{{{Dayan}}*{{2013}}}, *Nyberg*{{{etal}}*{{2022}}}, *Pronier*{{{etal}}*{{2023}}}, *Sharp*{2025}, Sosa_{{{Giocomo}}*{{2021}}}, *Tomar*{{{McHugh}}*{{2022}}}}. *The brain optimizes decision-making and guides future actions by encoding important information into long-term memory \cite{Shohamy*{{{Adcock}}*{{2010}}}}. Meanwhile, event relevance and individual emotional states modulate the strength of episodic memory formation, thereby influencing consolidation and retrieval efficiency \cite{Lloyd*{{{Nieuwenhuis}}_{{2024}}}}.*

Since episodic memories typically carry distinct emotional imprints, when this balance is disrupted, trauma-related scenes become erroneously encoded as "danger signals," triggering pathological avoidance and hypervigilance—the hallmark symptoms of PTSD. These findings not only explain the neural basis of memory disorders but also point toward therapeutic breakthroughs; elucidating the interaction mechanism will be key to clarifying the pathogenesis of AD and PTSD.

In terms of treatment strategies, neuromodulation of memory has gained increasing attention. For AD patients, studies show that deep brain stimulation (DBS) targeting the hippocampal dentate gyrus can significantly improve spatial memory decoding efficiency \cite{Mankin_{{{Fried}}*{{2020}}}}. *This research demonstrates that neuromodulation can not only enhance memory encoding efficiency but also strengthen memory capacity by reshaping hippocampal function \cite{Mankin*{{{Fried}}*{{2020}}}}. For PTSD patients, neuromodulation aims to reconstruct balanced memory retrieval: suppressing amygdala-mediated excessive fear responses*

\cite{Milad{{{Quirk}}{{2012}}}} while enhancing prefrontal emotional regulation of traumatic memories \cite{Schiller{{{etal}}{{2010}}}}, thereby helping transform rigid traumatic flashbacks into controllable ordinary memories \cite{Isserles{{{etal}}{{2021}}}}. Closed-loop modulation systems based on individualized brain network features can both monitor spatial memory fluctuations in AD patients in real-time to dynamically optimize stimulation parameters and rapidly intervene in memory reconsolidation processes when PTSD patients encounter trauma cues \cite{Oganesian{{{Shanechi}}{{2024}}}}, Shanechi{2019}}. Therefore, systematic analysis of episodic memory decoding and modulation mechanisms is not only crucial for revealing memory' s essence but also directly relevant to developing effective clinical intervention strategies.

3 Spatial Memory Decoding

Neural decoding mechanisms of spatial information have become a critical breakthrough in understanding memory processing \cite{Behrens_{{{etal}}{{2018}}}}, *Buzsaki{{{Tingley}}{{2018}}}*, *Eichenbaum*{2017a}, Eichenbaum_{2017b}, Buzsaki_{{{Moser}}{{2013}}}, *Hunt{{{etal}}{{2021}}}*, *Niv*{2019}, Whittington_{{{etal}}{{2022}}}*. Two core findings have emerged: First, hippocampal place cell populations precisely encode movement trajectories through theta rhythm phase precession \cite{Buzsaki{{{Tingley}}{{2018}}}}, Buzsaki{{{Moser}}{{2013}}}*. Second, entorhinal grid cells construct a metric coordinate system for spatial cognition through hexagonal firing patterns \cite{Chen{{{etal}}{{2024}}}}, Rowland{{{etal}}{{2016}}}, Rueckemann{{{etal}}{{2021}}}*. fMRI combined with multi-voxel pattern analysis (MVPA) shows that while machine learning algorithms can reconstruct spatial orientation and position coordinates to recover subjects' paths during virtual navigation, decoding accuracy remains only slightly above chance due to signal quality limitations, far from BCI application requirements \cite{Hassabis{{{etal}}{{2009}}}}*. Recent research has refined spatial memory decoding into three key dimensions: movement state decoding reveals how the brain generates path predictions during dynamic movement \cite{Seeber{{{etal}}{{2025}}}}; boundary cue decoding reflects edge detection and spatial boundary perception \cite{Hardcastle{{{etal}}{{2015}}}}, Long{{{etal}}{{2024}}}, Solstad{{{etal}}{{2008}}}}; and precise position decoding demonstrates high-fidelity neuronal responses to specific locations \cite{Wikenheiser{{{Redish}}_{{2015}}}}*. These findings provide critical theoretical foundations for optimizing BCI technology and neuromodulation strategies. Precise analysis of different dimensions of spatial memory neural representations can not only optimize path planning algorithms for motor assistive devices but also provide precise spatiotemporal references for targeted neuromodulation, enabling precise intervention for spatial memory disorders.

At the mechanistic level, spatial memory formation depends on continuous integration of velocity, position, and boundary information. Recent human single-cell studies confirm that spatial coding cells are conserved across

species \cite{Ekstrom_{{{etal}}{{2003}}}, *Jacobs*{{{etal}}{{2013}}}, *Killian*{{{etal}}{{2012}}}, *Nadasdy*{{{etal}}{{2017}}}}, *and similar functional representations exist in the prefrontal cortex* \cite{*Chen*{{{etal}}{{2021}}}, *Long*{{{etal}}{{2024}}}}. *Current research primarily employs invasive LFP-based electrophysiology, with the core challenge being reliable spatial information extraction from these signals* \cite{*Kunz*{{{etal}}_{{2019}}}}. Notably, experimental paradigms are undergoing an important shift from traditional virtual navigation to real-world environmental navigation, offering new perspectives for understanding spatial memory mechanisms. Below, we discuss recent advances in decoding key spatial elements like movement states and environmental boundaries within this paradigm shift.

3.1 Decoding Movement States in Spatial Memory

Hippocampal theta oscillations serve as a biomarker for movement states, providing crucial insights into the dynamic neural mechanisms of spatial navigation. Early desktop VR studies found transient theta power enhancement at movement onset, with positive correlation between movement distance and theta activation strength. However, these studies failed to observe sustained theta activation during continuous movement, differing markedly from rodent findings \cite{Herweg_{{{etal}}{{2020}}}}. *This discrepancy likely stems from VR paradigm limitations. Recent research using wireless depth electrodes in epilepsy patients navigating real environments has yielded breakthrough discoveries: First, movement states (stationary/moving) and velocity can be effectively decoded from theta power. Second, theta activity exhibits characteristic short bursts (averaging 400ms), with burst frequency positively correlated with movement speed. Third, blind subjects relying on somatosensory input show more persistent and frequent theta bursts* \cite{*Aghajan*{{{etal}}{{2017}}}, *Bohbot*{{{etal}}{{2017}}}}. *Beyond theta oscillations, gamma power also represents movement processes, and cross-frequency coupling between gamma power and theta phase effectively decodes spatial information integration strength* \cite{*Colgin*{{{etal}}{{2009}}}, *Griffiths*{{{Jensen}}{{2023}}}, *Heusser*{{{etal}}{{2016}}}, *Lisman*{{{Jensen}}{{2013}}}, *Tort*{{{etal}}_{{2009}}}}. This phase decoding mechanism provides important theoretical foundations for developing more precise movement state decoding algorithms and offers new perspectives for understanding real-world spatial navigation mechanisms.

3.2 Decoding Environmental Boundaries in Spatial Memory

Environmental boundary perception plays a crucial role in spatial memory formation and segmentation, providing important references for navigation and mechanisms for correcting position estimation errors. Early desktop VR studies revealed associations between human hippocampal subicular theta oscillations and boundary coding: theta power was significantly higher when target locations were near virtual environmental boundaries, negatively correlating with distance to the boundary \cite{Lee_{{{etal}}{{2018}}}}. *With the shift to real-world*

paradigms, a 2020 Nature *breakthrough study using wireless electrode recordings systematically compared boundary coding mechanisms during self-navigation versus observation tasks. Notably, both task modes showed enhanced medial temporal lobe theta and gamma power when spatial positions approached physical boundaries, confirming the cross-task universality of boundary reference neural coding. More importantly, this study first revealed task relevance modulation of boundary coding: when subjects invested more cognitive resources (e.g., actively searching for targets or judging others' positions), theta oscillation boundary responses became more pronounced \cite{Stangl{{{etal}}}{{2021}}}. Subsequent work further refined this mechanism, finding that medial temporal lobe theta enhancement effects were task-specific—only appearing when tasks explicitly required boundary attention \cite{Maoz{{{etal}}}{{2023}}}, Seeber{{{etal}}}_{{2025}}}}*. These findings collectively construct a "task-driven boundary coding" dual-layer neural mechanism model, deepening understanding of spatial memory' s neural basis and providing theoretical support for developing environment-cue-based memory enhancement neuromodulation.

3.3 Decoding Spatial Position in Spatial Memory

Neural decoding of current and target positions represents the core issue in spatial memory research, involving dynamic coding by grid cells and memory trace cells. Regarding entorhinal grid representations, two independent 2018 studies simultaneously discovered hexadirectional modulation of human entorhinal theta activity \cite{Chen_{{{etal}}}{{2018}}}, *Maidenbaum{{{etal}}}{{2018}}}, providing electrophysiological basis for similar fMRI findings \cite{Bao{{{etal}}}{{2019}}}, Bongioanni{{{etal}}}{{2021}}}, Julian{{{Doeller}}}{{2021}}}, Moon{{{etal}}}{{2024}}}, Nitsch{{{etal}}}{{2024}}}, Park{{{etal}}}{{2021}}}, Vigano{{{etal}}}{{2023}}}, Wagner{{{etal}}}{{2023}}}}. This representation not only correlates positively with spatial memory performance but also shows significant spatiotemporal dynamics—enhanced at environmental boundaries and gradually stabilizing with learning \cite{Chen{{{etal}}}{{2018}}}}. Notably, movement speed significantly modulates representation strength, becoming more pronounced during high-speed movement. Behavioral evidence further indicates that grid coding' s spatiotemporal dynamics can predict spatial memory biases \cite{Chen{{{etal}}}{{2015}}}}, while pathological studies reveal grid coding degeneration in both schizophrenia and Alzheimer' s patients \cite{Convertino{{{etal}}}_{{2023}}}}*, highlighting its critical role in spatial memory.

Regarding target location coding, Qasim et al. discovered "memory trace cells" in the entorhinal cortex that undergo firing rate remapping under different target cue conditions, with discharge patterns closer to subjects' subjective memory locations than objective coordinates \cite{Qasim_{{{etal}}}{{2021}}}}. *Population neural activity analysis confirmed that even with recall biases, neuronal discharge centers remained closer to subjective response locations, revealing the dominant role of memory reference frames in spatial coding. Subsequent re-*

search found that posterior hippocampal theta activity is modulated by target distance \cite{Liu{{{etal}}}{{2023}}}}, with stronger theta activity when subjects were farther from targets. Recent work has further expanded understanding of goal-directed processes in real-world navigation: Maoz et al. found that successful memory retrieval triggered significant medial temporal lobe theta power elevation 0.5 seconds before reaching target locations—a feature absent during erroneous retrieval or visible cue tasks \cite{Maoz{{{etal}}}{{2023}}}}. Seeber et al. compared real and imagined navigation, revealing theta oscillations' critical role in route segmentation coding—under both conditions, theta activity intermittently enhanced at turning nodes, with activation overlapping in left anterior hippocampus, confirming the endogenous nature of spatial memory coding mechanisms \cite{Seeber{{{etal}}}_{{2025}}}}. These findings collectively construct a dual decoding model for spatial memory: the grid cell system provides precise metric representations of current location through hexadirectional modulation, while memory trace cells and hippocampal theta dynamics construct target location reference frames based on episodic memory. Together, they support memory-based spatial navigation behavior, laying theoretical foundations for developing high-performance spatial memory neuromodulation.

Current spatial memory decoding research has made important progress, yet several key issues remain unresolved. Existing work primarily focuses on independent components of spatial memory, particularly the core role of hippocampal theta oscillations \cite{Herweg_{{{etal}}}{{2020}}}}. *However, achieving finer decoding requires future research in two directions: technically, high-density sampling of LFP signals across hippocampal subregions combined with complex navigation paradigms closer to real-world scenarios; theoretically, recognizing that spatial memory is not simply the sum of activities across brain regions but fundamentally depends on multi-regional coordination, particularly fronto-hippocampal circuits \cite{Eichenbaum{*2017b}, Klein-Flugge_{{{etal}}}{{2022}}}, Knudsen{{{Wallis}}}{{2022}}}}, Patai{{{Spiers}}}{{2021}}}}. Recent advances provide important clues: Chen et al. found that medial prefrontal cortex theta oscillations also exhibit grid-like representations synchronized with entorhinal grid orientation, suggesting theta-rhythmic coordination of grid information between these systems \cite{Chen{{{etal}}}{{2021}}}}. However, three factors limit current understanding: delayed discovery of prefrontal coding mechanisms, traditional experimental paradigms' insensitivity to prefrontal activity, and lack of effective network analysis methods \cite{Patai{{{Spiers}}}_{{2021}}}}*. Future spatial memory decoding research should focus on developing "prefrontal-hippocampal" network paradigms. This direction will help reveal whole-brain network mechanisms of spatial memory, develop more precise decoding algorithms, and drive the paradigm shift from single-region to network-based decoding. Only by understanding spatial memory' s neural basis at the systems level can we achieve complete decoding and application of its complex functions.

4 Decoding Emotional Valence

Episodic memory encoding and retrieval depend not only on spatial elements but are also profoundly modulated by emotional valence \cite{Bicanski_{{{Burgess}}{{2020}}}, *Boccara*{{{etal}}{{2019}}}, *Butler*{{{etal}}{{2019}}}, *Nyberg*{{{etal}}{{2022}}}, *Sosa*{{{Giocomo}}{{2021}}}}. *Emotion not only significantly affects information selection and encoding but also optimizes future choices and behaviors by strengthening memory for valuable experiences \cite{Shohamy{{{Adcock}}{{2010}}}}. Meanwhile, individual emotional states influence memory formation strength, thereby modulating consolidation and retrieval efficiency \cite{Lloyd{{{Nieuwenhuis}}{{2024}}}}. From an evolutionary perspective, approaching rewards and avoiding punishment constitute fundamental survival motivations, requiring spatial localization for foraging and threat avoidance. Spatial perception not only concerns survival but also supports complex behaviors and advanced cognitive processes \cite{Bellmund{{{etal}}{{2018}}}}. At the neural level, fear conditioning can induce hippocampal place cell remapping and promote representation stability \cite{Wang{{{etal}}{{2015}}}}, while hippocampal sequences integrate spatial representations, task states, and reward information \cite{Sosa{{{Giocomo}}{{2021}}}}. Emotional processing involves multiple brain regions: the insula encodes aversive emotions through 30-150 Hz gamma oscillations; ventral anterior cingulate processes positive emotions while dorsal subregions specifically participate in negative emotion processing \cite{Bellmund{{{etal}}{{2018}}}}. Amygdala beta activity closely correlates with subjective fear ratings, while ventral striatum preferentially encodes pleasure \cite{Xiao{{{etal}}{{2023}}}}. These functional differentiations establish the circuit basis for emotion regulation and provide potential targets for clinical intervention. For example, beta reduction in dorsolateral prefrontal cortex of depressed patients often accompanies symptom relief, but recent studies show high-frequency gamma activity may be more predictive of treatment efficacy \cite{Xiao{{{etal}}_{{2023}}}}. Common psychiatric disorders (e.g., anxiety, depression) often stem from dysregulation of negatively valenced avoidance motivation systems. Therefore, neuromodulatory interventions must simultaneously suppress excessive negative emotional responses while enhancing positive emotions to reestablish motivational balance. Based on these associations, we integrate research on neural mechanisms of emotion and motivation systems, emphasizing differential processing of negative and positive valence neural pathways in subsequent decoding and modulation strategies.

4.1 Decoding Negative Valence

Emotion network functional connectivity exhibits significant dynamic heterogeneity, with distinct coupling patterns across brain regions and frequency bands having specific functional significance. Orbitofrontal cortex encodes stimulus emotional value through beta-band activity, with phase synchronization to the amygdala participating in emotion-decision integration, while medial prefrontal cortex exerts top-down inhibition on the amygdala via theta bands,

playing a key role in fear extinction \cite{Sonkusare_{{{etal}}{{2023}}}}. *Threat memory formation, consolidation, and retrieval involve complex interactions among hippocampus, amygdala, and prefrontal cortex, with these regions' coordinated actions providing important clues for understanding neural mechanisms* *cite{Brown{{{etal}}{{2020}}}, Suarez-Jimenez{{{etal}}{{2018}}}, Tomar{{{McHugh}}{{2022}}}, Wise{{{etal}}_{{2021}}}}.

Specifically, dorsal hippocampal neurons alter their firing characteristics during fear and extinction learning, with different cell subpopulations preferentially encoding fear or safety information \cite{Wang_{{{etal}}{{2015}}}}. *The amygdala' s lateral and basal nuclei are considered key sites for fear memory storage* *cite{Fanselow{{{LeDoux}}{{1999}}}}. *The basolateral amygdala complex has long been viewed as a core structure for memory consolidation, remaining involved in long-term fear memory maintenance after consolidation completion* *cite{Gale{{{etal}}{{2004}}}}. *In animal experiments, place cells show clear avoidance behaviors when re-exposed to fear-conditioned environments* *cite{Wu{{{etal}}{{2017}}}}. *Research has also revealed functional connectivity mechanisms between amygdala, entorhinal cortex, and ventral hippocampus in contextual fear memory consolidation* *cite{Chaaya{{{etal}}{{2018}}}}. *Notably, the pathway from basolateral amygdala complex to entorhinal cortex is suppressed during fear memory acquisition and reactivation, primarily affecting glutamatergic neurons. Suppressing this pathway during acquisition induces freezing behavior deficits, while similar suppression during memory reactivation does not produce the same effect* *cite{Sparta{{{etal}}_{{2014}}}}. These studies collectively support the critical role of the amygdala-centered limbic network in negative emotion processing.

Recent research has shifted toward neural coding mechanisms of human limbic networks during natural emotional behaviors. An innovative study used computer vision to classify and label subjects' spontaneous emotional behaviors while synchronously recording neural activity, systematically exploring midbrain limbic network dynamics \cite{Bijanzadeh_{{{etal}}{{2022}}}}. *Researchers performed LFP time-frequency analysis on key nodes including insula, prefrontal cortex, cingulate, amygdala, and hippocampus, extracting power features in theta, alpha, beta, and gamma bands to construct a "spectral-spatial" joint feature matrix. Based on this, they developed an emotional behavior classifier using decision tree algorithms, validating the effectiveness of multi-scale neural oscillation features in parsing emotional behavior neural codes. However, this study did not deeply explore dynamic network properties among these brain regions. Kirkby et al. provided a powerful complement by integrating multiple key brain regions of the human limbic system (hippocampus, anterior cingulate, insular cortex, prefrontal cortex, and inferior temporal cortex), analyzing inter-regional frequency synchronization changes, and identifying a subnetwork centered on amygdala-hippocampus beta-band functional connectivity* *cite{Kirkby{{{etal}}_{{2018}}}}. Notably, this network' s dynamic properties closely relate to daily emotional states: during emotional deterioration, its connectivity pattern variability significantly increases, and individuals with

such features show more pronounced anxiety tendencies. This discovery provides not only a computational method for parsing behavior-relevant neural networks from high-dimensional neural data but also reveals a cross-individual conserved neural coding mechanism in the limbic system—where coordinated activity across brain regions at specific frequency bands participates in emotion regulation through dynamic adjustment of network connection strength.

Jackson' s team further explored the cellular basis of amygdala-hippocampus beta-band synchrony \cite{Jackson_{{{etal}}_{{2024}}}}. Using mouse models, they found that synchrony between basolateral amygdala and ventral hippocampal neuronal ensembles could predict anxiety-related behavior. In-depth research revealed this synchrony primarily depends on coordinated activity of somatostatin-expressing inhibitory interneurons in both regions. In anxiety-inducing environments, these neurons' synchronization levels significantly increase, peaking before avoidance behaviors appear. Optogenetic manipulation of neuronal synchrony bidirectionally altered mouse anxiety behaviors, further confirming the key role of specific inhibitory neural circuits in dynamic emotion regulation. These findings not only validate cross-species conserved emotion-motivation neural coding mechanisms but also provide important theoretical foundations for developing targeted neuromodulation strategies for mood disorders. Overall, this series of studies reveals the coordinated mechanisms of hippocampus, amygdala, and prefrontal cortex in fear learning and subsequent emotional memory storage and regulation, establishing a solid foundation for understanding emotion network function.

4.2 Decoding Positive Valence

Research on positive valence primarily focuses on interactions between the brain' s reward system and medial temporal lobe memory systems like the hippocampus \cite{Shohamy_{{{Adcock}}{{2010}}}}. *Reward-predictive stimuli often induce memory enhancement effects \cite{Knowlton{{{Castel}}{{2022}}}}. Reward or motivational relevance is jointly influenced by stimulus novelty and reward value. Under dopaminergic modulation from the ventral tegmental area (VTA) and amygdala projections to striatum and hippocampus, relevant memory information receives prioritized encoding \cite{Bromberg-Martin{{{etal}}{{2010}}}, Miendlarzewska{{{etal}}{{2016}}}}. Additionally, motivational salience may be partially restored each time previously rewarded memories are retrieved \cite{Luo{{{etal}}_{{2011}}}}*.

During novel environment exploration and reward-driven spatial tasks, dopamine release plays a crucial role in guiding subsequent trajectory replay, helping strengthen associations between new place cell assemblies and rewards \cite{Adamantidis_{{{etal}}{{2019}}}, *Girardeau*{{{etal}}{{2017}}}, *Klinzing*{{{etal}}{{2019}}}}. *Successful memory encoding under high-arousal stimuli is accompanied by stronger activation of midbrain dopaminergic regions and enhanced functional connectivity with the medial temporal lobe \cite{Bowen{{{etal}}{{2020}}}}. Early research identified midbrain regions,*

particularly the VTA, as primary sources of dopaminergic input to cortex and limbic system closely related to reward processing \cite{Ikemoto{2010}}. Midbrain dopaminergic inputs are thought to modulate hippocampal activity during learning, thereby enhancing encoding and hippocampus-dependent memory consolidation \cite{Gruber_{{{etal}}_{{2016}}}}.

During reward-related tasks, activation of dorsolateral and dorsomedial prefrontal cortex reflects motivational processing related to intention generation and cognitive control. Therefore, reward-related memory enhancement may be modulated through interactions between these prefrontal regions, both participating in motivation and cognitive control processes. Meanwhile, nucleus accumbens and striatum primarily mediate reward processing, while medial temporal lobe regions (including hippocampus and parahippocampus) handle episodic memory processing \cite{Shigemune_{{{etal}}_{{2017}}}}.

In spatial navigation, reward signals not only facilitate learning of reward locations or changes but also enhance recall and use of learned paths. After reward acquisition, dorsal hippocampal sharp-wave ripple activity significantly increases \cite{Sosa_{{{etal}}*{{2020}}}}, *synchronizing with reward-evoked dopamine release and potentially consolidating associations between recently experienced paths and reward outcomes* *cite{Foster{{{Wilson}}*{{2006}}}}. *Consistently, higher reward intensity increases reverse replay occurrence rates* *cite{Mattar{{{Daw}}*{{2018}}}} *and enhances matching between forward replay sequences and actual experience sequences* *cite{Bhattarai{{{etal}}*{{2020}}}}. *These studies demonstrate that replay processes are highly coupled with dopamine signals, establishing precise links between spatial positions of reward paths and outcomes* *cite{Sosa{{{Giocomo}}*{{2021}}}}. *Research also shows sharp-wave ripple activity supports inferential connections between reward-predictive cues and outcomes* *cite{Barron{{{etal}}_{{2020}}}}, suggesting replay applies not only to reward integration in spatial tasks but also to event associations in non-spatial contexts. In summary, the reward system participates in and modulates all stages of memory processing—including encoding, storage, and retrieval—through dopaminergic pathways, while complex and refined functional connectivity mechanisms between prefrontal regions and medial temporal lobe systems also play key roles in regulating memory formation and expression.

Compared to reward' s memory enhancement mechanisms, systematic research on interactions between negative valence (e.g., fear) and spatial memory remains lacking. A novel hypothesis gaining acceptance suggests that the hippocampal-entorhinal system' s key function is not limited to constructing spatial maps but rather generating event sequences that link individuals' spatiotemporal experiences to behavioral outcomes \cite{Buzsaki_{{{Tingley}}*{{2018}}}, *Rueckemann*{{{etal}}*{{2021}}}}. *Neuromodulatory signals can shape hippocampal-entorhinal representations, providing both local emotional value information and influencing global state distributions, thereby causing emotion-valence-dependent changes in spatial representations* *cite{Sosa{{{Giocomo}}*{{2021}}}}. *Studies*

have noted that hippocampus, amygdala, and prefrontal cortex jointly participate in reward and fear modulation of spatial memory, but the synchronization mechanisms among these regions remain unclear \cite{Bocchio{{{etal}}_{{2017}}}}. Whether reward (approach motivation) and fear (avoidance motivation) depend on different neural pathways lacks direct comparative research. Elucidating interactive coding mechanisms between emotional motivation and memory will not only help understand trauma survivors' generalized responses to specific contexts or spaces from a neurocomputational perspective but also provide important theoretical support for developing context-sensitive memory intervention strategies.

5 Open-Loop Neuromodulation of Spatial Memory and Emotion

Decoding and modulation constitute two key BCI components: precise decoding provides neural feature markers for targeted modulation, while effective modulation validates decoding mechanisms' reliability. In spatial memory, decoding studies of entorhinal theta oscillations and hippocampal place cell activity directly guide DBS target selection; emotion valence research identifying amygdala beta oscillations and reward system gamma activity provides biomarkers for mood disorder neuromodulation. This "decode-modulate" translation logic has been validated in multiple clinical studies and become an important strategy for memory and emotion neuromodulation.

5.1 Open-Loop Memory Modulation

Open-loop BCI memory modulation practice primarily relies on deep brain stimulation (DBS) of the hippocampal-entorhinal circuit. Research shows this circuit' s coding properties not only affect memory strength and duration but also provide intervention targets \cite{Kirkby_{{{etal}}*{{2018}}}}. *This circuit system evolutionarily retains spatial navigation mechanisms like place cells, grid cells, and border cells while integrating multimodal information and executing advanced cognitive functions (e.g., language and context construction) \cite{Whittington{{{etal}}_{{2022}}}}.* Therefore, modulating the hippocampal-entorhinal system can not only restore basic memory abilities but also potentially affect attention, decision-making, and social behavior.

The research lineage traces back to Ojemann team' s foundational work in the 1970s. They first discovered through electrical stimulation mapping of temporal and frontal cortex that interventions at different memory processing stages selectively affected semantic memory performance—whether verbal material recognition or visuospatial free recall \cite{Ojemann_{1978}}. Notably, the only stimulation target that improved memory was the ventrolateral thalamic nucleus, where stimulation during encoding significantly enhanced subsequent retrieval performance \cite{Ojemann_{1975}}. These early findings established the spatiotemporal specificity principle of memory modulation: intervention ef-

fects highly depend on precise matching between stimulation site and memory processing stage.

In the more complex domain of spatial memory, Suthana team' s 2012 *New England Journal of Medicine* study holds milestone significance \cite{Suthana_{{{etal}}{{2012}}}}. *Using a virtual reality navigation task (subjects played taxi drivers in a structured city), they first demonstrated that entorhinal cortex stimulation could improve navigation efficiency by resetting theta oscillations and enhancing hippocampal phase stability, manifested as improved path selection and task speed. This discovery broke through traditional hippocampal targeting limitations, revealing that upstream brain regions projecting to the hippocampus might offer superior modulation effects. However, Jacobs team' s 2016* Neuron *publication provided contradictory evidence, showing that 50 Hz DBS of entorhinal cortex significantly impaired object-location memory encoding in open-field environments, causing systematic recall position shifts \cite{Jacobs{{{etal}}_{{2016}}}}*. This contradiction may stem from fundamental task differences: structured environment navigation versus open-field object localization may involve different neural coding mechanisms. Subsequent research further refined these findings, with Kim et al. (2018) using intracranial EEG to confirm that theta-burst stimulation selectively disrupts functional coupling of spatial memory retrieval networks, causing spatial (but not temporal) memory retrieval-specific impairments.

5.2 Open-Loop Emotion Modulation

In emotion neuromodulation research, non-invasive stimulation techniques have become mainstream, including transcranial magnetic stimulation (TMS), transcranial direct current stimulation (tDCS), and transcranial alternating current stimulation (tACS). Weigand et al. used TMS to find that high-frequency stimulation of cingulate-dorsolateral prefrontal cortex connections could predict antidepressant effects, while high-frequency stimulation of ventrolateral prefrontal cortex enhanced voluntary emotion regulation capacity \cite{Weigand_{{{etal}}{{2018}}}}. *Such stimulation not only activates local regions but also triggers functional connectivity responses across prefrontal-subcortical networks, including emotion integration and subcortical emotion areas \cite{He{{{etal}}{{2023}}}}. However, TMS' s limited spatial resolution makes precise deep brain targeting difficult, and high-intensity stimulation may cause headaches, severely constraining clinical efficacy. Nitsche' s team (2012) used tDCS to demonstrate that left dorsolateral prefrontal cortex stimulation enhanced positive emotion recognition \cite{Nitsche{{{etal}}{{2012}}}}, while Fink and Exner' s (2019) bifrontal pole stimulation showed stable antidepressant effects \cite{Fink{{{Exner}}{{2019}}}}. Yet tDCS lacks sufficient penetration depth, and individual skull differences significantly affect current distribution, leading to inconsistent efficacy. Although tACS can improve emotion processing by modulating cortical rhythms \cite{Hu{{{etal}}_{{2021}}}}*, its mechanisms remain unclear and stimulation parameters lack standardization.

Despite non-invasive techniques' convenience, key emotion-regulating brain regions (amygdala, hippocampus, ventral striatum, orbitofrontal cortex) are deeply buried \cite{He_{{{etal}}}*{{2023}}}, *Weigand{{{etal}}}{{2018}}}}. *Traditional non-invasive neuromodulation suffers from insufficient spatial resolution and skull signal attenuation, making it difficult to precisely parse dynamic coding features of these nuclei or achieve targeted emotion circuit modulation. In contrast, invasive DBS technology, by directly implanting electrodes in these deep structures, achieves higher spatiotemporal resolution and precise modulation capability, offering new possibilities for treating refractory mood disorders, particularly treatment-resistant depression \cite{Sheth{{{etal}}}{{2022}}}}. *Common clinical DBS targets include subcallosal cingulate cortex, medial forebrain bundle, anterior limb of internal capsule, and ventral tegmental area \cite{Figee{{{Mayberg}}_{{2021}}}}. Mechanistically, Qasim' s research team (2023) employed a multimodal intraoperative neurosurgical paradigm, directly recording single-neuron discharges and LFPs from deep brain regions in epilepsy patients while synchronously applying targeted electrical stimulation. This strategy first confirmed in living human brains that during successful memory encoding, high-frequency activity (HFA) synchrony between hippocampus and amygdala positively correlates with stimulation-evoked emotional arousal. Critically, dual-intervention experiments (disruptive DBS and depression pathology controls) provided causal evidence: when this network' s HFA was artificially suppressed or affected by depressive symptoms, subjects' memory advantage for emotional stimuli selectively disappeared, accompanied by synchronous reduction in amygdala-hippocampus HFA coupling strength. This offers direct evidence for how noradrenergic system dysfunction impairs memory encoding via amygdala-hippocampus pathways. This research not only establishes theoretical foundations for DBS-based mood disorder treatments but also reveals neural oscillatory mechanisms of emotional memory encoding, providing crucial scientific basis for future precise neuromodulation strategies for memory disorders or PTSD.

Although open-loop BCIs have achieved 阶段性 progress in memory and emotion modulation, two core challenges remain: First, unclear neural mechanisms limit stimulation strategy design. While key physiological markers like theta rhythms and HFA synchrony have been identified, we cannot yet determine which neural activity patterns most directly contribute to new memory formation or successful emotion regulation. This mechanistic understanding gap directly affects the scientific basis and individualization of modulation parameters and target selection. Second, lack of dynamic adaptation mechanisms constrains modulation efficacy. Current DBS mostly uses fixed parameters, unable to adjust stimulation strategies in real-time according to individual neural state changes (e.g., mood fluctuations, fatigue, hormone levels, circadian rhythms). This "rigid input" may affect modulation efficacy or even produce counterproductive interference effects.

Consequently, increasing researchers are focusing on closed-loop neuromodulation technology—real-time neural activity detection with dynamic stimulation

adjustment to achieve precise, efficient, personalized neural regulation. Below we introduce representative achievements in this emerging direction.

Stimulation Target	Phase	Stimulation Parameters	Stimulation Duration	Open/Closed Loop	Measurement Task	Measurement Index	Stimulation Result	Reference
Hippocampus	Encoding	50Hz/0.5-1.5s	4.6-5s on / 4.6-5s off	Open-loop	Shortcut selection (structured field)	Path efficiency	Enhanced navigation	Suthana et al., 2012
Hippocampus	Encoding	50Hz/0.5-3s	4.6-5s on / 4.6-5s off	Open-loop	Object placement (open field)	Placement error	Impaired memory	Jacobs et al., 2016
Temporal lobe	Encoding	Theta burst	500ms	Open-loop	Verbal memory	Word recall rate	Enhanced memory	Kim et al., 2018
Amygdala-Hippocampus	Encoding	200Hz/7mA	20min	Open-loop	Emotional word memory	Negative word recall	Reduced negative memory	Inman et al., 2018
Lateral temporal	Encoding	50Hz/0.5-1.5mA	500ms	Open-loop	Visuospatial memory	Retrieval rate	Enhanced retrieval	Miller et al., 2015
Hippocampus-Entorhinal	Encoding	10, 25, 50, 200Hz/0.5-1.5mA	500ms	Open-loop	Spatial memory	Distance judgment	Impaired memory	Kucewicz et al., 2018
Lateral temporal	Retrieval	200Hz/0.5-1.5mA	500ms	Open-loop	Visuospatial working memory	Retrieval accuracy	Enhanced hippocampal theta synchronization	Ezzyat et al., 2018

6 Closed-Loop Invasive BCI: A Breakthrough Path for Memory Modulation

Addressing open-loop BCI limitations in mechanism clarity and adaptability, closed-loop neuromodulation technology, with its real-time monitoring and adaptive response capabilities, is gradually becoming the research frontier for memory and emotion intervention. Although no closed-loop studies have directly targeted spatial memory yet, multiple studies on semantic memory and sleep consolidation have preliminarily validated its advantages in temporal precision, stimulation targeting, and individualized intervention .

Memory consolidation depends on precise coordination of neural oscillations during sleep \cite{Adamantidis_{{{etal}}}*{{2019}}}, *Girardeau*{Lopes}-dos-Santos_{2021}, Klinzing_{{{etal}}}*{{2019}}}*. *Research indicates that during non-rapid eye movement sleep, coupling of slow oscillations (0.5-1 Hz), spindles (9-15 Hz), and sharp-wave ripples (80-140 Hz) is crucial for long-term memory formation. Slow waves regulate global neural synchrony, spindles assist information transfer, and ripples triggered by the hippocampus mediate memory replay and integration. This tripartite coordination forms the core mechanism converting short-term to long-term memory \cite{Boyce{{{etal}}}*{{2016}}}*, *Brodt*{{{etal}}}*{{2023}}}*, *Girardeau*{Lopes}-dos-Santos_{2021}, Maingret_{{{etal}}}*{{2016}}}*, *Parhizkar*{{{Holtzman}}}*{{2025}}}*, *Viejo*{{{Peyrache}}}*{{2020}}}*, *Zhang*{{{etal}}}*{{2025}}}*. *Based on this mechanism, Geva-Sagiv' s team constructed a closed-loop electrical stimulation system to enhance sleep-dependent memory consolidation \cite{Geva-Sagiv*{{{etal}}}_{{2023}}}*. Due to slow oscillations' high stability and detectability, researchers used them as BCI regulation markers. After epilepsy patients (with electrodes implanted in temporal and frontal lobes) completed word-pair association tasks, the system monitored slow-wave activity on temporal electrodes during non-REM sleep. Upon detecting enhanced slow-wave power, it immediately delivered brief high-frequency stimulation via frontal electrodes to achieve precise phase matching with slow waves. Results showed this closed-loop intervention significantly enhanced coordination among slow waves, spindles, and ripples, improving subjects' memory performance. This study first validated in humans that neural rhythm-based closed-loop stimulation can effectively promote sleep memory consolidation, providing important evidence for neuromodulation applications in memory.

Memory encoding efficiency can be enhanced through closed-loop neuromodulation. Kahana' s team proposed a closed-loop deep brain stimulation system that first achieved precise memory function modulation driven by real-time neural decoding \cite{Kahana_{{{etal}}}_{{2023}}}. Using word-list memory tasks (12 words/list from 3 semantic categories), they recorded neural activity in real-time during encoding and input it into a pre-trained logistic regression classifier. When predicted recall probability fell below 0.5, they immediately delivered a 200 Hz biphasic electrical stimulus (500 ms, 0.5 mA) to left temporal cortex. Key results showed this closed-loop stimulation improved recall rates by an average

of 19%, with neural patterns of increased high-frequency power and decreased low-frequency power stably predicting memory performance. This achievement not only validates closed-loop neuromodulation' s feasibility for enhancing memory encoding efficiency but also establishes a new "encode-decode-intervene" precise neuromodulation paradigm, providing an important model for cognitive enhancement strategies.

Closed-loop neuromodulation can reshape hippocampal network function. Kragel' s team innovatively employed closed-loop phase-locked stimulation to reveal hippocampal theta oscillations' regulatory mechanisms in cross-regional neural information transfer \cite{Kragel_{{{etal}}_{{2025}}}}. They tracked hippocampal theta phase in real-time during subjects' resting states and delivered precisely synchronized electrical stimulation to lateral temporal cortex. The study revealed three key findings: First, when external stimulation achieved phase-locking with hippocampal theta activity, it significantly enhanced hippocampal theta rhythmic neural synchrony during stimulation. Second, after stimulation intervention, functional connectivity between hippocampus and neocortex showed sustained enhancement, manifesting as steadily increased theta-band phase synchrony and enhanced hippocampal response magnitude to cortical stimulation. Third, control groups receiving same-frequency but non-phase-locked stimulation showed no significant changes in these network dynamics parameters. This study causally validates theta oscillations' core role in memory information flow and proposes a rhythm-synchronization-based closed-loop modulation strategy, offering new pathways for regulating hippocampus-dependent cognitive functions.

Despite breakthroughs in multiple closed-loop modulation instances, current research remains limited: task ecological validity is insufficient, with studies primarily using simple memory paradigms like word-pair or free recall, not yet extending to more ecologically valid spatial episodic memory. One non-invasive study attempted this in a VR memory game environment. Rudoler and colleagues (2024) designed a closed-loop device using spatial episodic memory tasks, applying multivariate decoding methods to EEG data and controlling stimulus presentation timing based on decoded brain states. Results showed scalp EEG signals could effectively distinguish successful from failed memory states, with decoding accuracy closely related to recall performance changes, providing feasibility evidence for closed-loop regulation in real interactive scenarios \cite{Rudoler_{{{etal}}_{{2024}}}}.

Comprehensively, future closed-loop memory modulation systems require breakthroughs in three aspects: First, temporally covering the entire memory process, including encoding, retrieval, and sleep consolidation phases. Second, content-wise distinguishing specific neural mechanisms for different memory types (semantic, spatial, temporal, emotional). Third, technologically enabling real-time monitoring of neural dynamics features like oscillatory coupling. Through intelligent adjustment of decoder parameters and stimulation strategies, systems can achieve dynamic adaptive regulation, ultimately attaining dual goals: providing

personalized precise treatment for memory disorder patients while developing safe and effective neural enhancement protocols for healthy populations.

7 Future Outlook

With rapid advances in machine learning, particularly deep learning, increasing attention focuses on how to use LFP signals from human invasive electrodes for real-time brain state decoding and modulation. Above we reviewed progress in episodic memory, particularly spatial memory and its key influencing factor —emotional valence. Spatial memory depends on sequential coding patterns of cell ensembles including place cells, grid cells, and head direction cells in the hippocampal-entorhinal system, modulated by specific oscillations including sharp-wave ripples at rest and theta oscillations during movement. Recent studies have successfully decoded individuals' navigation positions and movement directions in simple environments (e.g., T- or W-mazes) using these neural oscillations. Additionally, successful memory encoding, retrieval, and modulation involve specific frequency bands in broader brain regions like amygdala and prefrontal cortex. For instance, emotional motivation as a crucial component of episodic memory correlates with beta oscillations in large-scale brain networks. These frequency-specific field potential patterns provide novel perspectives for dynamic episodic memory decoding. However, real-world information flow is highly dynamic and high-dimensional, with complex state transitions during memory processes. How to efficiently mine LFP signal features and leverage advanced machine learning models for real-time monitoring, precise decoding, and effective intervention has become a critical challenge. We discuss this from two dimensions: brain mechanism understanding and technical implementation pathways.

7.1 Brain Mechanism Bottlenecks

Current understanding of human memory neural mechanisms remains limited. Research shows memory is not accomplished by single brain regions but depends on dynamic coordinated interactions in distributed neural networks \cite{Clarke-Williams_{{{etal}}}*{{2024}}}, *Kirkby{{{etal}}}{{2018}}}}. *Precise spatiotemporal coordination between hippocampus and neocortex is crucial for memory formation and retrieval, while emotional motivation processing relies on complex dynamic coupling between limbic and cortical regions. Individual differences and state dependencies greatly increase neural representation complexity. Factors like age, gender, and lifestyle significantly affect neural signal features, while psychological variables like attention level and cognitive load dynamically alter brain network functional states. In P300 paradigms, researchers observed a counterintuitive phenomenon: individuals with lower empathy produced stronger P300 amplitudes, reflecting that advanced cognitive function representation mechanisms may not follow intuitive assumptions *cite{Jin*{{{etal}}}_{{2012}}}}. These findings highlight the complexity and plasticity of advanced cognitive function neural representations, posing

enormous challenges for BCI technology.

Current challenges underscore the urgent need to construct refined neuroscientific theoretical frameworks. Recent frontier advances in computational neuroscience—particularly dynamic systems theory characterizing neural circuit spatiotemporal dynamics and population coding models parsing distributed neural representations—have opened new paradigms for studying memory' s neural coding mechanisms. These theoretical breakthroughs not only reveal the computational essence of neural activity state dependence but also provide key design principles for next-generation BCI technology by establishing quantitative mapping relationships between "dynamic coding-cognitive function." It is crucial to emphasize that only causal (not merely correlational) understanding of cognitive neural mechanisms can enable the paradigm shift from empirically driven coarse decoding to principle-guided precise modulation, ultimately propelling the field into a new stage of mechanism-targeted intelligent intervention.

7.2 Technical Progress and Challenges

Achieving high-precision, stable, and individualized neuromodulation systems represents the core technical challenge for invasive BCIs. Major challenges concentrate on signal acquisition hardware, stimulation intervention strategies, and neural signal decoding. As the core information acquisition component, electrode system performance determines overall system stability and parsing precision. Current commonly used silicon-based rigid electrodes, despite high spatial resolution, face signal decay (typically 40% within 6 months), poor biocompatibility-induced gliosis, and mechanical mismatch causing neuronal damage (mortality up to 15-20%), severely limiting practicality. Researchers are addressing these bottlenecks through four directions: flexibility, high-density integration, new materials, and nanoscale fabrication. For example, Neuralink' s "neural lace" uses 4 m polyimide fibers for flexible implantation; Precision' s Layer7 system integrates 1024 channels on micron-scale flexible substrates; graphene electrodes with single-atomic-layer thickness (0.335nm) and high optical transparency become important materials for optoelectronic fusion interfaces; Harvard' s 50nm silicon nanowire electrodes achieve cellular-precision neural recording. These advances are pushing electrode systems toward "unfelt implantation, lifetime stability."

Meanwhile, stimulation patterns and parameter configurations critically determine neuromodulation efficacy. Current research shows stimulation effects are highly task-dependent. For instance, 50 Hz hippocampal stimulation significantly improves spatial memory in structured path planning tasks but may produce opposite effects in open-field navigation, indicating stimulation parameters must be finely matched to task type and current brain state. Additionally, closed-loop stimulation patterns are gradually replacing traditional open-loop approaches. For example, Kahana et al.' s temporal lobe closed-loop intervention automatically adjusts stimulation timing based on EEG-decoded states, significantly improving intervention efficacy across multiple memory

tasks \cite{Kahana_{{{etal}}}_{{2023}}}}.

Future modulation systems will further rely on neural feedback signals to achieve individualized, dynamically adjustable stimulation-response strategies. "Model-driven" closed-loop neuromodulation systems represent the main research direction. Traditional closed-loop strategies primarily rely on preset thresholds triggering stimulation when neural signals reach predetermined states, lacking predictive capability for complex neural dynamics. New-generation closed-loop systems learn the functional relationship between stimulation input and neural response through data-driven modeling, enabling automatic optimization of stimulation parameters (frequency, amplitude, rhythm). However, this approach faces multiple challenges: First, the vast parameter space requires efficient optimization algorithms. Second, stimulation may introduce strong artifacts interfering with authentic neural response acquisition. Third, neural systems exhibit extreme state dependence—individuals may produce completely different responses to identical stimulation parameters across emotional, arousal, or pathological states. Therefore, future closed-loop systems should integrate dynamic predictive models, state recognition mechanisms, and adaptive control algorithms to form "self-learning" capabilities, thereby supporting long-term stable operation in real-world environments.

Exploration of multi-target coordinated stimulation mechanisms is also becoming a research hotspot. For example, Kragel et al. found that low-frequency stimulation of lateral temporal cortex can enhance hippocampal theta rhythm synchrony, providing new neuromodulation mechanism support for interactions between spatial memory and emotion regulation \cite{Kragel_{{{etal}}}_{{2025}}}}. This suggests future attempts could coordinate modulation of multi-node pathways like hippocampus-prefrontal cortex-amygdala at more complex network levels, particularly improving intervention efficiency in complex scenarios like spatial navigation with emotional load. To avoid network instability and functional suppression risks from multi-point intervention, it is necessary to introduce modeling methods like dynamic causal modeling (DCM) to predict regulatory effects of different stimulation combinations, thereby achieving precise optimization of multi-target modulation.

Neural signal decoding capability directly determines intervention systems' ability to capture cognitive state changes. Currently, traditional machine learning methods (e.g., support vector machines, linear discriminant analysis) remain widely used for LFP or cortical signal classification and prediction. These methods have low computational cost suitable for low-latency scenarios but show clear limitations in handling nonlinear, non-stationary, multimodal signals. Recently, deep learning models have significantly improved decoding performance. Convolutional neural networks can extract spatial channel distribution patterns, recurrent neural networks excel at modeling temporal sequence dynamics, while Transformer architectures with self-attention mechanisms demonstrate stronger expressive power in long-term sequence modeling. These models support end-

to-end training, reduce manual feature dependencies, and achieve higher classification accuracy in spatial navigation and emotion recognition tasks. However, due to deep models' reliance on large samples and high computational resources, their application in small-sample and online real-time environments remains limited, requiring future development of few-shot transfer, model compression, and incremental learning technologies for practical implementation.

In summary, invasive neuromodulation system development is advancing synergistically across three directions: hardware engineering, neural modeling, and algorithmic intelligence. Through continuous optimization of electrode interface technology, refined stimulation pattern design, improved neural state decoding capability, and construction of intelligent closed-loop control architectures, future systems may achieve efficient, precise, and individualized intervention for spatial and emotional memory systems, providing entirely new technical support pathways for neuropsychiatric disease treatment. With deep integration of neuroscience and artificial intelligence, BCIs promise to open a new era of human-machine interaction, potentially reshaping medical rehabilitation paradigms and redefining the boundaries of human cognition and perception.

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Note: Figure translations are in progress. See original paper for figures.