Neural Mechanisms of Executive Function and Digital Intervention in Amnestic Mild Cognitive Impairment in Older Adults

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Abstract

Alzheimer's disease exhibits extremely high incidence and mortality rates. As a clinical prodromal stage, investigating the formation and development mechanisms of amnestic mild cognitive impairment (aMCI) contributes to the prevention of Alzheimer's disease onset. Existing research demonstrates that deficits across multiple executive domains are closely associated with memory decline in aMCI; however, critical scientific questions regarding which executive domain constitutes the key pathogenic factor and optimal intervention target remain unresolved. To overcome the limitations of previous studies that conceptualized executive function as either a unitary construct or fragmented elements, the present study proposes to examine the comprehensive structure of executive function. Building upon a hypothesis concerning the relationship between executive function and memory impairment in aMCI, we will systematically investigate the time-domain, time-frequency, and dynamic brain network characteristics of three executive function subcomponents—inhibition, updating, and shifting—in aMCI using EEG technology. Additionally, we will employ three-dimensional convolutional neural networks to screen and identify specific neural markers for executive function deficits, exploring the potential of incorporating inhibition domain-related neural markers into early aMCI identification. Finally, through a longitudinal causal design, we will analyze the training effects and neural underpinnings of different targeted digital interventions in aMCI patients, thereby revealing the crucial role of the inhibition domain-related frontoparietal control network in interventions. This study is expected to elucidate, from a computational cognitive neuroscience perspective, that inhibition represents a novel cognitive target for executive function deficits and interventions in aMCI, thus providing evidence-based support for early aMCI identification and the development of precision diagnostic and therapeutic protocols.

Full Text

Neural Mechanisms and Digital Intervention of Executive Function in Older Adults with Amnestic Mild Cognitive Impairment

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Abstract

Alzheimer's disease (AD) carries an extremely high morbidity and mortality rate. Amnestic mild cognitive impairment (aMCI), as a clinical prodromal stage of AD, offers a critical window for exploring its pathogenic mechanisms to prevent AD onset. Existing research demonstrates that deficits across multiple executive domains are closely associated with memory decline in aMCI, yet key scientific questions remain unanswered: Which executive domain constitutes the critical pathogenic factor? What represents the key therapeutic target? To overcome the limitations of previous studies that treated executive function either as a monolithic construct or as fragmented elements, this study adopts a comprehensive view of executive function structure. Building upon a hypothesis regarding the relationship between executive function and memory impairment in aMCI, we will systematically investigate the temporal, time-frequency, and dynamic brain network characteristics of three executive function sub-components—inhibition, updating, and switching—using EEG technology. By integrating three-dimensional convolutional neural networks, we will screen and identify specific neural targets of executive function deficits and explore the feasibility of incorporating inhibition-related neural markers into early aMCI identification. Finally, through longitudinal causal designs, we will analyze the training effects and neural underpinnings of different targeted digital interventions in aMCI patients to reveal the crucial role of inhibition-related frontoparietal control networks in intervention efficacy. This study aims to elucidate inhibition as a novel cognitive target for executive function deficits and intervention in aMCI from a computational cognitive neuroscience perspective, thereby providing evidence-based support for early identification and precision diagnosis and treatment planning.

Keywords: executive function, amnestic mild cognitive impairment, cognitive neural mechanism, digital intervention, deep learning

1. Research Significance

More than a century has passed since German physician Alois Alzheimer reported the first case of Alzheimer's disease in 1906, yet the global number of people suffering from dementia (including AD) continues to rise, with approximately one new case diagnosed every three seconds. It is projected that by 2025, the number of dementia patients worldwide will reach 131.5 million (Bondi et al., 2017). In 2020, China had 15.07 million dementia patients among individuals aged 60 and above, with the disease's healthcare costs and income losses estimated to reach $1.88718 trillion by 2050 (Jia et al., 2018). Importantly, if the onset of dementia could be delayed by just five years, the prevalence and associated healthcare costs would decrease by approximately 40% over the subsequent 25 years (Anderson, 2019).

Mild cognitive impairment (MCI) represents an intermediate state between normal aging and early-stage dementia, characterized by self-reported cognitive deficits and objective impairment while basic daily living abilities remain largely intact (Petersen et al., 1999). Among MCI subtypes, amnestic MCI (aMCI) is the most common, with an 80% probability of progressing to AD within six years of diagnosis (Gauthier et al., 2006). While episodic memory impairment is considered the core symptom of aMCI, many researchers argue that executive function deficits represent the initial characteristic of the disease (da Costa Armentano et al., 2013; Rabi et al., 2020) and may cause or exacerbate memory symptoms, thereby increasing the risk of progression to AD (Panza et al., 2010; Yuan et al., 2016). Consequently, targeting executive function may reveal novel targets for early identification and intervention in aMCI.

Executive function, often used interchangeably with terms such as "executive control," "central executive," and "executive attention," refers to a set of neurocognitive skills involving conscious, top-down control of thoughts, actions, and emotions—abilities essential for complex social functions including reasoning, volitional action, and emotion regulation (Blair & Clancy, 2016; Chatzikostopoulos et al., 2022; Marks, 2019). According to Baddeley's working memory model, executive function influences subsequent inhibition of interfering information, updating of working memory representations, and mental set shifting, which collectively impair the ability of aMCI patients to encode and recall events, thereby producing memory symptoms (Baddeley et al., 1992; Schmeichel, 2007). Neuroimaging studies also indicate that the frontoparietal control network, which is closely related to executive function and forms a neural circuit connecting the dorsolateral frontal lobe, dorsolateral head of the caudate nucleus, and parietal cortex, exhibits mutual regulatory interactions with the hippocampus, which is responsible for learning and memory (Taylor et al., 2020). This provides crucial neurobiological evidence for understanding the relationship between executive function and memory symptoms in aMCI, suggesting that executive function assessment may serve as an important pathway for early identification.

However, current neuropsychological assessments of executive function in clin-

ical practice still rely primarily on questionnaires and interviews, which suffer from low sensitivity, strong subjectivity, and may fail to detect certain executive domain deficits in the early stages of aMCI (Guo et al., 2012). Task-based EEG (event-related potentials, ERP) offers high temporal resolution and can sensitively capture neural activity abnormalities underlying executive function tasks across different time scales, providing a new avenue for objective assessment. Research indicates that executive function structure exhibits both unity and specificity, with "inhibition" potentially serving as the underlying common cognitive process for other sub-components such as updating and switching (Friedman & Robbins, 2022; May & Kana, 2020). This suggests that focusing on executive function structure may help identify specific neural targets of deficits in aMCI. While researchers typically use latent variable structural equation modeling to validate theoretical structures of psychological components, traditional statistical methods struggle to integrate multidimensional, non-stationary EEG signals reflecting different executive sub-component processes (May & Kana). Deep learning, in contrast, can integrate spatiotemporal information from high-dimensional EEG data and demonstrates superior performance in identifying and classifying aMCI (Wen et al., 2021). Therefore, it is necessary to introduce deep learning algorithms from artificial intelligence, combined with EEG technology, to screen and identify specific neural targets of executive function deficits in aMCI, thereby providing empirical evidence for early clinical identification.

Targeted digital intervention represents a novel cognitive digital therapy in the era of universal internet access. Leveraging mobile internet platforms and high-temporal-resolution EEG technology, researchers have revealed the intervention effects of individual executive function sub-components and their associated EEG signal changes in cognitively normal older adults, confirming strong neuroplasticity of executive function (Anguera et al., 2013; Tusch et al., 2016). However, as aMCI is a brain network disorder characterized by dynamic neural network decline, whether these training protocols and dosages can be directly transferred to aMCI populations remains uncertain. Furthermore, the nested factor model of executive function suggests that "inhibition" may be the cognitive target underlying structural deficits in aMCI patients (Friedman & Robbins; Karr et al., 2018), yet it remains unclear whether digital interventions targeting this structural deficit would demonstrate superior training and transfer effects compared to other sub-component training.

This study will focus on executive function as an entry point, employing cross-sectional designs to explore structural characteristics and cognitive neural mechanisms of executive function in aMCI patients, and further combine deep learning algorithms to screen and identify specific neural targets of executive function deficits. Finally, through longitudinal intervention designs, we will identify which executive function sub-components yield stronger training effects and elucidate the mechanisms of intervention efficacy, training transfer, dosage effects, and key factors underlying intervention effectiveness. This project is expected to provide new cognitive intervention targets for precision medicine in older adults

with aMCI and offer evidence-based support for national health departments to develop novel prevention and treatment strategies.

2.1 Abnormal Neurophysiological Activity Related to Executive Function in Amnestic Mild Cognitive Impairment

Current domestic and international assessments of executive function in aMCI rely primarily on neuropsychological tests, which suffer from strong subjectivity, susceptibility to patients' education levels, and low sensitivity in early disease stages (Babiloni et al., 2021). Since executive function typically operates in rapidly changing environments, assessment cannot depend solely on traditional neuropsychological tests but must employ more sensitive task-based neurophysiological techniques—specifically event-related potentials (ERP). Time-locked neurophysiological signals can clarify the relative contributions of critical events such as preparatory cues, target stimuli, and correct or incorrect responses to executive function processing at the temporal scale. Therefore, investigating the neural mechanisms underlying executive dysfunction in aMCI from an ERP perspective may capture the primary link for early identification.

2.1.1 Temporal and Time-Frequency Characteristics

Executive function is typically measured across three domains: inhibition, updating, and switching (Karr et al., 2018). Current neurophysiological research on executive function in aMCI has largely focused on single sub-components. For instance, studies using Go/No-go, N-back, and task-switching paradigms to examine neural activity characteristics of inhibition, updating, and switching in aMCI have consistently found that N200 and P300 amplitudes evoked in frontoparietal regions during Go/No-go tasks are lower in patient groups than in cognitively normal controls, while P300 amplitudes in parietal regions during N-back and switching tasks show similar patterns. Additionally, P300 latency during switching tasks is delayed in aMCI patients compared to cognitively normal older adults (see Table 1). However, no study has systematically and comprehensively compared EEG signal characteristics across all three executive function sub-components—inhibition, switching, and updating—in aMCI patients. Literature review in Table 1 suggests that EEG signal characteristics across these three sub-components may exhibit both overlap (e.g., in EEG components and brain regions) and specificity, indicating that neural activity patterns of executive function in aMCI may possess both unity and specificity.

Nevertheless, previous studies have reported inconsistent findings. Some research has found delayed N200 and P300 latencies in aMCI patients during Go/No-go and N-back tasks compared to cognitively normal groups (Chiang et al., 2018), while others have found no statistically significant group differences in these component latencies (Gu et al., 2019). These inconsistencies may arise because most neurophysiological studies on executive function in aMCI rely on

ERP group difference analyses, which typically compare amplitudes and latencies of certain components across multiple electrode sites. This approach either increases the probability of false-positive effects due to multiple comparisons (Fields & Kuperberg, 2020) or reduces statistical power when adjusting alpha error levels using Bonferroni or similar methods (Stahl et al., 2012). Therefore, it is necessary to explore novel algorithms superior to traditional spatiotemporal averaging methods to more effectively integrate such high-dimensional data and further identify characteristic targets of executive function structural damage in aMCI.

Table 1. Summary of EEG Studies on Executive Function in Amnestic Mild Cognitive Impairment
Note: HC = Healthy Controls; md-aMCI = multiple domain aMCI; sd-aMCI = single domain aMCI; NS = Not Significant.

2.1.2 Brain Network Connectivity Characteristics

All human cognitive processing involves synchronized activity of neuronal populations within and between brain regions. The collaborative relationships between brain regions form the material basis for effective cognitive task completion and can be quantitatively characterized through brain network analysis at three spatial scales: microscopic (neuronal level), mesoscopic (neuronal clusters), and macroscopic (brain regions).

Brain network analyses of executive function in aMCI have primarily utilized functional MRI (fMRI), employing methods such as Pearson correlation analysis, coherence analysis, and phase synchronization index to characterize dynamic coordination of blood oxygen activity between local brain regions (functional connectivity), while using Granger causality models (GCM), partial directed coherence, and dynamic causal models to characterize causal and regulatory relationships between brain regions (effective connectivity) (Zhong et al., 2022). For example, Wang et al. (2019) used Pearson correlation analysis to find that decreased working memory (updating) performance in aMCI patients was associated with compensatory increases in low-frequency amplitude fluctuations in the right ventrolateral prefrontal cortex, right dorsolateral prefrontal cortex, and left supplementary motor area. Huang et al. (2023) employed Granger causality coefficient analysis to reveal that reduced effective connectivity between the posterior cingulate cortex and left medial temporal lobe in aMCI patients was negatively correlated with neuropsychological test performance (Clock Drawing Test).

Although fMRI-based brain network analysis has conducted substantial admirable work on the mechanisms of executive dysfunction in aMCI, the temporal dynamics of hemodynamics limit its ability to capture transient neural activity changes. Since EEG offers high temporal resolution and enables non-invasive monitoring of cortical neural electrical activity, brain network construction based on EEG signals should be considered to explore the neural mecha-

nisms of executive dysfunction in aMCI.

As a brain network disorder characterized by dynamic neural network decline, aMCI exhibits unique neural network properties: first, connectivity changes follow non-linear trends, with compensatory connectivity enhancement in early disease stages shifting to connectivity decline and even disconnection based on varying degrees of cortical atrophy; second, community structure modularity decreases, characterized by tightly connected node groups with fewer connections to nodes outside local groups; and finally, prefrontal brain regions regulate cognitive processing in posterior parietal regions through top-down mechanisms, with related neural activities exhibiting regulatory and regulated patterns (Hillary & Grafman, 2017). Time-varying multilayer network models, as a form of multilayer network analysis, offer advantages over single-layer network analysis by capturing complete neural information from multi-band, multi-scale, multi-layer communities, and spatiotemporal datasets (Li et al., 2017), perfectly matching the analytical needs of brain networks in aMCI patients. Therefore, it is necessary to employ time-varying multilayer network models for community reconstruction to explore the dynamic brain network mechanisms underlying executive function processing in aMCI.

2.2 Theoretical Structure and Data Modeling of Executive Function

Meta-analyses of neuroimaging assessments of executive function have found that the three neurocognitive skills of inhibition, updating, and switching activate partially overlapping regions within the frontoparietal control and dorsal attention networks (May & Kana, 2020), while also showing specific activations in prefrontal, anterior/mid-cingulate, and subcortical regions involved in updating and switching tasks (Iachini et al., 2021). This neurobiological commonality and specificity suggests that the three sub-components of executive function are not entirely independent, with the "inhibition" sub-component potentially serving as the underlying common cognitive process for other sub-components. For instance, updating tasks require "inhibition" to prevent irrelevant information from entering working memory and to remove irrelevant information from working memory when necessary. Similarly, switching tasks require "inhibition" of information unrelated to the current task set and inhibition of irrelevant task sets during rule switching.

Latent variable research indicates that nested factor models of executive function in adults provide better fit than single-dimension or three-factor models (Friedman & Robbins, 2022; Karr et al., 2018). These models suggest that inhibition is not an independent, specific executive function sub-component but rather a more fundamental executive function than updating and switching. In other words, most executive functions can be described as requiring some form of inhibition (Bull & Scerif, 2001). This suggests that executive function structure

may contain general (G) and specific (S) factors analogous to intelligence theory. However, these nested factor models were developed in cognitively normal adults, leaving open whether "inhibition" serves as the underlying common cognitive process across executive function sub-components in aMCI patients (see Figure 1). Moreover, these models were constructed based on behavioral data such as reaction time and accuracy, which reflect the sum total of psychological processes from stimulus presentation to behavioral response. Some researchers note that initial attentional orienting may occur too rapidly to capture before attention shifts (Kappenman et al., 2015). Therefore, it is necessary to use high-temporal-resolution EEG technology to validate the theoretical structure of executive function in aMCI populations.

Figure 1. Nested Factor Model Structure of Executive Function (adapted from Karr et al., 2018)

Since EEG signals involve multidimensional datasets across temporal (e.g., latency, amplitude) and time-frequency (energy, phase coherence) domains, such data reflect the complexity of neural activity underlying executive function. However, traditional latent variable analysis methods struggle to integrate such high-dimensional data (Ou & Wu, 2020). Machine learning, as a branch of artificial intelligence, can extract meaningful information from high-dimensional, noisy EEG signals. Currently, researchers have primarily combined machine learning with resting-state EEG to classify and identify aMCI patients, achieving classification sensitivity of 60-73%, specificity above 70%, and accuracy exceeding 90% (Youn et al.; Kim et al., 2022; Musaeus et al., 2018). However, few studies have used machine learning algorithms with task-based EEG to explore executive function structure. Upon literature review, only Krumpe et al. (2018) used traditional machine learning algorithms (support vector machines) for cross-classification validation of ERPs, power spectra, and pupil diameter during Flanker and N-back tasks in healthy adults to extract potential overlapping information of neural correlates between classes, finding that executive function sub-components "updating" and "inhibition" each possess unique features while sharing some common features. Since traditional machine learning algorithms separate feature extraction and classification into two steps and require substantial prior knowledge and experience from researchers, deep learning offers superior classification performance by fitting complex custom models through multi-layer architectures and directly extracting relevant features to complete EEG signal processing in one step (Zhang et al., 2023). Recently, Michmizos' team proposed a three-dimensional convolutional neural network (CNN) that is highly interpretable from a neurophysiological perspective, capable of capturing spatiotemporal characteristics of EEG features during movement while preserving crucial temporal components of brain-evoked activity (Kumar & Michmizos, 2022). Additionally, domestic researchers have developed a deep learning algorithm based on EEG signals—a single-scale multi-input convolutional neural network classification model—that achieves over 95% accuracy in classifying aMCI patients with type 2 diabetes mellitus from normal populations (Wen et al., 2021). Therefore, it is reasonable to propose that using deep learning

technology for EEG feature extraction, cross-classification validation, and cross-population validation can more objectively verify theoretical structural models of executive function in aMCI patients, thereby clarifying that the G factor of executive function—"inhibition"—represents the target of executive function deficits and a potential pathogenic factor for memory symptoms in aMCI.

2.3 Digital Intervention and Neural Mechanisms of Executive Function in Older Adults

The American Academy of Neurology's 2017 clinical guideline update for mild cognitive impairment stated that no strong evidence supports the efficacy of pharmacological interventions for symptom relief (Petersen et al., 2018). Conversely, empirical studies have found that cognitive training using computer systems targeting attention, memory, logical reasoning, and other cognitive domains can improve overall cognitive function, working memory, verbal memory, visual memory, attention, and psychomotor learning in older adults with aMCI (Sherman et al., 2017). These findings suggest that non-pharmacological cognitive training can enhance neuroplasticity of executive function in aMCI patients.

In the mobile internet era, targeted digital intervention is a novel cognitive digital therapy based on neuroplasticity theory. It utilizes digital media such as smartphones and tablets, with video games as carriers, to scientifically design intervention paradigms and dosages adapted to individuals' current cognitive function models (Kollins et al., 2020). This approach offers potential advantages in accessibility, convenience, cost-effectiveness, and non-invasiveness, while its highly standardized nature allows for targeted interventions in specific cognitive domains while controlling other variables, thereby facilitating better understanding of cognitive training mechanisms (Domhardt et al., 2021; Holmes et al., 2018). However, few studies have reported on targeted digital interventions and their neural mechanisms in aMCI patients, with most research focusing on training effects in cognitively normal older adults. For instance, *Nature* reported in 2013 that a four-week conflict control digital intervention improved cognitive performance, with cognitive changes associated with increased theta power in midline prefrontal regions (Anguera et al., 2013). Subsequent studies found that six weeks of adaptive working memory (updating) training improved cognitive function and increased P300 amplitude at midline parietal sites (Tusch et al., 2016), while six weeks of global executive function training correlated with increased CNV amplitude at midline parietal locations (Chainay et al., 2021). These results confirm strong neuroplasticity of executive function in older adults, but these studies either trained single sub-components or global executive function without addressing which targeted sub-component or dosage makes interventions effective. Moreover, whether these digital intervention contents, frequencies, and durations can be directly transferred to older adults with aMCI remains unverified. Moshe et al. (2021) proposed that participant characteristics, intervention paradigms, and dosage are key factors influencing

digital intervention efficacy. Therefore, it is essential to compare the training, transfer, dosage effects, and neural underpinnings of targeted digital interventions focused on different executive function sub-components in aMCI patients to reveal the pathways of intervention efficacy, clarify relationships between training-related cognitive and neural changes, and provide more precise intervention protocols for digital cognitive therapy in aMCI.

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3. Research Questions

This study focuses on structural characteristics of executive function to understand impairments in aMCI populations and uses this as a target to explore the effects and neural foundations of different targeted digital interventions, thereby revealing the important role of inhibition-related frontoparietal control networks in interventions. We propose the following questions:

First, how can we identify "inhibition" as the characteristic target of executive function structural damage in aMCI at the neurophysiological level? Baddeley's working memory model points to an interactive relationship between executive function and episodic memory but does not specify which executive sub-component impairment triggers or exacerbates memory symptoms in aMCI. Since pathological brain changes precede the emergence of memory symptoms, this study will employ high-temporal-resolution EEG technology and leverage deep learning's ability to integrate multidimensional EEG spatiotemporal features. We will focus on examining whether convolutional neural network classification models built on inhibition-related EEG features can be validated in datasets from the other two executive sub-components—"updating" and "switching"—and evaluate the model's performance in classifying symptomatic populations, thereby clarifying from a neurophysiological perspective whether inhibition function represents the G factor of executive function theory.

Second, which executive function sub-component target and what training "dosage" can effectively enhance neuroplasticity and improve memory symptoms in aMCI patients? Are targeted digital interventions focusing on the G factor—inhibition—superior to those targeting updating and switching? Previous online cognitive training studies for aMCI patients have typically involved multiple cognitive domains with varying intervention durations, making it difficult to identify key mechanisms underlying neuroplasticity improvements. Based on this, our study will scientifically design intervention paradigms targeting different executive function sub-components with difficulty adaptation based on patients' current training performance. We will examine intervention, transfer, and dosage effects and corresponding changes in neurophysiological indicators and dynamic brain network connectivity at 4-week and 8-week intervals, focusing particularly on whether targeted inhibition interventions improve episodic memory in aMCI patients more effectively than updating- or switching-targeted interventions.

4. Research Framework

This study follows the path of "neurophysiological spatiotemporal assessment →characteristic target identification →targeted digital intervention" for executive function in aMCI patients, integrating behavioral and ERP-EEG technologies with deep learning and longitudinal intervention methods. First, we will use EEG technology with three paradigms—Go/No-go, N-back, and set-shifting tasks—to characterize neural activity features of different executive function sub-components in aMCI (Study 1). Next, we will use deep learning to screen reliable features and construct three-dimensional convolutional neural network classification models for inhibition, updating, and switching sub-components, followed by cross-classification and cross-population validation to identify specific neural targets of executive function deficits in aMCI (Study 2). Finally, through longitudinal intervention studies, we will test the intervention, transfer, and dosage effects and corresponding neural foundations of targeted digital interventions focused on different executive function sub-components to clarify intervention mechanisms (Study 3). See Figure 2.

Figure 2. Overall Research Framework

4.1 Neurophysiological Activity of Executive Function in Amnestic Mild Cognitive Impairment Patients

Study 1 employs high-temporal-resolution EEG technology to investigate neurophysiological activity across different executive function sub-components in aMCI patients. This component includes one baseline EEG experiment and three executive function EEG experiments. By comparing temporal, time-frequency, and dynamic brain network connectivity changes between aMCI and cognitively normal older adult groups during Go/No-Go, N-back, and switching tasks, we will reveal the cognitive neural mechanisms and brain functional network damage characteristics of aMCI patients across inhibition, updating, and switching sub-components. The study adopts a 2 (group: aMCI vs. cognitively normal older adults) ×2 (stimulus type: X vs. Y) mixed design, with group as a between-subjects factor and stimulus type as a within-subjects factor. In the Go/No-go, N-back, and switching tasks, the within-subjects factor (X vs. Y) corresponds to Go vs. No-Go, congruent vs. incongruent, and repeat vs. switch rules, respectively. To ensure experimental material homogeneity, stimuli for all tasks are arrows pointing in four different directions (up, down, left, right). In the Go/No-go task, participants respond quickly and accurately to green flashing arrows while withholding responses to red flashing arrows. In the N-back task, participants determine whether the current arrow direction matches the arrow from N trials back. In the switching task, participants respond congruently to green arrows (repeat rule) and incongruently to red arrows (switch rule). We hypothesize that aMCI patients will perform significantly worse than cognitively normal older adults on these executive function

tasks, with neural manifestations including changes in N200 amplitude, P300 amplitude, and power in alpha, theta, and other frequency bands. Additionally, due to neurodegeneration, aMCI patients may exhibit different brain network connectivity patterns across executive function tasks.

4.2 Construction and Validation of a Deep Learning-Based Executive Function Structure Model for Amnestic Mild Cognitive Impairment

Study 2 leverages deep learning's advantage in integrating multidimensional EEG data to construct three-dimensional convolutional neural network classification models for three executive function sub-components—inhibition, updating, and switching—in aMCI patients, demonstrating that "inhibition" is the underlying common cognitive process across sub-components (i.e., the G factor). The specific pipeline is as follows (Figure 3): (1) **Frequency domain feature extraction**: Extract EEG data from aMCI patients during different executive function tasks from Study 1, forming multispectral images from theta, alpha, and beta frequency bands of ERPs arranged in RGB channel order. Multispectral images from different brain regions are input simultaneously into different convolutional channels, with three 2D convolutional layers and three pooling layers extracting frequency features. (2) **Spatiotemporal feature extraction**: Use brain topographic maps from different tasks at different time points as inputs, employing five 3D convolutional layers and one 2D convolutional layer to generate spatial feature maps. Gradient-weighted Class Activation Mapping (Grad-CAM) through backpropagation identifies brain regions the network focuses on for classifying the three executive sub-components, further extracting spatial features of key brain regions. (3) **Brain functional connectivity feature extraction**: First, extract brain connectivity features based on topology-based complex network measures from task-based EEG; second, extract connectivity features across different frequency bands as input for integrated 3D CNN classifiers; finally, convert 1D vectors of connectivity complex network features across frequency bands into 2D tensors as 1D input to further extract brain functional connectivity features of key regions. (4) **Deep learning model construction**: Fuse the aforementioned multidimensional neurophysiological EEG frequency and spatiotemporal features, perform feature combination cluster analysis to screen effective feature values, distinguish four factor levels (baseline, inhibition, updating, switching), build machine learning classification architecture, and train one classifier for each executive sub-component versus baseline condition. Through 5-fold cross-validation, preliminary models for inhibition, updating, and switching in aMCI will be constructed. (5) **Cross-classification validation**: Use EEG feature values from other executive sub-components as test sets for pairwise cross-validation of the aMCI inhibition, updating, and switching models, comparing accuracy, sensitivity, and specificity to examine the degree of "overlap" between neural features of different sub-components. (6) **Cross-population validation**: Following Study 1's procedures, conduct ERP experiments on 30 cognitively normal older adults. Using clinical diagnosis as the gold standard, validate classification per-

formance (accuracy, sensitivity, specificity) of the aMCI inhibition, updating, and switching neural correlation models across populations. We hypothesize that cross-classification validation accuracy between the aMCI inhibition neural model and updating/switching sub-components will be significantly above chance level, and that the inhibition neural model will demonstrate superior classification performance in cross-population validation compared to updating and switching models.

4.3 Intervention Effects and Neural Mechanisms of Targeted Digital Intervention in Amnestic Mild Cognitive Impairment

Figure 3. Deep Learning Technology Roadmap

Building on previous studies, Study 3 aims to identify targeted digital intervention protocols with strong intervention effects for specific executive function sub-components. Using targeted digital interventions combined with EEG technology, we will examine the training, transfer, and dosage effects and neural foundations of targeted digital interventions focused on different executive function sub-components in aMCI patients. The study adopts a 4 (group: inhibition/updating/switching/active control) $\times 3$ (measurement time: pre-test/post-test 1/post-test 2) mixed design, with group as a between-subjects variable and measurement time as a within-subjects variable. The inhibition, updating, and switching groups will receive difficulty-adaptive targeted digital interventions ("Whack-a-Mole," "Picturesque Scenery," and "Divided Attention," respectively), while the active control group will receive processing speed training only. Training will occur three times weekly for 30 minutes per session, with post-tests conducted at weeks 4 and 8. Pre- and post-test tasks will be identical to Study 1. We hypothesize that inhibition function training in aMCI patients will involve activity in frontoparietal control network-related brain regions, demonstrate the best intervention effects, and may show far transfer to updating and switching tasks.

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5. Theoretical Construction

This study proposes a hypothesis regarding the relationship between executive function and memory impairment in aMCI. From the perspective of executive function unity, training higher-order control systems should benefit various executive sub-components; from a modular perspective, transfer scope should depend on the degree of overlap in specific neural foundations between trained and transfer tasks (Ulbl & Rakusa, 2023). This leads to predictions about possible transfer effects of executive function training in aMCI: training effects on inhibition sub-components should transfer to updating and switching, whereas training benefits from updating and switching should not transfer to each other. Furthermore, given the mutual regulatory relationship between the dorsolateral prefrontal cortex (which governs executive function) and the

hippocampus (which governs learning and memory) in the corticolimbic dorsal pathway, we propose that training inhibition sub-components—which involve larger frontoparietal control network ranges—should be more effective in reducing or delaying memory impairment in aMCI patients (see Figure 4).

Figure 4. Schematic Diagram of the Hypothesized Relationship Between Executive Function and Memory Impairment in aMCI

This study features three innovative aspects. **First**, it focuses on executive function deficits—a high-level cognitive process abnormality in early-stage aMCI—and deeply explores its cognitive neural mechanisms. Executive function deficits are closely related to working memory, episodic memory, visual semantic processing, and other cognitive impairments, and affect subsequent high-level cognitive functions including planning, reasoning, decision-making, and problem-solving. This provides an important entry point for identifying key pathogenic cognitive factors and developing early precision interventions in aMCI. By systematically elucidating neural characteristics and intervention regulatory mechanisms of executive function structure in aMCI, this study provides theoretical guidance for deep learning modeling and targeted digital intervention, reflecting substantial theoretical foundation and distinctive features.

Second, this study insists on method innovation driven by scientific questions. Given the high-dimensional, noise-sensitive characteristics of task-based EEG signals, we specifically employ 3D convolutional neural networks to analyze EEG spatiotemporal information features, making it possible to reveal executive function structure at the neural level. Additionally, we use temporal, time-frequency, and dynamic brain functional network analysis methods to capture time-frequency-space coupling information in inhibition, switching, and updating tasks, depicting spatiotemporal characteristics of neural activity at multiple levels. Following the approach of "typical abnormal EEG features →key brain regions of interest →primary driving brain regions →specific pathogenic features," we attempt to explore and clarify candidate intervention targets for aMCI. Moreover, leveraging advantages of multimodal EEG indicator systems, we further reveal the critical role of early qualitative connectivity decline in aMCI brain networks, particularly the frontoparietal network, in pathological changes.

Third, based on the above, we strive to validate intervention effects of different targeted digital intervention methods in clinical cognitive rehabilitation applications. Through precise targeted regulation of different executive function sub-components, we aim to improve clinical cognitive performance in aMCI patients. By focusing on the potentially specific damage target ("inhibition") as a key intervention target and carefully comparing its intervention, transfer, and dosage effects with other targets ("updating," "switching"), while clarifying changes in dynamic brain functional connectivity, we achieve a closed-loop regulatory strategy of "memory symptoms →target identification →cognitive training →executive function neuroplasticity →memory improvement." This demonstrates technological application innovation. Through the academic and

clinical advantages of medical-science integration, this study not only facilitates technological innovation in novel targeted digital interventions but also provides empirical evidence for aMCI executive dysfunction theory and neural mechanisms through actual intervention effects.

In summary, this study will investigate the theoretical structural characteristics and cognitive neural mechanisms of executive function in aMCI patients at the neurophysiological level, using deep learning for EEG feature extraction, cross-classification validation, and cross-population validation to verify the nested factor structure model of executive function and further demonstrate that inhibition is the characteristic target of executive function deficits. Additionally, by implementing targeted digital interventions focused on different executive function sub-components, we will compare the near-transfer, far-transfer, and dosage effects of different interventions at both behavioral and neurophysiological levels to identify executive function sub-components with strong intervention effects and their neurophysiological markers. We aim to elucidate the critical role of the executive function G factor (inhibition)-related frontoparietal control network in targeted digital interventions, thereby demonstrating the effective pathway of "cognitive training →executive function neuroplasticity →memory improvement."

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