Proceedings of ICBioMed 2025 Symposium: Computational Modelling and Simulation for Biology and Medicine
DOI: 10.54254/2753-8818/2025.LD26747

A Review of Strategies for Deploying Stage of Disease-Based Brain-Computer Interfaces for Communicative Functional Substitution in Amyotrophic Lateral Sclerosis

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Abstract. Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease characterised by a gradual loss of motor function and communication. Brain-computer interfaces (BCI), as an alternative means of communication without the need for muscle control, have demonstrated a unique potential for applicability in different disease stages of ALS. In this paper, we propose a set of BCI deployment strategies that match the disease stage based on the King clinical staging system, the MiToS functional staging system, and the evolutionary pathway of communication ability. In the early stage of the disease, when the patient's visual and attentional functions are still good, it is recommended to deploy non-invasive BCI systems, such as SSVEP and P300, because of their low training burden and high recognition efficiency. Priority is given to highly robust BCI paradigms that do not require active cooperation, such as trained auditory/tactile P300 systems, or implantable cortical systems to maintain residual communication abilities. This review emphasises that BCI training should be initiated as early as possible in ALS's early to middle stages to build a stable decoding model and lay the foundation for effective communication later. Future development of BCI should focus on stage adaptation, deployment feasibility and system durability improvement.

Keywords: Brain-computer interfaces, Amyotrophic lateral sclerosis, MiToS staging system, King's staging syste

1. Introduction

Amyotrophic Lateral Sclerosis is a severe, progressive neurodegenerative disease. Its core feature is the progressive degeneration of Upper Motor Neurons (UMN) and Lower Motor Neurons (LMN). This is characterised by a progressive loss of muscle strength in different regions, ultimately affecting key functions such as speech, swallowing, respiration, and limb movement [1]. However, ALS has traditionally been viewed as a disease centred on motor dysfunction. However, in recent years, more studies have redefined it as a multisystem degenerative disease. Approximately 15% of patients have comorbid frontotemporal dementia (FTD), and 30%-50% of patients have cognitive deficits at diagnosis. Cognitive deficits are present at diagnosis, with symptoms ranging from frontotemporal dementia to milder executive dysfunction or behavioural dysfunction [2-4]. These

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DOI: 10.54254/2753-8818/2025.LD26747

non-motor symptoms not only accelerate the disease's progression but also directly impact the integrity of communication skills and the efficiency of communicative intent.

Among the many dysfunctions of ALS, the loss of speech and communication is recognised as one of the most devastating and far-reaching in terms of quality of life. Despite significant heterogeneity at the individual level, more than 80-95% of ALS patients experience a sustained loss of communication ability as the disease progresses, ranging from mild dysarthria to an eventual "Locked-in State" (LIS) or even a "Completely Locked-in State" (CIS). "Completely Locked-in State"(CLIS), which means a complete loss of all voluntary movement and traditional communication [5,6]. The loss of language function not only deprives patients of the ability to express their needs and participate in communication and medical decision-making, but also seriously affects their social connection and sense of being.

Despite current advances in the diagnosis and treatment of ALS, the disease still lacks an effective cure. Approved drugs such as riluzole and edaravone only delay the course of the disease with limited improvement in functional status [2,7-8,9-10]. Antisense oligonucleotide therapies targeting mutations in SOD1, C9orf72, and other genes are still in the experimental stage and are only applicable to a small number of patients with familial ALS [11]. Clinical interventions rely mainly on supportive therapy, including antispasmodic drugs, nutritional support, respiratory assistance and speech rehabilitation training [5,12-14]. Regarding the maintenance of communication function, Augmentative and Alternative Communication (AAC) systems, such as eye trackers and facial electromyography input devices, are widely used in early and middle-stage patients. However, they are highly dependent on muscle activity and attention maintenance. They are often challenging to sustain in the advanced stages (especially complete locked-in state, CLIS) when motor function is severely impaired or the level of consciousness fluctuates [15,16].

In the face of the functional bottlenecks of the above interventions, the Brain-computer interface, a communication system that does not rely on peripheral neuromuscular output pathways, has demonstrated its irreplaceable clinical value in the mid- to late-stage ALS. The BCI provides the last technological channel to maintain autonomy, communication ability and social connectivity by recording and decoding brain signals to realise external expression of the patient's intentions. The BCI provides the last technological channel for maintaining autonomy, communication ability and social connectivity. Especially after entering the CLIS, the BCI system may become the only means of interaction to access an individual's subjective awareness and communicative intentions. Based on the staging framework of ALS, this review systematically explores the suitability and deployment strategies of different types of brain-computer interfaces, including non-invasive and invasive systems, at various stages of the disease. Given ALS patients' high degree of heterogeneity in terms of clinical manifestations and neurophysiological status, this paper further proposes a theoretical basis for individualised BCI design. It attempts to construct a dynamic model of "overall disease progression - speech function status - BCI interface". This paper further proposes the theoretical basis for individualised BCI design and attempts to construct a dynamic matching model between "overall disease progression - speech function status - BCI interface". The review will analyse each deployment stage's feasibility, risks, and technical challenges in the light of representative BCI application cases reported so far, aiming to provide theoretical support and strategic guidance for the future personalised design and clinical deployment of communicative BCI systems for ALS patients.

DOI: 10.54254/2753-8818/2025.LD26747

2. ALS staging framework

2.1. King's staging system

The King's staging system is based on the order of disease involvement in different anatomic regions. It delineates ALS's four main stages (stages I-IVB) from single-site onset to extensive multiregional progression, with good longitudinal traceability and sensitivity to progression (Figure 1). It reflects the temporal evolutionary trajectory of ALS in the anatomical dimension by identifying the path of lesion expansion from local to contralateral and other anatomical functional regions. Thus, King's system not only assists neurologists in tracking the dynamic process of lesion dissemination. Correlating with changes in neural network connectivity reveals its potential value in identifying intervention windows in BCI deployment strategies [17,18].

2.2. MiToS staging system

The MiToS (Milano-Torino staging system) is based on the patient's determination of loss of ability in four key daily function domains (movement, self-care, communication, and swallowing) and emphasises progressive changes in independence of living. The system categorises ALS into stages 0 to 4 and is sensitive to early signs of loss of daily functioning (Figure 1). As a result, MiToS is more closely aligned with the evolution of actual functional ability and is suitable for guiding the timing of BCI deployment with the goal of "functional replacement. For example, patients can enter the BCI training stage earlier than the loss of independent communication ability, thus prolonging their social participation ability and quality of life [17, 19].

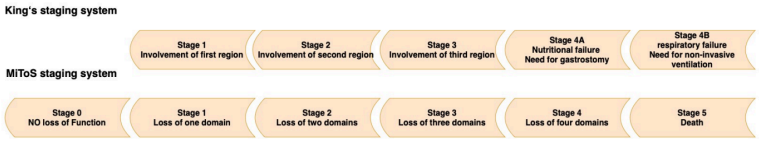

Figure 1. The diagram shows the framework for the progression of the King's staging system and the MiToS staging system in the course of ALS [20]

In the clinical management of ALS with BCI deployment, the two show complementarity on the timeline: the King's system applies a higher resolution in the early and middle stages, and MiToS is more sensitive to functional decline in the middle and late stages, especially changes in communication and swallowing ability. The joint use helps to form a structure-function bi-dimensional disease course portrayal framework, providing a precise temporal anchor point for BCI deployment [17, 21].

3. Characterisation of speech dysfunction in ALS

Since the rate of speech deterioration may not be consistent with the deterioration process of other parts of the motor system, and it directly affects the timing of the deployment of brain-computer interfaces (BCIs) in the replacement of communicative functions and the way of adaptation, it is necessary to conduct a special study on the process of speech deterioration in ALS [22]. Clinical observations and studies have shown that ALS patients show a high degree of individual variability in speech deterioration, with the site of onset being a key factor in determining the rate of speech deterioration [22]. Compared with patients with spinal cord onset, patients with medullary onset

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ALS showed lower speech rate and intelligibility at symptom onset (approximately 51 w/m and 14% lower, respectively), and the rate of decline was more rapid, with speech rate and intelligibility decreasing by 4.16 w/m and 1.61% per month, respectively. In contrast, patients with spinal cord onset had a significantly slower rate of decline (1.74 w/m and 0.28% per month, respectively), and the majority were able to maintain functional speech five years after onset [5, 12, 22]. More notably, the decline in speech rate usually precedes significant changes in intelligibility, where 120 w/m is considered a predictive threshold for rapid decline in intelligibility. Once speech intelligibility begins to decline, its degradation tends to be accelerated, rapidly leading to the loss of communication ability, which is highly detrimental to the deployment of BCI in the mid- to late-stage [15]. Therefore, recognising early signals of speech deterioration and intervening in conjunction with the individual's stage of the disease process are key prerequisites for developing communication replacement strategies for BCI.

4. BCI timely referral for communication support

Despite the significant potential of brain-computer interfaces (BCIs) as an alternative means of communication in ALS, existing research suggests that patients, families, and healthcare teams are generally hesitant or even avoidant of BCIs in the early stages of the process. Sicilia et al. (2021), in a survey of rehabilitation professionals, noted that despite the majority of positive attitudes expressed toward BCIs, they are often reluctant to recommend their use in real-world clinics due to a lack of experience, poor access to the technology, and concerns about privacy risks. Immaturity, poor equipment accessibility, and concerns about patient privacy risks make them reluctant to recommend its use. Similarly, Sattler and Pietralla (2022) reported that the general public is more inclined to accept BCIs for medical purposes but is significantly resistant to invasive BCIs, especially women, the elderly, and the religiously devout, who are considerably lower in terms of ethical acceptance and willingness to use [23,24]. In several ALS-related studies, the majority of patients (66.7%) preferred non-invasive BCIs, and some surveys showed that up to 29% of severely paralysed patients explicitly rejected implantable devices. Together, these results suggest that despite the potential benefits of BCI technology, its dissemination still needs to face realistic barriers to acceptance [25]. Therefore, when promoting the use of BCIs in the ALS population, priority should be given to developing non-invasive solutions that focus on comfort, independence, and manoeuvrability, complementing user-centred design to improve compliance and system satisfaction. At the same time, BCIs (e.g., P300 and SSVEP systems) should be deployed in the early stages of ALS to establish signal modelling and operating habits, so that a smooth transition to higher-performance semi-invasive or invasive solutions can be achieved after disease progression, to achieve a balance between technology acceptance and system performance.

The value of BCI in ALS has been well documented, especially around the time of entry into MiToS verbal function score decline or King's staging stage III, where BCI is often the only residual mode of active communication. Therefore, early deployment strategies based on staging systems are critical to extend the window of practical use, improve adherence, and slow communication deprivation. Unfortunately, this widespread resistance may delay the timely deployment of BCIs, compromising the opportunity for ALS patients to access alternative channels before communication function declines. The assessment of performing a BCI and the appropriate timing of the intervention remain the most critical clinical decision-making issues.

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5. System adaptation and multimodal deployment strategies for BCIs in various phases

In recent years, the usability and user experience of non-invasive BCI systems have continued to improve, and they have gained an initial base of application in ALS patients, showing practical value as an alternative communication method [26]. Meanwhile, invasive BCIs have also demonstrated good signal stability and long-term usability in several clinical studies. Considering that individuals with ALS differ significantly in terms of the type of disease onset, speed of functional deterioration, and pathway, the deployment of BCI systems is highly heterogeneous in practice. A systematic review of the deployment cases and adaptation strategies of different types of BCIs at various stages of ALS disease can help promote clinical understanding, enhance the confidence of patients and caregivers in their feasibility, and provide a practical reference for selecting individualised communication aids.

5.1. Application and training window of the BCI system in early ALS

In the early stages of ALS (King's stage 1 to 2 or MiToS stage 0 to 1), patients still retain good visual, cognitive, and partial motor functions, providing a critical window for the initial deployment of the BCI system. To capitalise on this stage's neurological and cognitive advantages, it is recommended to carry out BCI-related processes early, including signal acquisition, initial training of classifiers, adaptation of feedback mechanisms, and establishment of habits of use [27]. Especially for those with medullary onset, whose phonological abilities deteriorate faster than spinal cord onset type, the window period is more limited, thus making anterior BCI deployment more necessary [28].

In the early stages of ALS, SSVEP and P300 are two of the most practical non-invasive BCI paradigms available.SSVEP-BCI achieves efficient, limbless movement-free intention recognition by inducing a steady-state response of the visual cortex to stroboscopic stimuli, with high information transfer rates and real-time interaction potential. The SSVEP-BCI system developed by Lee et al. (2022) combined with an improved Modular Continuously Restricted Boltzmann Machine (MCRBM) with a command recognition accuracy of 96.14%, validating its potential for efficient application in ALS patients [29]. A positive voltage deviation is observable about 300 ms after the trigger event. It recognises the user's attentional response to the target stimulus, and is widely used for brain-controlled spelling and communication aids. Its low training threshold and intuitive operation suit pre-ALS patients with fair cognitive function [30].

Both of the above paradigms can be deployed in advance when patients' functions are still preserved to establish a stable alternative interaction pathway, which can provide critical support for the decline of communication ability in the middle and late stages. Introducing a non-invasive BCI system in the early stage not only helps to prolong the functional autonomy of patients, but also creates a technically and psychologically feasible basis for potential invasive systems to be deployed in the future, reflecting the clinical translation path of BCI of "advanced adaptation and progressive integration".

5.2. Application of the BCI system in intermediate ALS with a training window

Entering the intermediate stage of ALS (King's stage 3/MiToS stage2-3), patients have usually progressed to the point where they have impaired function in three anatomical regions, as evidenced by a wide range of motor dysfunctions, in particular severe weakness in the upper limbs as well as significant deterioration in balance function. This makes it difficult to maintain traditional

DOI: 10.54254/2753-8818/2025.LD26747

communication methods that rely on physical or spoken language, and oral expression is often significantly impaired, with some patients progressively losing their language skills. However, most patients retain limited eye movement control, some facial muscle activity, and basic concentration at this time, offering the possibility of continued use of non-invasive brain-computer interface (BCI) systems [3, 27].

To ensure the effectiveness and sustainability of the BCI system at this stage, the focus should be on the continuity of model training and the stability of signal classification. On the one hand, the quality of patients' neuroelectric signals needs to be assessed regularly to prevent signal degradation from affecting the decoding performance; on the other hand, the complexity of the BCI interaction interface should be reduced, and the cognitive burden and operational fatigue of patients should be alleviated by decreasing the number of stimuli, adjusting the frequency of visual blinks, or simplifying the decision logic. In addition, changes in cognitive and attentional functions, such as shortening of attention maintenance duration, response delay, or decline in executive function, should be dynamically monitored. The parameter settings of the evoked paradigm (e.g., stimulus duration, target-stimulus ratio, and feedback tempo) should be flexibly adjusted accordingly to maintain the system's response efficiency and experience of use.

At the same time, the mid-term phase is also a critical window for evaluating the need to transition from a non-invasive BCI system to an implantable BCI system. As the disease progresses and the patient's ability to manipulate the upper limbs and attentional regulation decreases, non-invasive systems (e.g., P300 or SSVEP) may face the following dilemmas [27]:

1. Decrease in signal stability: due to the presence of ambient noise interference in the arrangement of the scalp electrodes, coupled with fluctuations in the patient's daily state (fatigue, inattentiveness, and reduced visual adaptation), which may lead to unstable evoked potential signal amplitude and a significant decrease in system decoding accuracy;
2. Frequent interruptions and recalibration: Non-invasive systems often require frequent recalibration or calibration of model parameters, which puts high demands on cognitive resources and nursing assistance, leading to a deterioration of the patient's experience of using the device.
3. Increased subjective fatigue of the user: due to the frequent visual stimuli, high task repetitiveness, patients are prone to visual fatigue, attention slippage, and operational burnout, further weakening the willingness and efficiency of communication;

Therefore, an assessment of the feasibility of implantable BCIs should be performed as early as possible once the clinical team observes a significant decrease in the frequency of use of the non-invasive system, an increase in the rate of misrecognition, an increase in the subjective resistance of the patient, or a decrease in their reliance on daily communication. This assessment should include ethical informed consent from the patient and family, cognitive assessment, electrophysiologic activity testing of brain regions, and availability of long-term maintenance and care resources. For intermediate-term patients who still have some cognitive status and training data, transitioning to electrocorticography (ECoG) or cortical microelectrode array systems not only provides higher signal-to-noise ratios and classification stability but also enables longer cycles and more independent communication pathways, which is a core strategy for future high-quality communication assurance.

5.3. BCI feasibility and options in advanced ALS (LIS/CLIS)

In the LIS stage (king (4A 4B)/MiToS stage 4), despite quadriplegia and loss of speech, patients often retain limited eye-movement control or facial electromyographic activity, providing the potential for the application of non-invasive BCI systems, while the CLIS stage represents the

DOI: 10.54254/2753-8818/2025.LD26747

ultimate form of ALS communication deficits - the patient is awake and cognitively capable, but unable to use any external output channels, including eye movements or speech, often described as "consciousness trapped in the body". Any external output channels, including eye movements, facial expressions, or speech, are often described as "consciousness trapped in the body". At this stage, the deployment of BCI systems faces significant challenges, as patients can no longer perform active tasks, are incapable of cooperating, and are difficult to train or calibrate in any real-time manner [31,32].

Despite severe limitations in motor and visual function in patients with advanced ALS, the non-invasive P300-BCI system remains practical and deployable in some patients, especially in the LIS stage. Through multimodal inputs (e.g., visual, tactile, or auditory), the P300 system can maintain basic communication and emotional expression without invasive implants. This addresses the resistance of some patients to invasive BCI modalities. Holz et al. (2015) reported that a woman with ALS who was in atresia and had only oculomotor function was able to communicate with the visual P300-BCI system "Brain Painting" through autonomous painting, selecting brushes and colours from a 6×8 matrix, and completed 200 paintings in 14 months. The patient completed 200 painting tasks in 14 months, was highly satisfied with the feedback, and wanted to use the system daily [33]. This case demonstrates that the Vision P300-BCI not only has the potential to maintain communication function in the later stages, but also demonstrates unique value in enhancing patients' emotional expression and quality of life. To address the limitation of being unable to gaze at visual stimuli in the CLIS stage, researchers developed the mindBEAGLE system based on haptic P300 evoked potentials, which induce ERP responses through wrist and back vibratory stimuli without visual or motor cooperation. Guger et al. (2017) tested the system on 12 patients with ALS (including 3 with CLIS), of which 2 CLIS patients Guger et al. (2017) tested 12 ALS patients (including 3 CLIS), of which 2 CLIS patients accomplished "yes/no" semantic communication through the VT3 paradigm with an accuracy of 90% and 70%, respectively, which provides a feasible pathway for interaction in extreme disabling states [34]. In another study, Lugo et al. (2016) tested the ERP responses of 11 LIS patients with the auditory P300 paradigm. Although the spelling accuracy was lower than the visual system's, some ALS patients could induce stable responses under active conditions. This suggests that the auditory P300 can also be used as an auxiliary channel for patients with visual limitations [35].

However, due to the high dependence of the LIS state on residual channels and the risk of rapid transition to CLIS, if BCI training and deployment are not completed at this stage, training opportunities will be lost entirely in the ensuing loss of communication. Therefore, introducing semi-invasive or invasive BCIs needs to be evaluated in advance to safeguard the continuity of communication ability and system stability.

Recent studies have shown that implantable cortical BCI systems, especially long-term recording devices based on ECoG (cortical electroencephalogram), have demonstrated better stability and accuracy in CLIS patients [32]. During ECoG signal acquisition, no electrodes penetrate the brain, thus minimising damage to the cortex and neurons beneath the implant [25,26]. Vansteensel et al. (2016) implanted subdural ECoG electrodes in the left motor cortex of a female patient with ALS, causing LIS. They designed a communication system that could be used at home for long periods. The patient was trained to autonomously type two letters per minute by attempting right-hand motor control of a cursor and "brain click" tasks. The system achieved unassisted use after 197 days, providing a long-term home-adaptive paradigm for advanced BCI deployment in ALS [33]. The subdural ECoG system offers the advantages of high stability and long-term use at home, with favourable user feedback in late ALS. Communication pathways are preserved for ALS patients in a

DOI: 10.54254/2753-8818/2025.LD26747

fully locked-in state. In addition, ECoG signals have a higher signal-to-noise ratio and spatial-temporal resolution than conventional EEG, which is especially suitable in preserved cognitive ability but complete loss of behavioural ability. Therefore, it is recommended that the deployment of the invasive BCI system and model training in the middle and late stages of ALS be completed to realise the seamless transition to the CLIS state and to guarantee the patient's right to autonomous expression.

6. Conclusion and prospects

The continued development of BCI technology and its clinical value as a functional alternative to communication in ALS is becoming increasingly evident. In this paper, we systematically sorted out the deployment strategies of non-invasive and invasive BCIs at different ALS stages based on the disease course's stage-specific features. We pointed out the complementary advantages of King staging and MiToS functional domain scores in guiding individualised deployment. In the early phase, focus should be placed on low-burden, easy-to-access non-invasive systems (e.g., P300 vs. SSVEP) to supplement existing communication modalities and build user awareness of BCI; the mid-phase is a critical window for transitional deployment, where signal decoding models need to be trained ahead of time in conjunction with the functional decompensation trajectory and to reinforce system usage habits; In the later stages, especially the complete locked-in state (CLIS) stage. At this stage, non-invasive P300 systems should be prioritised, especially multimodal P300 paradigms that combine tactile or auditory channels. If non-invasive signal quality is insufficient, invasive systems (e.g., ECoG) offer higher signal stability and long-term applicability and are a central means of maintaining residual communicative capacity.

However, the widespread deployment of BCIs in ALS still faces several challenges, including inter-individual variability at different stages, the effects of signal decay and fatigue, system accessibility, and ethical acceptance by patients. Current research focuses on system performance validation and lacks a framework for continuous deployment that centres on the dynamic needs of patients throughout the disease course. In the future, interdisciplinary collaboration should be strengthened to promote progress in the following areas: First, developing less-trained or zero-trained BCI systems with more generalization capabilities to improve the adaptability and transfer ability of the system during the disease; second, constructing a multi-modal monitoring system (e.g., combining indicators such as ALSFRS-R, eye movement, and speech rate) to provide real-time feedback on the patient's status and optimize the timing of deployment; Third, improving public and social acceptance of the BCI system from an ethical and social perspective; and third, improving public and social acceptance of the BCI system from an ethical and social viewpoint. Third, from a social perspective, we should enhance the public and clinical team's knowledge and acceptance of BCI to create a better supportive environment for early intervention and home deployment.

To summarise, BCI should not be regarded as a "rescue tool" in the advanced stage of ALS, but rather as a technical guarantee that serves individuals' dignity and communication rights throughout the disease. A more phased, precise and sustainable deployment strategy is needed to promote BCI development from experimental to clinical and family scenarios.

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