ACCSCIENCE PUBLISHING

Journal of Clinical and Translational Research

ORIGINAL ARTICLE

Task-related handwriting and drawing features for early detection of Alzheimer's disease: A pilot study

Maria Santina Ler[1]*, Miriam Veneziano[1†], Alfonsina D'Iorio[1†], Gennaro Cordasco[2†], Gabriella Santangelo[1†], and Anna Esposito[1†]*

[1]Department of Psychology, Faculty of Psychology, University of Campania Luigi Vanvitelli, Caserta, Italy

[2]Department of Computer Science, Faculty of Computer Science, University of Salerno, Salerno, Italy

Abstract

Background: Dementia causes significant disability worldwide and has no cure. The only way to improve the quality of life of those affected is through early intervention. For this reason, the development of effective diagnostic tools is a priority for healthcare systems and researchers. Handwriting and drawing, which engage multiple cognitive and motor areas, have shown promise in detecting early signs of dementia. However, findings in this field remain inconsistent, largely due to a lack of standardized protocols. **Aim:** This study aims to investigate the discriminatory power of graphomotor analysis in distinguishing individuals with Alzheimer's disease (AD) from healthy controls (HC) by examining the contribution of dynamic handwriting features and task-related characteristics within an easy-to-use and multi-task protocol. **Methods:** Patients with AD (n = 14) and HC (n = 25) were asked to complete five drawing and two writing tasks, and their online data were recorded using a digital tablet. **Results:** Significant differences (p<0.05) between groups were observed for time- and ductus-related features in almost all tasks, while pressure, space, and inclination features did not differ significantly. **Conclusion:** Although certain graphomotor characteristics are more sensitive than others, analyzing them together yields a detailed functional profile of patients. Overall, the study provides evidence of the effectiveness of handwriting analysis in identifying several symptoms associated with dementia. The protocol warrants further validation with a larger sample. **Relevance for patients:** The proposed protocol highlights the potential of a handwriting-based tool as an ecologically valid, objective, and accessible method for assessing and monitoring dementia. Adopting up-to-date digital approaches responds to the need for more sensitive tools that align with technological and cultural changes within the population. This could consequently simplify screening, improve access to treatment, and enhance the quality of life for patients and their caregivers.

Keywords: Dementia screening; Alzheimer's disease; Handwriting analysis; Online feature; Kinematic parameters

†These authors contributed equally to this work.

***Corresponding authors:**
Maria Santina Ler (mariasantina.ler@unicampania.it)
Anna Esposito (anna.esposito@unicampania.it)

Citation: Ler MS, Veneziano M, D'Iorio A, Cordasco G, Santangelo G, Esposito A. Task-related handwriting and drawing features for early detection of Alzheimer's disease: A pilot study. *J Clin Transl Res.* 2025;11(6):50-63. doi: 10.36922/JCTR025380063

Received: September 18, 2025

Revised: October 30, 2025

Accepted: November 19, 2025

Published online: December 4, 2025

1. Introduction

The growing prevalence of dementia worldwide poses a significant public health challenge, compounded by the economic and social strain it places on healthcare systems. Despite its profound impact, dementia diagnoses are often delayed due to a limited understanding of early markers. Recently, dynamic handwriting analysis has become increasingly relevant for early diagnosis of neurocognitive disorders because it is a non-invasive, economical, and reliable method of detecting dementia, especially Alzheimer's disease (AD).[1] Writing is a complex skill that requires the combined integration of executive, visuo-spatial, linguistic, and fine motor functions. Despite its potential, the lack of standardized and shared protocols hinders the systematic adoption of this approach in clinical practice. An important insight drawn from the literature is the substantial heterogeneity of the graphomotor characteristics selected for analysis, in contrast to an increasing convergence in the types of tasks proposed. The most frequent tasks can be categorized into three primary categories:

(i) Drawing simple geometric shapes, such as straight lines, circles, or spirals, is commonly used to assess fine motor skills and visuospatial coordination.[2-4]

(ii) Writing tasks which include various exercises, such as letter repetition (involving ascending and descending characters),[2,5,6] word writing (including irregular or non-sense words with distinct phonological and orthographic features),[7,8] and simple sentence writing. These tasks are proposed in different modalities, including copying, dictation, and spontaneous production.

(iii) Complex productions include the clock-drawing test (CDT), writing articulated sentences or paragraphs, performing backward tasks, and engaging in dual-task conditions.[3,4,9] These activities require the integration of a wider range of cognitive functions, including planning, working memory, attention, language, and visuospatial organization.

Although tasks are frequently categorized into broad groups, such as writing, drawing, and complex productions, their quantity and variability remain high, and the correlation among these tasks and discriminative graphomotor characteristics remains unclear. A noteworthy contribution to the digital writing domain is the multi-task protocol developed by Cilia *et al.*[10] for the DARWIN dataset,[11] which comprises 25 graphical and writing tasks of increasing complexity. They employed a task-informed machine learning approach that combines general and specific graphomotor features of individual writing tasks to enhance classification accuracy. Nevertheless, its extension has led numerous researchers to select specific components extracted from the whole protocol, tailoring them to their temporal and contextual requirements. Previous studies have shown that kinematic characteristics of handwriting are effective in identifying cognitive and mood disorders.[12-15] In particular, the pressure exerted on the paper and the time taken with the pen in flight have proven highly discriminatory, resulting in slower, less stable movements, and variable pressure during task performance in patients with AD. It is noteworthy that in patients with mild cognitive impairment (MCI), kinematic parameters, such as flight time, were particularly sensitive to cognitive status.[16-18] Nevertheless, the specific contribution of each graphomotor feature to task performance remains unclear, and further research is required to determine which parameters are most informative and the conditions under which they offer the greatest discriminatory power. Notably, people with AD have been observed to move more slowly and irregularly when performing complex activities, such as aiming tasks or curvilinear movements like circle drawing; however, these symptoms are less pronounced when simpler tasks, such as drawing straight lines or looped letters, are performed.[2] Longer execution times and slower writing speeds have also been observed in the early stages of the disease, particularly when writing in block letters.[16] Plonka *et al.*[8] investigated the relationship between cognitive demands and handwriting kinematics in different clinical populations, discovering that subjects with AD exhibited higher mean pressure in non-linguistic cognitive tasks, whereas subjects with primary progressive aphasia showed increased pressure in linguistic tasks, indicating a selective interaction between the cognitive domain elicited and the motor response. These findings underscore the importance of considering the task's impact on outcomes when examining graphomotor characteristics in writing and drawing, such as cognitive effort and the nature of movements performed.[17,18] In this regard, Garrè-Olmo *et al.*[17] used discriminant analysis to categorize participants based on their cognitive functioning as determined by graphomotor features. They observed that classification accuracy varied across task types and group comparisons, supporting the hypothesis that kinematic parameters were less informative when considered in isolation. In a multimodal integration study, Yamada *et al.*[19] analyzed graphomotor, vocal, and gait signals in individuals with cognitive decline, discovering that classification accuracy was the highest when combining the three behavioral modalities, with each modality outlining a distinct profile: graphical analyses revealed significant increases in pressure variability, decreases in speed, and prolonged pauses in the AD group during the writing process. These alterations were particularly pronounced during complex tasks, such as the Trail Making Test, and were also observed in MCI patients, highlighting the potential of complex tasks for early detection of dementia. All these

evidences[8,13-19] suggest that handwriting-related tasks are a promising tool for early dementia diagnosis. However, further investigation is needed, as the heterogeneity of protocols and outcomes limits the generalizability of results. Although specific graphomotor characteristics and task types have been identified, the most informative potential lies in their interactions, a topic that remains unexplored in the literature. Furthermore, many recent studies focus exclusively on classification models. Despite their ability to recognize complex patterns, these models have significant limitations, especially in interpretability, which can lead to the neglect of crucial information about the mechanisms of the graphomotor system and the underlying cognitive processes, both of which are clinically relevant. For this reason, a pilot study was conducted to evaluate the discriminative power of dynamic handwriting and drawing data in distinguishing between subjects diagnosed with probable AD and healthy controls (HCs). The main objective was to test a short-term screening method based on a combined writing and drawing protocol that could collect a wide range of information useful for the early identification of dementia. Specifically, we hypothesized that certain graphomotor features would be more sensitive to specific tasks. Therefore, the study examines the contribution of handwriting and drawing characteristics to the tasks performed, assessing whether their discriminatory capacity is task-specific or reflects more generalizable properties. These initial analyses aim to establish an empirical foundation for selecting tasks and key parameters for a future digital cognitive screening tool. By refining these tasks and identifying critical parameters, we hope to improve the accuracy and reliability of early dementia detection. Ultimately, this could lead to better outcomes through timely intervention and personalized support for those at risk.

In this regard, in line with the three-level functional structure (graphic, written, and complex tasks), this study proposes an independent and original protocol designed for future clinical application, which has been successfully validated in the Emotion Recognition from Handwriting and Drawing Project, where it was used to detect emotional states such as anxiety, depression, and stress through handwriting analysis on digital tablets by a sample of 129 subjects.[12] The current objective is to provide a preliminary validation of this protocol in detecting cognitive impairment. To this end, we explored the discriminatory power of online handwriting analysis in distinguishing between AD and HC subjects. Moreover, we investigated the specific contributions of individual tasks and related writing features to assess whether these features were task-dependent or task-independent. Although this is a pilot study with a small sample size and further large-scale validation is needed, our goal is to assess whether this approach shows potential as a feasible tool for future clinical applications.

2. Materials and methods

2.1. Selection criteria and participant recruitment

This pilot study recruited 39 participants (Participants were recruited between September 2024 and March 2025): 14 with probable AD (10 females and 4 males; mean age = 76; standard deviation [SD] = 6.42) and 25 healthy subjects (15 females and 10 males; mean age = 69.12; SD = 8.53). The sample size for this pilot study was determined through an a priori power analysis conducted using G*Power 3 software. Considering a comparison between two groups (clinical versus control) and the simultaneous analysis of an average of four dependent variables, it was hypothesized that the effect size would be medium to large, corresponding to an $f^2(V)$ value of 0.37. With a significance level of $\alpha = 0.05$ and a desired statistical power of 80% ($\beta = 0.20$), the minimum total sample size required was approximately 38 participants. The sample size adopted is consistent with that of comparable studies in the literature and accounts for the challenges of recruiting clinical subjects from sensitive populations. It is also proportionate to the exploratory and preliminary nature of the study.

All participants were right-handed and of Italian nationality. AD patients were recruited from the Memory Clinic at the University of Luigi Vanvitelli in Caserta. They were selected based on clinical and cognitive criteria consistent with mild-to-moderate disease, as outlined in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition[20] and the National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association criteria.[21] A multidisciplinary team of healthcare experts made the diagnosis based on clinical assessment, caregiver interviews, and standardized cognitive tests. The assessment covered a wide range of cognitive domains, including executive functions, short-term and long-term memory, language, and attention. Aspects of affective emotional functioning were also considered, with particular attention paid to the presence of depression, apathy, and mood swings, using validated tools and clinical observations. Participants' functional state and level of autonomy were evaluated by collecting data on activities of daily living and instrumental activities of daily living, supplemented by caregiver information from the Caregiver's Inventory for Neuropsychological Diagnosis of Dementia.[22] Where possible, the clinical evaluation was supported by blood tests and neuroimaging. No time criteria were applied for

disease duration; however, participants taking psychotropic medications, including antidepressants or other treatments known to alter cognitive or motor performance, were excluded. Additional exclusion criteria included a known diagnosis of motor disorders (including Parkinson's disease, Parkinsonism, and other conditions that could affect writing ability) and severe cognitive impairment, as determined by specialists. Cognitively, HCs were recruited at the Memory Clinic and through local communities (e.g., associations). They reported no history of neurological or psychiatric disorders, or sensory or motor impairments. Cognitive profiles were assessed using the Mini-Mental State Examination (MMSE)[23] and the Montreal Cognitive Assessment (MoCA).[24] Only subjects with MMSE scores ≥24 and MoCA scores ≥23 were included.[25-27] Table 1 shows the summary of cognitive test scores, age, education, and other demographic variables in the two groups. The experiment adhered to the ethical principles of privacy and confidentiality and received approval from the Ethics Committee of the University of Campania Luigi Vanvitelli, under protocol number 16/2024. All participants received detailed information about the study and provided written informed consent. They received a copy of the consent form. For the clinical group, caregivers also reviewed and confirmed their comprehension of the study, its methods, and its purposes.

2.2. Data acquisition and apparatus

The experimental environment was designed to enhance the ecological validity of the interaction, maintaining the natural characteristics of the graphic gesture as much as possible, even in a digital acquisition setting. For this purpose, a digital tablet was utilized, equipped with an ink-stamped pen that allowed writing on traditional A4 sheets of paper superimposed on the active surface. This approach provided participants with consistent, familiar visual feedback, thereby mitigating the artificial effects of digitization and fostering fluid and spontaneous writing.

Table 1. Demographics and psychometrics of participants (*n*=39)

Demographics and psychometrics	Healthy control	Alzheimer's disease
Number of participants	25	14
Age (mean and SD)	69.12 (±8.53)	76 (±6.42)
Gender (female: male)	15: 10	10: 4
Years of education (mean)	11.6	7.29
MoCA (mean)	25.54	18.21
MMSE (mean)	27.40	21.07

Abbreviations: MMSE: Mini-mental state examination; MoCA: Montreal cognitive assessment; SD: Standard deviation.

The tablet used was the Intuos 4 (Wacom Co., Ltd., Japan), featuring a 224 × 148 mm active surface and a 5,080 lines per inch resolution. The pen had 8192 levels of pressure sensitivity and up to 60 levels of tilt detection, allowing for the precise capture of variations in stroke kinematics. The data were sampled at 8-millisecond intervals, recording real-time coordinates (x, y), pressure, tilt, azimuth angle, and pen-up/down states. The collected data was subsequently archived in CSV format for processing. The tablet was connected to a laptop, allowing the researcher to view the traces made by the participants in real time. This ensured continuous monitoring and facilitated prompt intervention as necessary.

2.3. Tasks and features

Participants were required to complete seven tasks, including two writing tasks and five drawing activities. These tasks were specifically selected from a wide range of already validated neuropsychological tests used to evaluate psychological and cognitive skills. Figure 1 illustrates the battery of tasks selected for the study, with the drawing tasks presented in the upper section and the writing tasks in the lower section. This protocol was meticulously designed to encompass a broad spectrum of executive complexity, ranging from basic geometric tracing to tasks requiring high-order cognitive functions, such as planning, semantic memory, and phonological integration. The proposed tasks include the following:

(i) Pentagon (Task 1): Copying two intersecting pentagons, taken from the MMSE,[23] is a classic visuo-constructive task requiring eye-hand coordination and spatial integration.

(ii) House (Task 2): Copying a three-dimensional house, inspired by personality projective tests, which combines the reproduction of horizontal, vertical, and oblique straight lines.

(iii) Word (Task 3): Writing four Italian words in capital letters; "*BIODEGRADABILE*," "*FLIPSTIM*," "*CHIUNQUE*," and "*SMINUZZAVANO*" (English translation: "biodegradable," "flipstrim," "anyone," and "they chop up"), selected to include regular, irregular and non-sense word, according to established paradigms in the literature on orthographic and phonological processing.

(iv) Circles (Tasks 4 and 5): Drawing circular loops first with the non-dominant hand and then with the dominant hand. This is a simple task useful for assessing motor fluency, control of curvilinear movements, and differences related to hemispheric dominance.

(v) Clock (Task 6): The CDT was adapted from the MoCA.[24] It represents a complex task requiring

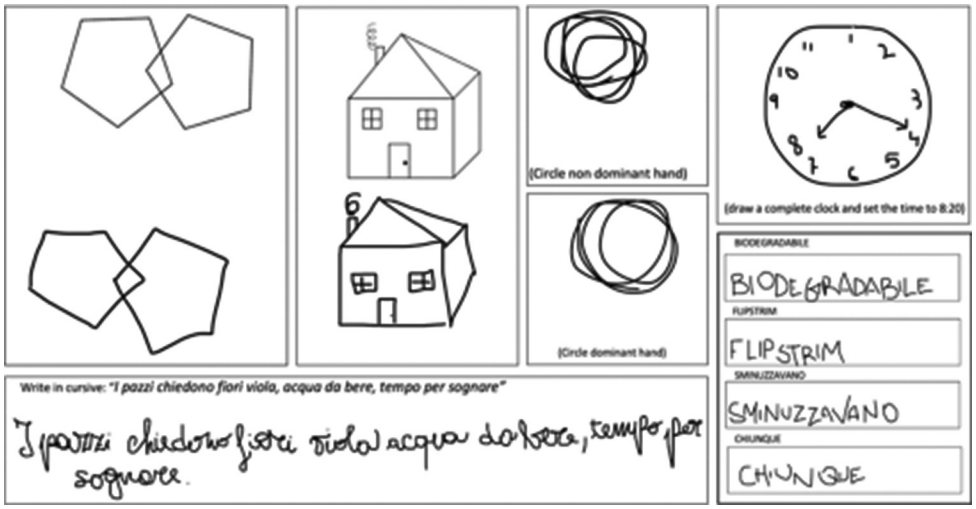

Figure 1. Illustration of the two task types. Drawing tasks are displayed on the top (pentagon, house, circle, and clock drawing) while writing tasks are shown on the bottom (word and sentence copy).

sequential planning, symbolic representation, and visuospatial integration.

(vi) Sentence (Task 7): Cursive copying of a phonologically complete Italian sentence: "*I pazzi chiedono fiori viola, acqua da bere, tempo per sognare*" (translated into English as "Crazy people ask for purple flowers, water to drink, and time to dream"), an exercise that simultaneously activates fine motor skills, sustained attention, linguistic processes, and working memory.

This heterogeneous battery enabled a sensitive examination of multiple motor, cognitive, and linguistic domains commonly affected by cognitive decline, thereby supporting a multi-level analysis of the graphomotor process. At the end of the experimental session, the raw data collected for each task were processed to extract a structured set of features. Specifically, 17 features were derived for each of the seven tasks, totaling 119 features, which were then grouped into five graphomotor categories: pressure, time, space, ductus, and inclination. Table 2 provides a detailed description of the features considered in the analysis, categorized by their type.

Table 2. Description of handwriting and drawing features according to their category

Category	Corresponding feature and description
Ductus	N_{up}: Length of movement performed in air
	N_{down}: Length of movement performed on paper
	N_{idle}: Strokes unrecognized by the tablet
Time	T_{up}: Time spent with the pen in the air
	T_{down}: Time spent with the pen on paper
	T_{idle}: Duration of pen status unrecognized by tablet
	T_{total}: Total time required to complete the task
Pressure	P_{min}: Minimum pressure value applied
	P_{max}: Maximum pressure value applied
	P_{avg}: Mean value of the applied pressure
	P_{sd}: Standard deviation of the applied pressure
	P_{10}: Lower 10th percentile of applied pressure
	P_{90}: Lower 90th percentile of applied pressure
Space and inclination	S_{bb}: Value derived from calculating the area of the smallest bounding box aligned to the axis that includes the stroke
	S_{avg}: Average length of the blank space between consecutive strokes
	S_{tot}: Total length of the blank space between consecutive strokes
	L_{avg}: Average inclination of the diagonals of the bounding boxes enclosing the strokes

2.4. Statistical analysis

Multivariate analysis of covariance (MANCOVA) was conducted using the Statistical Package for the Social Sciences (SPSS 21.0, IBM, United States) to evaluate the ability of graphomotor parameters to distinguish between individuals with cognitive impairment (AD) and HC subjects. Group affiliation (clinical versus control) was included as a fixed factor, while age and educational level were included as covariates to control for their potentially confounding effects on the dependent variables. The dependent variables were the graphic features extracted from each task and organized by graphomotor category (Table 2). A total of 28 separate MANCOVAs were performed, corresponding to an analysis of each of the four graphomotor categories (time, pressure, ductus, space, and inclination—the latter two analyzed jointly) for each of the seven proposed tasks. Each analysis included

all features belonging to the specific graphomotor category for that task as dependent variables. For example, the ductus-related features were analyzed in each of the seven tasks, and the same was performed for the other categories. Instead of conducting a single comprehensive analysis that included all 17 features simultaneously (17 features × 7tasks = 119 tests), we adopted an analytical design to limit the complexity of the statistical model, given the small number of participants. Such an analysis would have entailed a high risk of Type I error (false positives due to multiple comparisons) and a significant reduction in statistical power (Type II error), potentially compromising the reliability of the results and increasing the likelihood of misleading conclusions. Conversely, using 28 separate MANCOVAs enabled the simultaneous evaluation of the group's effect on multiple related variables, while accounting for interdependencies between features within each category and minimizing the risk of statistical errors. Where significant multivariate effects were present, *post hoc* univariate analyses of covariance were performed with Bonferroni correction for multiple comparisons to identify the features responsible for the differences between groups. Significance level was set at $p<0.05$. In the results sections, only the most relevant effects are reported. A complete, detailed view of the statistical results, including all *post hoc* analyses, is provided in the supplementary material (Table S1).

3. Results

3.1. Global effects of graphomotor categories across tasks

Multivariate analyses of covariance were used to estimate the overall effect of graphomotor categories (time, pressure, ductus, and space and inclination) on different groups for each task, while controlling for age and level of education. The results showed a significant difference between groups for time and ductus, whereas only one significant difference was observed for space and inclination. No statistically significant differences were found for pressure.

For time, the groups demonstrated a significant difference for Tasks 1 (F [4.32] = 3.675, p=0.014), 2 (F [4.32] = 9.335, p=0.000), 3 (F [4.32] = 6.559, p=0.001), 5 (F [3.33] = 5.181, p=0.005), 6 (F [4.32] = 3.274, p = 0.023), and 7 (F [4.32] = 2.926, p=0.036), indicating that participants with AD differed from the HC group in both drawing and writing tasks. In addition, a significant effect of age was observed in Task 6 (p=0.019), suggesting that age may influence execution times in clock drawing.

Regarding ductus, significant difference between groups was observed for Tasks 1 (F [3.32] = 3.955, p=0.017), 2 (F [3.33] = 3.921, p=0.017), 5 (F [2.34] = 7.606, p=0.002), 6 (F [3.33] = 3.348, p=0.031), and 7 (F [3.33] = 3.257, p=0.034), confirming graphical differences between groups in multiple writing and drawing conditions.

For space and inclination, a significant difference between groups was observed for Task 7 (F [4.32] = 2.691, p=0.049), whereas in Task 6, only the age covariate was significant (p=0.041). This suggests that spatial variations are more closely related to age than to clinical condition during CDT.

For pressure, no significant difference was observed between the groups.

Overall, the analyses indicate significant differentiation between groups in temporal and ductus measures, with age influencing clock drawing to some extent. Detailed statistical values for each graphomotor category and task are presented in Table 3.

3.2. Univariate analysis

Univariate analyses revealed several significant differences between the AD and HC groups across various writing features and tasks. While the space and inclination category showed an overall effect in Task 6 in the MANCOVA, this was not confirmed by the univariate analyses. Instead, statistically significant differences between the two groups emerged in the time and ductus categories. The results of the univariate analyses are reported in Table 4, which specifies the statistical significance, effect size, and mean values with SDs for each significant feature in the two groups (AD and HC). A complete overview of all results, including those that were not significant, is presented in the supplementary material (Table S1).

For the ductus category, the strokes unrecognized by the tablet (N_{idle}) feature were significant in all tasks, as indicated by the MANCOVAs. However, the N_{up} (length of movement performed in the air) and N_{down} (length of movement performed on paper) showed significant effects only in Tasks 5 and 7. Comparing the means revealed a homogeneous profile, with AD patients having higher scores than controls. Clinically, AD patients produced a greater number of strokes, both on paper and in the air, as well as more "empty" strokes. Notably, the N_{idle} feature represents movements that are not recognized by the tablet and can be interpreted as hand wandering, reflecting unstructured and non-purposeful motor activity. This phenomenon emerged consistently across tasks, regardless of whether they involved writing or drawing. During circle drawing with the dominant hand and cursive sentence writing, patients with AD exhibited not only increased N_{idle} but also a higher number of N_{up} and N_{down} strokes compared to HCs. This indicates an increased gesture segmentation, hesitation, and a loss of fluency in writing.

Table 3. Multivariate analysis of covariance results by group and covariates across all tasks and graphomotor categories

Category	Task	Wilks' Λ	*F* (df)	*p*	$\eta^2 p$	Age (*p*-value)	Education (*p*-value)
Ductus	1	0.729	3.955 (3.32)	0.017*	0.271	0.791	0.656
	2	0.737	3.921 (3.33)	0.017*	0.263	0.419	0.883
	3	0.898	1.243 (3.33)	0.310	0.102	0.201	0.851
	4	0.906	1.138 (3.33)	0.348	0.094	0.556	0.962
	5	0.691	7.606 (2.34)	0.002*	0.309	1.000	0.436
	6	0.767	3.348 (3.33)	0.031*	0.233	0.363	0.676
	7	0.772	3.257 (3.33)	0.034*	0.228	0.666	0.708
Time	1	0.685	3.675 (4.32)	0.014*	0.315	0.490	0.968
	2	0.461	9.335 (4.32)	0.000*	0.539	0.622	0.825
	3	0.549	6.559 (4.32)	0.001*	0.451	0.221	0.688
	4	0.796	2.054 (4.32)	0.110	0.204	0.234	0.914
	5	0.680	5.181 (3.33)	0.005*	0.320	0.693	0.370
	6	0.710	3.274 (4.32)	0.023*	0.290	0.019*	0.282
	7	0.732	2.926 (4.32)	0.036*	0.268	0.961	0.430
Pressure	1	0.737	1.783 (6.30)	0.136	0.263	0.626	0.235
	2	0.942	0.311 (6.30)	0.926	0.058	0.546	0.107
	3	0.761	1.567 (6.30)	0.191	0.239	0.181	0.114
	4	0.748	1.688 (6.30)	0.158	0.252	0.328	0.257
	5	0.785	1.370 (6.30)	0.259	0.215	0.755	0.755
	6	0.862	0.799 (6.30)	0.578	0.138	0.272	0.539
	7	0.845	0.920 (6.30)	0.494	0.155	0.844	0.617
Space and inclination	1	0.928	0.620 (4.32)	0.652	0.072	0.180	0.913
	2	0.867	1.225 (4.32)	0.320	0.133	0.447	0.710
	3	0.927	0.628 (4.32)	0.646	0.073	0.213	0.753
	4	0.835	1.579 (4.32)	0.204	0.165	0.322	0.245
	5	0.794	2.069 (4.32)	0.108	0.206	0.117	0.167
	6	0.896	0.930 (4.32)	0.459	0.104	0.041*	0.719
	7	0.748	2.691 (4.32)	0.049*	0.252	0.892	0.247

Notes: Task 1: Pentagon; Task 2: House; Task 3: Word; Tasks 4 and 5: Circles; Task 6: Clock; Task 7: Sentence. Statistical significance determined at $*p<0.05$.

Abbreviation: df: Degree of freedom.

For the time category, univariate analyses revealed significant group differences in almost all tasks. Notably, all temporal features were significant for Tasks 1, 2, and 3. No significant differences emerged for Task 4, aligning with the initial MANCOVA. In Tasks 5 and 7, all temporal features were significant, except for the time spent with the pen on paper (Tdown); in Task 6, only the duration of pen status unrecognized by the tablet (T_{idle}) was significant. Overall, a consistent pattern emerged from the mean scores, showing that the AD group exhibited higher values than the control group for all features and tasks, even when statistical significance was not achieved. A similar trend was also observed for the ductus category. These results suggest that patients with AD spend more time with the pen either in the air or in contact with the surface, thereby increasing total execution time. Furthermore, the T_{idle} parameter (i.e., the time not recognized by the system) was consistent with the increase in unrecognized strokes observed in the ductus category. Taken together, these two parameters suggest longer execution times and less fluid movement overall, which may indicate psychomotor slowing and reduced automation of graphomotor processes, even in simple tasks, such as drawing a circle with the dominant hand.

4. Discussion

The present study investigated a non-invasive method for distinguishing individuals with dementia from healthy subjects by integrating analyses of online drawing and writing tasks.

Table 4. Significant univariate results ($p<0.05$) for each feature and task, with group means and standard deviations

Category	Task	Feature	*F* (df)	*p*-value	η^2 *p*	AD mean±SD	HC mean±SD
Ductus	1	N_{idle}	12.091 (1.34)	0.001	0.262	14.890±2.201	4.622±1.545
	2	N_{idle}	11.627 (1.35)	0.002	0.249	16.241±2.348	5.505±1.648
	5	N_{up}	11.495 (1.35)	0.002	0.247	3.074±0.545	0.598±0.382
		N_{down}	11.495 (1.35)	0.002	0.247	4.074±0.545	1.598±0.382
		N_{idle}	7.181 (1.35)	0.011	0.170	1.925±0.480	0.202±0.337
	6	N_{idle}	7.597 (1.35)	0.009	0.178	16.350±2.615	6.684±1.836
	7	N_{up}	4.237 (1.35)	0.047	0.108	63.050±6.100	46.212±4.282
		N_{down}	3.957 (1.35)	0.050	0.102	63.629±6.186	47.128±4.342
		N_{idle}	5.430 (1.35)	0.026	0.134	17.090±2.963	7.830±2.080
Time	1	T_{up}	6.880 (1.35)	0.013	0.164	21,820.942±3,106.290	10,894.513±2,180.492
		T_{down}	5.503 (1.35)	0.025	0.136	17,132.331±2,126.358	10,443.255±1,492.619
		T_{idle}	6.527 (1.35)	0.015	0.157	19,021.266±4,492.789	3,628.291±3,153.760
		Total	13.832 (1.35)	0.001	0.283	57,976.077±6,618.315	24,966.757±4,645.794
	2	T_{up}	15.714 (1.35)	0.000	0.310	36,364.274±3,690.602	16,744.447±2,590.656
		T_{down}	7.112 (1.35)	0.012	0.169	24,180.190±2,769.910	14,273.774±1,944.367
		T_{idle}	11.534 (1.35)	0.002	0.248	12,366.581±2,192.672	2,380.035±1,539.168
		Total	20.558 (1.35)	0.000	0.370	72,917.563±6,499.348	33,398.245±4,562.284
	3	T_{up}	17.302 (1.35)	0.000	0.331	78,945.333±8,599.585	30,975.333±6,036.568
		T_{down}	12.929 (1.35)	0.001	0.270	37,686.454±3,296.460	21,791.026±2,313.984
		T_{idle}	5.849 (1.35)	0.021	0.143	32,822.920±6,340.780	12,257.445±4,450.976
		Total	16.966 (1.35)	0.000	0.326	149,465.100±15,286.424	65,025.264±10,730.463
	5	T_{up}	13.549 (1.35)	0.001	0.279	3,226.461±596.140	283.742±418.467
		T_{idle}	4.909 (1.35)	0.033	0.123	888.350±259.278	117.964±182.003
		Total	10.893 (1.35)	0.002	0.237	11,199.746±1,447.436	4,793.382±1,016.043
	6	T_{idle}	7.756 (1.35)	0.009	0.181	18,528.158±3,799.641	4,337.071±2,667.197
	7	T_{up}	11.746 (1.35)	0.002	0.251	42,545.297±5,243.194	18,446.794±3,680.514
		T_{idle}	6.197 (1.35)	0.018	0.150	13,352.760±2,628.629	4,577.254±1,845.194
		Total	12.131 (1.35)	0.001	0.257	81,485.894±8,358.319	42,445.139±5,867.208

Notes: Task 1: Pentagon; Task 2: House; Task 3: Word; Tasks 4 and 5: Circles; Task 6: Clock; Task 7: Sentence. Refer to Table 2 for a description of the features.
Abbreviations: AD: Alzheimer's disease; df: Degree of freedom; HC: Healthy control; SD: Standard deviation.

The results revealed clear differences between AD patients and controls in ductus- and temporal-related features. Regarding execution time, AD patients showed slower performance in both writing and drawing tasks, compared to controls. This slowdown is likely due to reduced processing speed and psychomotor retardation, which impair attention and action planning; these difficulties have been reported in the literature to be reflected in reduced autonomy in daily activities.[28] Particularly, pen-up time was highly effective at distinguishing between groups, even on simple tasks such as looping circles with the dominant hand. These observations confirm previous reports that in-air trajectories are an early indicator of cognitive impairment, which can distinguish between different stages of the disease.[8] Flight time may reflect a disorder in gesture planning, affecting the ability to decide when and how to initiate movement. Therefore, it is sensitive to tasks that require less complex integration between cognitive processes and motor control. Another consideration is the times observed in Task 6. Unlike the other tasks, no statistically significant differences in execution times were observed in the CDT, except for T_{idle}. The traditional CDT is highly sensitive to cognitive impairment but mainly assesses execution accuracy, i.e., the spatial arrangement of elements, the number of errors, and the overall quality of the final product. Therefore, time-related features may lack specificity for this task. Furthermore, the tasks in the present study involved imitating a model and provided clear guidance on what participants had to do. In contrast, CDT required

the participants to create the drawing from scratch without any prompts. This can create an "illusion of completion:" Patients may proceed with the drawing without fully understanding the necessary corrections, taking a similar amount of time to controls but producing a poor-quality result containing numerous errors. In other words, while execution times may be comparable, the difference lies in the accuracy and richness of detail, providing a coherent explanation for the observed statistical results. Regarding Task 4, the lack of statistical significance may be due to the effort required, given that it involves right-handed participants using their non-dominant left hand. This may cause even cognitively healthy participants to perform more slowly, thus attenuating the differences between groups. Therefore, any observed difficulty using the non-dominant hand may depend more on biomechanical and laterality factors than on specific cognitive deficits, which could explain the absence of statistical significance.

As for the ductus category, it was observed that AD patients tend to produce more strokes in writing and drawing tasks—both in the air and on paper—especially during sentence writing and in the circle loop with the dominant hand. Furthermore, they produced more unrecognizable strokes in most tasks. These results could arise from reduced motor control and altered spatial organization, leading to less precise, more fragmented writing, in line with findings observed for the temporal category.[29,30] Taken together, these two parameters help us to understand how hesitations and disfluencies in writing contribute to longer execution times. Conversely, such disfluencies and irregularities could result from a general psychomotor slowdown and impaired coordination.

Regarding pressure, as well as space and inclination, no statistically significant differences were found. This result can be interpreted as indicating that these parameters predominantly represent a biomechanical and automatic aspect of the graphic performance. These aspects may be less influenced by central cognitive processes and, therefore, could be more easily compensated for. Indeed, graphomotor skills are in part automated, meaning that parameters, such as pressure or stroke inclination, may remain relatively unaffected in the early and moderate stages of the disease. Conversely, kinematic and temporal characteristics—related to fluidity and execution speed—are highly susceptible to cognitive decline, since they could reflect higher cognitive functions, such as planning, executive control, and continuous movement monitoring.[31] This helps to explain why ductus features and execution times have greater discriminative power than other types of features, as supported by previous literature.[30-33] According to these studies, inclination does not appear to be a reliable or consistent parameter for distinguishing between normal and pathological aging. However, it could be effective in identifying mood alterations, such as symptoms of depression, where a more pronounced inclination could indicate reduced motor activation and cognitive effort.[34] In this context, inclination may have exploratory value and could be useful in differential diagnosis when considered in conjunction with other features. Regarding spatial aspects, it is important to recognize that spatial features reflect biomechanical, visuo-constructive, and spatial components.

In the present study, the absence of significant differences may be due to task performance being partially guided by a model to be copied, thereby reducing the cognitive demands placed on participants. Furthermore, using a bounding box likely provided external spatial cues, enabling participants to achieve a spatial distribution similar to that of the control group. In any case, the lack of statistical significance does not rule out genuine alterations; the small sample size in the AD group ($n = 14$) may have limited the analyses' statistical power. With a larger sample size, these measures may demonstrate a consistent trend with the visuospatial decline typically observed in AD. In addition, methodological differences across studies in the literature, including sample sizes and measurement tools, make direct comparison of results challenging and contribute to heterogeneity in reported data. Similarly, the same methodological considerations can be applied to pressure measurements, which are among the most controversial parameters in the literature. While our analyses do not contradict the results reported by Delazer *et al.*,[35] our data belong to a highly heterogeneous context in which empirical findings are often discordant and sometimes contradictory.[4,15] This variability can be attributed, at least in part, to differences in experimental protocols, measurement instruments, and sample selection criteria. These differences make direct comparisons between studies difficult and limit our ability to draw effective conclusions about the role of pressure in the analyzed graphomotor processes.

From a neurobiological perspective, although this study did not include biomarkers, literature suggests that alterations in fine motor skills are closely linked to underlying neurodegenerative processes, while the neural mechanisms remain poorly understood. Neuroimaging studies of motor function in patients with AD have revealed compensatory neural patterns during gross movement tasks (such as walking or gross coordination), while research into fine motor coordination remains limited.[36] Investigations into brain connectivity during manual dexterity tasks in individuals experiencing early stages of cognitive decline have not revealed significant differences compared to those without the condition, suggesting that

more subtle motor alterations emerge only in later stages of the disease.[37] The observed motor alterations in AD patients appear to result from an interaction between cognitive deficits and sensorimotor dysfunctions caused by neurodegenerative processes.[22,30] From this perspective, the observed slowing and graphomotor disfluency represent a loss of efficiency in the cognitive control mechanisms of movement, rather than a primary motor deficit. Understanding these differences is essential for improving our comprehension of the pathophysiological mechanisms of AD and for making differential diagnoses with other neurodegenerative diseases where movement disorders are predominant, such as Parkinson's disease.[5] Handwriting and drawing analysis may therefore represent a link between observable clinical manifestations and pathophysiological mechanisms, offering a multidimensional view of cognitive and functional decline. Moreover, graphomotor features are best interpreted in the context of the task, since certain motor patterns reflect the demands of the activity rather than specific deficits. This emphasizes the importance of considering the overall complexity of the graphomotor process rather than focusing on individual parameters in isolation.

Although several questions remain unanswered, the overall results confirm the existing literature on slowness and disfluency as distinctive features of AD patients.[35,38] Observed alterations, such as reduced execution speed, disorganized motor patterns, and an increased number of unrecognizable strokes, result in practical difficulties, including slower document completion, illegible handwriting, and impaired coordination of movements. These deficits directly affect autonomy in instrumental activities of daily living and overall quality of life, as they are often associated with reduced functional independence. Simple graphomotor tasks can therefore provide valuable insight into a patient's functional status. The proposed multi-task protocol is straightforward and fully non-invasive, with potential clinical applications, particularly for the early screening of dementia and the longitudinal monitoring of disease progression. Its use of short, easily replicable tasks enables frequent assessments in outpatient or home settings, supporting timely, patient-centered interventions to preserve autonomy, and quality of life. Furthermore, the quantitative and objective nature of the analysis minimizes human error, thereby enhancing the reliability and reproducibility of the results compared with those of traditional neuropsychological tests, which are based on subjective assessments and are susceptible to inter- and intra-examiner bias. In this context, the proposed protocol improves existing tools, such as the CDT, by offering a more detailed quantitative analysis. Continuous, objective measurements enable the detection of subtle variations that are often invisible in traditional assessments. This enhances sensitivity for long-term monitoring, supporting the early diagnosis of AD and the personalization of treatment pathways.

5. Limits and future direction

Several limitations should be considered when interpreting the results of this study. First, the small sample size ($n = 39$) and the imbalance between the AD and HC groups are significant methodological constraints. However, as this was a pilot study, the primary aim was to verify the feasibility of the experiment and to explore whether the proposed protocol could discriminate between the two groups by analyzing the relationships between different tasks and specific graphomotor features. The intention was not to draw definitive conclusions, but rather to identify potentially sensitive parameters and assess the consistency of the experimental paradigm with relevant clinical and neuropsychological assumptions. In this regard, the study advances our understanding of a field characterized by many uncertainties, including the neurodegenerative mechanisms underlying graphomotor skills, the specificity of graphomotor markers across different profiles of cognitive decline, and the relationship between higher cognitive processes and motor parameters in writing. Recruiting participants with neurodegenerative diseases poses logistical and organizational challenges due to strict inclusion criteria and limited access to vulnerable clinical groups. This justifies the use of a small but methodologically controlled sample, as is common in the literature. A similar issue arises with the age imbalance, with AD participants being older on average. Since age is a known confounding factor for motor slowing and cognitive decline, it may have influenced the results. While this was partially addressed by including age as a covariate in the MANCOVAs, future studies should aim to include larger, age- and education-matched samples to enhance statistical validity and generalizability. In addition, the homogeneity of the sample, comprising only Italian participants, prevented cross-cultural validation. Future studies should address the influence of cultural and educational factors on graphomotor and cognitive performance. Extending the protocol to different sociocultural contexts would enable the reproducibility of the results to be evaluated, as well as the impact of culture, language, and education on the generalizability of the findings.

In summary, the results of this study are a first step toward developing a complementary neuropsychological assessment tool based on graphomotor parameter analysis in writing and drawing tasks. However, as this is a pilot study with a small, unmatched sample, the results should be interpreted with caution. While the statistical analysis

controlled for confounding variables, such as age and education, future studies should validate these results using larger, more balanced populations that are more thoroughly characterized clinically. This may clarify some open methodological aspects, such as: (i) the stability of the parameters in relation to the method of acquisition (digital pen, tablet, or touchscreen); (ii) the sensitivity of the protocol in detecting early stages such as MCI; and (iii) the use of longitudinal approaches to observe the evolution of writing patterns over time and detect the progression of cognitive decline. Finally, future analyses may explore multivariate predictive models or classifiers that combine the most informative parameters to improve diagnostic accuracy and provide objective support for clinical practice. From this perspective, handwriting becomes a quantifiable window into cognitive functions and their impairment, rather than being observed only in qualitative terms.

6. Conclusion

This pilot study highlights the potential of a multi-task protocol, supported by dynamic graphic parameter analysis, as an innovative tool for early identification of neurodegenerative disease, particularly AD. Combining tasks and dynamic graphomotor features enables effective discrimination between clinical subjects and HCs, although a more in-depth evaluation is needed. Overall, the results suggest that time- and ductus-related features are particularly robust within the context of the proposed protocol. In contrast, no significant group differences were revealed for other features, such as pressure, as well as spatial and inclination parameters. This discrepancy does not imply that these features are uninformative; rather, it suggests that they vary in their discriminative power and likely reflect different underlying neurophysiological and cognitive processes. Clinically, patients with mild-to-moderate AD exhibited longer execution times and disfluencies with signs of uncertainty or hesitation in writing. This is consistent with a profile of psychomotor retardation and slower processing speed, which are typically associated with AD. As these graphomotor changes may appear before more evident cognitive symptoms, handwriting analysis could serve as a sensitive, non-invasive marker for early diagnosis. Furthermore, such measures could contribute to differential diagnosis by helping to distinguish AD from other neurodegenerative or psychiatric conditions that present with similar symptoms but different motor profiles. Longitudinal assessment of these parameters can also help clinicians track disease progression and evaluate treatment response. Finally, identifying specific motor and cognitive patterns enables the development of personalized rehabilitation strategies to preserve fine motor control and daily life autonomy.

From a technological perspective, identifying informative graphomotor parameters sensitive to cognitive decline is crucial for developing classification models and optimizing predictions. This paves the way for future digital developments and big data- and artificial intelligence-based applications. Technological progress and clinical relevance are closely linked, as the development of sensitive, accessible, affordable, and rapid screening tools is essential for developing person-centered, accessible medicine. As there is still no cure for AD, optimizing and streamlining diagnostic processes using cutting-edge tools is crucial to ensuring timely access to treatment and providing families with the right support. This is important because patients and carers often feel disorientated, confused, and socially isolated when facing the disease; receiving support to help them manage it can significantly improve their quality of life. While these objectives remain unattained, it is important to emphasize their prospective significance. These preliminary data provide a deeper understanding of the processes underlying handwriting in neurodegenerative diseases and offer the potential to integrate technological innovation into a clinical framework. While several questions remain unanswered, this research nonetheless represents a significant step toward developing dementia screening methods that combine scientific rigor, technological innovation, and clinical relevance.

Acknowledgments

We are grateful to the healthcare staff and research team of the Memory Clinic of L. Vanvitelli University in Caserta, Italy, for granting us access to the local patient community and for collecting the participants' clinical data. We acknowledge the valuable assistance of postdoctoral researchers Marialucia Cuciniello and Terry Amorese in improving the manuscript's English language.

Funding

This study received funding from the EU-H2020 program (grant no. 101182965, CRYSTAL), the EU NextGenerationE PNRR Mission 4 Component 2 Investment 1.1 (D.D 1409 del 14-09-2022) PRIN 2022 under the IRRESPECTIVE project (code P20222MYKE, CUP: B53D23025980001), and PNRR MUR under AI-PATTERNS FAIR Project (E63C22002150007).

Conflict of interest

The authors declare that they have no competing interests.

Author contributions

Conceptualization: Anna Esposito, Gennaro Cordasco
Formal analysis: Maria Santina Ler

Investigation: Maria Santina Ler, Miriam Veneziano, Alfonsina D'Iorio, Gabriella Santangelo
Methodology: Maria Santina Ler, Anna Esposito, Gennaro Cordasco
Writing–original draft: Maria Santina Ler
Writing–review & editing: Maria Santina Ler

Ethics approval and consent to participate

The experiment adhered to ethical principles of privacy and confidentiality and received approval from the Ethics Committee of the University of Campania Luigi Vanvitelli, under protocol number 16/2024. All participants received detailed information about the study and provided written informed consent to participate voluntarily. They received a copy of the consent form. For the clinical group, caregivers also reviewed and confirmed their comprehension of the study, its methods, and its purposes.

Consent for publication

All participants provided written consent for the publication of their data and its use for research and scientific purposes. To protect privacy, sensitive data were anonymized.

Availability of data

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

References

1. Smith AD. On the use of drawing tasks in neuropsychological assessment. *Neuropsychology*. 2009;23(2):231-239.

   doi: 10.1037/a0014184

2. Yu NY, Chang SH. Kinematic analyses of graphomotor functions in individuals with Alzheimer's disease and amnestic mild cognitive impairment. *J Med Biol Eng*. 2016;36:334-343.

   doi: 10.1007/s40846-016-0143-y

3. Ghaderyan S, Abbasi A, Saber S. A new algorithm for kinematic analysis of handwriting data; towards a reliable handwriting-based tool for early detection of Alzheimer's disease. *Expert Syst Appl*. 2018;114:428-440.

   doi: 10.1016/j.eswa.2018.07.052

4. Kairamkonda DD, Mandeleeka PS, Favaro A, *et al*. Analysis of interpretable handwriting features to evaluate motoric patterns in different neurodegenerative diseases. In: *2022 IEEE Signal Processing in Medicine and Biology Symposium (SPMB)*. Philadelphia, PA, USA: IEEE; 2022. p. 1-6.

   doi: 10.1109/spmb55497.2022.10014966

5. Slavin MJ, Phillips JG, Bradshaw JL, Hall KA, Presnell I. Consistency of handwriting movements in dementia of the Alzheimer's type: A comparison with Huntington's and Parkinson's diseases. *J Int Neuropsychol Soc*. 1999;5:20-25.

   doi: 10.1017/s135561779951103x

6. Kahindo C, El-Yacoubi MA, Garcia-Salicetti S, Rigaud AS, Cristancho-Lacroix V. Characterizing early-stage Alzheimer through spatiotemporal dynamics of handwriting. *IEEE Signal Process Lett*. 2018;25(8):1136-1140.

   doi: 10.1109/lsp.2018.2794500

7. Impedovo D, Pirlo G, Barbuzzi D, Balestrucci A, Impedovo S. Handwritten processing for pre diagnosis of Alzheimer disease. In: *Proceedings of Biodevices 2014*; 2014. p. 193-199.

   doi: 10.5220/0004900701930199

8. Plonka A, Mouton A, Macoir J, *et al*. Primary progressive aphasia: Use of graphical markers for an early and differential diagnosis. *Brain Sci*. 2021;11(9):1198.

   doi: 10.3390/brainsci11091198

9. Bensalah A, Parziale A, De Gregorio G, Marcelli A, Fornés A, Lladós J. I can't believe it's not better: In-air movement for Alzheimer handwriting synthetic generation. In: *Proceedings of the International Graphonomics Conference*. Cham, Switzerland; 2023. p. 136-148.

   doi: 10.48550/arXiv.2312.05086

10. Cilia ND, De Stefano C, Fontanella F, Di Freca AS. An experimental protocol to support cognitive impairment diagnosis by using handwriting analysis. *Procedia Comput Sci*. 2018;141:466-471.

    doi: 10.1016/j.procs.2018.10.141

11. Cilia ND, De Gregorio G, De Stefano C, Fontanella F, Marcelli A, Parziale A. Diagnosing Alzheimer's disease from on-line handwriting: A novel dataset and performance benchmarking. *Eng Appl Artif Intell*. 2022;111:104822.

    doi: 10.1016/j.engappai.2022.104822

12. Likforman-Sulem L, Esposito A, Faundez-Zanuy M, Clémençon S, Cordasco G. EMOTHAW: A novel database for emotional state recognition from handwriting and drawing. *IEEE Trans Hum-Mach Syst*. 2017;47(2):273-284.

    doi: 10.1109/thms.2016.2635441

13. Impedovo D, Pirlo G. Dynamic handwriting analysis for the assessment of neurodegenerative diseases: A pattern recognition perspective. *IEEE Rev Biomed Eng*. 2019;12:209-220.

    doi: 10.1109/rbme.2018.2840679

14. Schröter A, Mergl R, Bürger K, Hampel H, Möller HJ, Hegerl U. Kinematic analysis of handwriting movements in patients with Alzheimer's disease, mild cognitive impairment, depression and healthy subjects. *Dement Geriatr Cogn Disord*. 2003;15(3):132-142.

    doi: 10.1159/000068484

15. Qi H, Zhang R, Wei Z, *et al*. A study of auxiliary screening for

Alzheimer's disease based on handwriting characteristics. *Front Aging Neurosci*. 2023;15:1117250.

doi: 10.3389/fnagi.2023.1117250

16. Kawa J, Bednorz A, Stępień P, Derejczyk J, Bugdol M. Spatial and dynamical handwriting analysis in mild cognitive impairment. *Comput Biol Med*. 2017;82:21-28.

doi: 10.1016/j.compbiomed.2017.01.004

17. Garre-Olmo J, Faúndez-Zanuy M, López-De-Ipiña K, Calvó-Perxas L, Turró-Garriga O. Kinematic and pressure features of handwriting and drawing: Preliminary results between patients with mild cognitive impairment, Alzheimer disease and healthy controls. *Curr Alzheimer Res*. 2017;14(9):960-968.

doi: 10.2174/1567205014666170309120708

18. Müller S, Preische O, Heymann P, Elbing U, Laske C. Diagnostic value of a tablet-based drawing task for discrimination of patients in the early course of Alzheimer's disease from healthy individuals. *J Alzheimers Dis*. 2016;55(4):1463-1469.

doi: 10.3233/jad-160921

19. Yamada Y, Shinkawa K, Kobayashi M, *et al*. Combining multimodal behavioral data of gait, speech, and drawing for classification of Alzheimer's disease and mild cognitive impairment. *J Alzheimers Dis*. 2021;84(1):315-327.

doi: 10.3233/jad-210684

20. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA work group under the auspices of department of health and human services task force on Alzheimer's disease. *Neurology*. 1984;34(7):939-944.

doi: 10.1212/wnl.34.7.939

21. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Arlington, VA: American Psychiatric Association; 2013.

22. Petersen RC, Jack CR Jr., Xu YC, *et al*. Memory and MRI-based hippocampal volumes in aging and AD. *Neurology*. 2000;54(3):581-587.

doi: 10.1212/wnl.54.3.581

23. Folstein MF, Robins LN, Helzer JE. The mini-mental state examination. *Arch Gen Psychiatry*. 1983;40(7):812.

doi: 10.1001/archpsyc.1983.01790060110016

24. Nasreddine ZS, Phillips NA, Bédirian V, *et al*. The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. *J Am Geriatr Soc*. 2005;53(4):695-699.

doi: 10.1111/j.1532-5415.2005.53221.x

25. Conti S, Bonazzi S, Laiacona M, Masina M, Coralli MV. Montreal Cognitive Assessment (MoCA)-Italian version: Regression based norms and equivalent scores. *Neurol Sci*. 2015;36(2):209-214.

doi: 10.1007/s10072-014-1921-3

26. Carson N, Leach L, Murphy KJ. A re-examination of montreal cognitive assessment (MoCA) cutoff scores. *Int J Geriatr Psychiatry*. 2018;33(2):379-388.

doi: 10.1002/gps.4756

27. Measso G, Cavarzeran F, Zappala G, *et al*. The mini-mental state examination: Normative study of an Italian random sample. *Dev Neuropsychol*. 1993;9(2):77-85.

doi: 10.1080/87565649109540545

28. De Paula JJ, Albuquerque MR, Lage GM, Bicalho MA, Romano-Silva MA, Malloy-Diniz LF. Impairment of fine motor dexterity in mild cognitive impairment and Alzheimer's disease dementia: Association with activities of daily living. *Braz J Psychiatry*. 2016;38:235-238.

doi: 10.1590/1516-4446-2015-1874

29. Neils-Strunjas J, Groves-Wright K, Mashima P, Harnish S. Dysgraphia in Alzheimer's disease: A review for clinical and research purposes. *J Speech Lang Hear Res*. 2006;49(6):1313-1330.

doi: 10.1044/1092-4388(2006/094)

30. Yan JH, Rountree S, Massman P, Doody RS, Li H. Alzheimer's disease and mild cognitive impairment deteriorate fine movement control. *J Psychiatr Res*. 2008;42(14):1203-1212.

doi: 10.1016/j.jpsychires.2008.01.006

31. Guarino A, Favieri F, Boncompagni I, Agostini F, Cantone M, Casagrande M. Executive functions in Alzheimer disease: A systematic review. *Front Aging Neurosci*. 2019;10:437.

doi: 10.3389/fnagi.2018.00437

32. Fernandes CP, Montalvo G, Caligiuri M, Pertsinakis M, Guimarães J. Handwriting changes in Alzheimer's disease: A systematic review. *J Alzheimers Dis*. 2023;96(1):1-11.

doi: 10.3233/JAD-230438

33. Werner P, Rosenblum S, Bar-On G, Heinik J, Korczyn A. Handwriting process variables discriminating mild Alzheimer's disease and mild cognitive impairment. *J Gerontol B Psychol Sci Soc Sci*. 2006;61(4):P228-P236.

doi: 10.1093/geronb/61.4.p228

34. Greco C, Raimo G, Amorese T, *et al*. Discriminative power of handwriting and drawing features in depression. *Int J Neural Syst*. 2024;34(2):2350069.

doi: 10.1142/s0129065723500697

35. Delazer M, Zamarian L, Djamshidian A. Handwriting in Alzheimer's disease. *J Alzheimers Dis*. 2021;82(2):727-735.

doi: 10.3233/jad-210279

36. Koppelmans V, Silvester B, Duff K. Neural mechanisms of motor dysfunction in mild cognitive impairment and

Alzheimer's disease: A systematic review. *J Alzheimers Dis Rep.* 2022;6(1):307-344.

doi: 10.3233/adr-210065

37. Crockett RA, Hsu CL, Best JR, Beauchet O, Liu-Ambrose T. Head over heels but I forget why: Disruptive functional connectivity in older adult fallers with mild cognitive impairment. *Behav Brain Res*. 2019;376:112104.

doi: 10.1016/j.bbr.2019.112104

38. Kobayashi M, Yamada Y, Shinkawa K, Nemoto M, Nemoto K, Arai T. Automated early detection of Alzheimer's disease by capturing impairments in multiple cognitive domains with multiple drawing tasks. *J Alzheimers Dis*. 2022;88(3):1075-1089.

doi: 10.3233/jad-215714