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Unlocking the silent signals: Motor kinematics as a new frontier in early detection of mild cognitive impairment

Nagamine T *et al*. A revolution in MCI screening

Abstract

The increasing global prevalence of mild cognitive impairment (MCI) necessitates a paradigm shift in early detection strategies. Conventional neuropsychological assessment methods, predominantly paper-and-pencil tests such as the Mini-Mental State Examination and the Montreal Cognitive Assessment, exhibit inherent limitations with respect to accessibility, administration burden, and sensitivity to subtle cognitive decline, particularly among diverse populations. This commentary critically examines a recent study that champions a novel approach: The integration of gait and handwriting kinematic parameters analyzed *via* machine learning for MCI screening. The present study positions itself within the broader landscape of MCI detection, with a view to comparing its advantages against established neuropsychological batteries, advanced neuroimaging (*e.g.*, positron emission tomography, magnetic resonance imaging), and emerging fluid biomarkers (*e.g.*, cerebrospinal fluid, blood-based assays). While the study demonstrates promising accuracy (74.44% area under the curve 0.74 with gait and graphic handwriting) and addresses key unmet needs in accessibility and objectivity, we highlight its cross-sectional nature, limited sample diversity, and lack of dual-task assessment as areas for future refinement. This commentary posits that kinematic biomarkers offer a distinctive, scalable, and ecologically valid approach to widespread MCI screening, thereby complementing existing methods by providing real-world functional insights. Future research should prioritize longitudinal validation, expansion to diverse cohorts, integration with multimodal data including dual-tasking, and the development of highly portable, artificial intelligence-driven solutions to achieve the democratization of early MCI detection and enable timely interventions.

Key Words: Mild cognitive impairment; Early detection; Motor kinematics; Gait analysis; Handwriting analysis; Digital biomarkers; Machine learning

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Core Tip: This study proposes a paradigm shift in mild cognitive impairment screening, moving from subjective cognitive tests to objective, quantifiable measures of gait and handwriting kinematics. This novel approach uses readily observable behaviors and non-invasive technology (like digital pens) to circumvent barriers of traditional neuropsychological assessments, such as language dependency and cultural bias. By measuring motor kinematics, which capture the real-world effect of cognitive-motor changes, the method offers ecological validity and reflects functional status, distinguishing it from biomarkers focused only on pathology. The integration of gross and fine motor abilities provides a scalable and accessible foundation for early, proactive mild cognitive impairment detection, paving the way for better intervention.

INTRODUCTION

The global landscape of cognitive health is increasingly characterized by the rising prevalence of mild cognitive impairment (MCI). MCI is positioned as a critical intermediary stage between normal cognitive aging and the more severe manifestations of dementia. It is characterized by measurable cognitive decline that does not yet significantly impede daily living activities. Despite its substantial global prevalence, estimated at over 15% among individuals over 50, a profound diagnostic and intervention gap persists[1]. A substantial proportion of older adults with MCI remain unaware of their condition, and a significant percentage go undiagnosed and untreated[1-3]. This critical oversight is largely attributable to insufficient public awareness and the inherent limitations of conventional screening tools.

The prevailing approach in current MCI screening involves the utilization of scale-based assessments, such as the Mini-Mental State Examination and the Montreal Cognitive Assessment. While these tools are invaluable in clinical settings, they demand specialized administration, extended time, and professional expertise, severely restricting their widespread utility, particularly in primary care environments with limited resources[4]. Consequently, there is an urgent need to develop screening

solutions that are not only accurate but also inherently more accessible and practical for broad application.

The convergence of motor function decline and cognitive impairment offers a compelling avenue for novel detection strategies[5]. Cortical atrophy, a hallmark of cognitive decline, has been demonstrated to affect both cognitive and motor domains. It has been demonstrated that older adults diagnosed with MCI exhibit consistent alterations in gait parameters. These alterations include, but are not limited to, reduced velocity, decreased stride length, and lengthened double support time. Moreover, these alterations in gait frequently precede the onset of overt cognitive decline, underscoring their potential as sensitive biomarkers. Beyond gross motor skills, fine motor deficits - particularly evident in complex tasks like handwriting - also manifest in MCI. Individuals with MCI exhibit reduced writing speeds, diminished pressure, and elevated error rates, thereby underscoring the interconnected nature of cognitive and fine motor control.

While single-modality analyses of gait or handwriting kinematics have demonstrated efficacy in distinguishing MCI from normal cognition, the potential for enhanced screening accuracy through their integration remains largely unexplored[6]. The incorporation of gross and fine motor assessments provides a more comprehensive evaluation of motor function, ensuring a broader capture of impairment. The burgeoning field of machine learning (ML) provides a powerful analytical framework for synthesizing these multimodal data streams[5,6]. This commentary positions a recent study, which for the first time applies ML algorithms for an integrated analysis of gait and handwriting kinematics in MCI screening, as a pivotal development in the pursuit of an objective, accessible, and accurate diagnostic tool[7].

CURRENT ARSENAL OF MCI DETECTION: STRENGTHS AND SHORTCOMINGS

To comprehend the innovations presented by the motor kinematic approach, it is essential to contextualize it within the existing landscape of MCI detection methods.

Each method possesses unique strengths for specific clinical and research purposes, but also significant limitations for large-scale, accessible screening.

Neuropsychological assessments: The clinical cornerstone

The strengths of the aforementioned approach include its widespread availability, its assessment of comprehensive cognitive domains, and its cost-effectiveness. The following are considered to be among the subject's weaknesses: Performance is heavily influenced by the administrator's skill, the participant's education level, cultural background, and motivation. A considerable number of tests are developed in Western contexts, necessitating extensive and frequently imperfect validation for diverse populations. These assessments are also time and resource-intensive for a comprehensive diagnosis and may have ceiling effects in highly educated individuals[8,9].

Advanced neuroimaging: Illuminating brain pathology

The following list enumerates the subject's strengths: Direct visualization of brain structure and function is crucial for differential diagnosis. The following are considered to be among the subject's weaknesses: The high cost and limited accessibility of these tests, in addition to their invasiveness (positron emission tomography), and the occurrence of pathological changes often after initial cognitive symptoms have been observed, limit their utility for ultra-early screening[10,11].

Fluid biomarkers: The biochemical window

The following list enumerates the subject's strengths: The presence of direct molecular evidence of neurodegeneration has been demonstrated, and blood-based tests offer the advantage of ease of collection. The following are considered to be among the subject's weaknesses: The following factors must be considered: Invasiveness (cerebrospinal fluid), ongoing challenges with standardization and validation for blood-based markers, and a lack of direct functional correlation[12,13].

MOTOR KINEMATICS: A PROMISING NEW FRONTIER

The present study, which integrates gait and handwriting kinematic parameters, presents a highly compelling alternative to the methods discussed above, directly addressing many of their inherent limitations.

The objective is to identify quantifiable biomarkers

A notable benefit of this approach is its inherent objectivity and quantifiability. Contrary to the subjective responses elicited by cognitive scales, the measurement of gait and handwriting kinematics is achieved with precision through the utilization of specialized sensors. This methodological approach serves to mitigate the influence of observer bias, thereby ensuring the reproducibility and standardization of assessments. The non-invasive nature of the gait measurement equipment, which does not require sensors to be worn by participants, further enhances data objectivity and patient comfort[14].

The objective of this study is to examine the accessibility and practicality of widespread screening

The practical implementation of this method holds immense promise for democratizing MCI screening. The administration of both gait and handwriting assessments is relatively straightforward and does not necessitate highly specialized clinical training to operate the equipment[15]. These characteristics render them particularly well-suited for integration into primary care settings, community health centers, and even elder care facilities, where the majority of older adults receive their initial health assessments[16].

The present study explores the concepts of ecological validity and functional relevance in the context of ecological psychology

Motor function is inextricably linked to cognitive function. Deficits in executive function, attention, processing speed, and visuospatial abilities frequently manifest as subtle changes in motor performance. Gait is theorized to function as a cognitive mirror. The findings reveal that the observed characteristics in MCI patients, including slower gait speeds, increased stride time variability, and prolonged double support times, are not merely physical limitations. These findings are indicative of declines in higher-order cognitive control, which is necessary for efficient and adaptive walking, including planning, inhibition, and multitasking[14,15]. The concept of a "shared neural substrate" that links gait slowing to cognitive decline underscores this profound connection.

Handwriting can serve as a valuable tool for examining fine motor-cognitive interaction. Handwriting is a complex process that demands precise integration of fine motor control and multiple cognitive domains. The observed prolonged in-air time, slower writing speeds, reduced pressure, and increased writing errors in MCI patients are direct reflections of impaired visuospatial abilities, executive function, and processing speed. The graphic copying tasks are of particular concern due to their reliance on complex visuospatial and planning abilities, which are frequently impacted during the early stages of cognitive decline[16,17]. By evaluating these behaviors, which are relevant to daily functioning, the motor kinematic approach provides a direct insight into the impact of cognitive impairment on motor performance. This approach offers a more comprehensive understanding than isolated cognitive scores or molecular markers[18].

The power of multimodal integration and ML

The study's most significant innovation lies in its multimodal integration and the application of ML. While unimodal analyses of gait or handwriting demonstrated individual potential (*e.g.*, graphic handwriting attained 73.44% accuracy with an area under the curve of 0.75), their integration resulted in a substantial enhancement of diagnostic efficacy. The highest level of accuracy, 74.44% (area under the curve = 0.74),

was achieved through the integration of gait and graphic handwriting tasks[7]. This finding provides substantial support for the study's hypothesis and the expanding consensus that a multi-biomarker approach offers enhanced diagnostic capability in complex conditions, such as MCI. ML algorithms are computational models designed to learn patterns from data and make predictions or classifications. In this study, ML functions as a sophisticated pattern recognition engine, enabling researchers to: (1) The identification of discriminative features is paramount in this regard. ML algorithms have the capacity to systematically analyze a vast array of kinematic parameters, thereby identifying the most salient factors that differentiate individuals with MCI from those who are cognitively normal; (2) It is imperative to ascertain the intricate interrelationships that underpin the subject matter. ML models have the capacity to discern intricate, multi-dimensional patterns and interactions between various kinematic parameters that may be overlooked by conventional statistical methods; (3) The construction of predictive models is imperative. These models can be utilized to categorize novel individuals that have not been previously observed; (4) The management of high-dimensional data is a critical component of this field. ML algorithms are engineered to process vast quantities of features with optimal efficiency; and (5) Robust evaluation: The employment of ten-fold cross-validation serves to ensure that the model's performance metrics are not merely a consequence of a particular data division, but rather, they are more indicative of the model's generalizability to unseen data.

NAVIGATING THE CHALLENGES: LIMITATIONS AND FUTURE DIRECTIONS

Despite its considerable strengths, the study provides a foundation for future research by highlighting critical limitations that must be addressed for this approach to achieve its full potential in clinical practice.

The imperative of longitudinal validation: An examination of the necessity for replication in longitudinal research

The most significant constraint of this study is its cross-sectional design. While it identifies differences between existing MCI and cognitively normal groups, it cannot establish the predictive power of these kinematic biomarkers. For a screening tool to be considered truly transformative, it must demonstrate its capacity to identify individuals at risk of developing MCI prior to the full establishment of clinical symptoms, or to predict the progression from MCI to dementia. The execution of large-scale, multi-year longitudinal studies is of the utmost importance in addressing this issue.

Expanding the horizon: A case study of variation in sample size and diversity

The study's sample size of 95 participants is relatively small for developing highly robust and generalizable ML models. Moreover, the fact that the subject was recruited from a particular region of China calls its generalizability to other ethnic, cultural, and linguistic groups around the world into question. Future studies must prioritize the recruitment of significantly larger and more diverse cohorts spanning different geographical regions, ethnicities, and educational backgrounds.

The objective of this study is to enhance sensitivity, the power of dual-task paradigms

The study's observation that "stride time variability is more sensitive to dual-task gait assessments" is a critical point. Cognitive-motor interference, defined as the performance of a motor task while simultaneously engaging in a cognitive task, has been shown to amplify subtle cognitive-motor deficits. The present study, which is predicated on single-task assessments, may have resulted in an underestimation of the full discriminatory power of kinematic parameters. The incorporation of dual-task paradigms into assessments of both gait and handwriting is imperative to achieve more sensitive and specific kinematic biomarkers.

Beyond the lab: The present study will examine the relationship between wearable technology and ecological assessment

While the GAITRite® system and digital pens offer objective measures in a controlled environment, the future of accessible screening lies in more portable and ecologically valid solutions. Research should explore the use of widely available wearable sensors (*e.g.*, smartwatches, accelerometers in smartphones) for passive, continuous monitoring of gait and fine motor activities in individuals' natural environments. This could provide early warning systems and more accurate data reflecting functional impairment in everyday life.

The present study explores the refinement and interpretability of ML models

While the present study demonstrates the utility of ML, further efforts are necessary to refine the models and enhance their interpretability. The identification of the kinematic features and their combinations that most strongly influence the model's decisions will increase clinicians' confidence in these "black box" tools.

A holistic diagnostic ecosystem: The integration of this variable with other biomarkers is a subject that merits further investigation

The ultimate objective should be to integrate motor kinematic data with other promising biomarkers. This could entail the integration of digital biomarkers with cognitive performance data, behavioral data, biological biomarkers, and genetic risk factors. A comprehensive "digital phenotyping" approach, powered by advanced artificial intelligence, has the potential to provide a more robust, personalized risk assessment. Ultimately, this could result in more precise diagnostic and prognostic tools for MCI[20,21].

CONCLUSION

The study, signifies a pivotal advancement in the quest for accessible and objective MCI detection. By leveraging the quantifiable insights embedded in everyday movements and the analytical power of ML, it effectively addresses critical limitations inherent in traditional screening methods. This research paves the way for a paradigm shift,

moving beyond specialized, clinic-bound assessments towards scalable, community-based screening that is sensitive to subtle cognitive changes.

Nevertheless, for this technology to genuinely transform the field of MCI detection, further evolution is imperative. To proceed, it is imperative to implement rigorous longitudinal validation to substantiate its predictive capabilities, expand the study to encompass larger and more diverse global cohorts, and integrate dual-task paradigms to elucidate more nuanced cognitive-motor deficits. Moreover, advancements in wearable technology and explainable artificial intelligence will be crucial for seamless integration into daily life and clinical practice. The future of MCI detection is contingent upon a holistic, multi-modal approach, wherein motor kinematics function as a vital, accessible, and proactive early warning system. This system enables timely interventions that can substantially alter the trajectory of cognitive decline and enhance the quality of life for millions worldwide.

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