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Handwriting Process Variables Discriminating Mild Alzheimer's Disease and Mild Cognitive Impairment

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This study's aims were (a) to examine kinematically the handwriting process of persons with mild cognitive impairment (MCI), compared with those with mild Alzheimer's disease and healthy controls; (b) to assess the importance of these measures for the differentiation of the groups; and (c) to assess characteristics of the handwriting process across different functional tasks. Thirty-one persons with MCI, 22 with mild Alzheimer's disease, and 41 healthy controls performed functional tasks while using a computerized system. We found significant differences between the groups in almost all measures, with the MCI group assuming a position between the other groups. Temporal measures were higher and pressure was lower in more cognitively deteriorated groups. Information gathered about kinematic measures, together with cognitive functioning, allowed us to classify 69% to 72% of the participants correctly, although the classification for the MCI group was relatively poor.

ALZHEIMER'S disease (AD) is a degenerative disease that attacks the brain, causing memory loss, cognitive impairment, and, in late stages, deterioration of motor skills and withdrawal from social contacts. AD is characterized by a gradual onset of symptoms and irreversible decline to a near vegetative state (Small et al., 1997).

Recently, there has been an increase in research focusing on evidence that the onset of AD is preceded by a phase of loss in cognitive functioning in general and in memory functioning in particular (Goldman & Morris, 2001). This phase has been termed *mild cognitive impairment* (MCI; Petersen et al., 1999), and it has been defined as "a transitional but progressively degenerative cognitive phase that precedes the onset of AD" (Shah, Tangalos, & Petersen, 2000, p. 65), although naturalistic studies show that not all persons with MCI progress and some even recover.

Handwriting is a complex human activity that entails an intricate blend of cognitive, kinesthetic, and perceptual-motor components (Reisman, 1993), including visual and kinesthetic perception, motor planning, eye–hand coordination, visual-motor integration, dexterity, and manual skills (Tseng & Cermak, 1993). These characteristics of the handwriting process suggest that it might be sensitive to age-related impairments in cognitive functioning, and thus assessments of handwriting might facilitate the diagnosis of such impairments. We designed the present research to address this possibility.

Significant handwriting difficulties were already reported by Alois Alzheimer when describing the first patient with AD in 1907: "when writing, she reduplicated the same syllable and forgot some others, in general, finished very rapidly by stopping" (p. 226, Croislie, 1999). The evolution of agraphic impairments in AD was described in 1989 (Platel et al., 1993) and included lexicosemantic disturbances at the beginning of the disease, with impairments becoming more and more phonological as the dementia becomes more severe.

In several studies, researchers examined this proposed sequence by using writing tests. Results of these studies showed that handwriting difficulties were well correlated with the severity of the disease and the concomitant cognitive impairment. Croislie (1999), using results from LaBarge, Smith, Dick, and Storandt (1992), concluded that AD patients give the visual impression of a studious and hesitant writing. Croislie thought that graphic motor skills were impaired early in AD because they require cognitive decision making in order to perform automatic retrieval. Other studies reported that, compared with controls, mild to moderate AD patients significantly increased their writing thickness and pressure of the pen (LaBarge et al.).

Despite these encouraging findings by Croislie (1999), LaBarge and colleagues (1992), and others, their conclusions are limited by the methodologies used. Indeed, most studies focused on the linguistic aspects of the writing product or its content (Croislie; Kemper et al., 1993; Hughes, Graham, Patterson, & Hodges, 1997; Nakamura, Nakanishi, Hamanaka, Nakaaki, & Yoshida, 2000; Shwartz, Marin, & Saffran, 1979). The kinematic characteristics of handwriting in AD patients were not widely assessed, although this complex everyday skill can supply important information about the perceptual-motor process.

Kinematic Assessment of Handwriting

By analyzing a rich set of handwriting measures, recent developments in data-collection technology permit the researcher to examine the writing process rather than its outcome. With the aid of a digitizing tablet and an instrumented pen, the researcher can monitor the handwriting in real time and store it in a format amenable to sophisticated kinematic and kinetic analyses (Slavin, Phillips, Bradshaw, Hall, & Presnell, 1999). The use of such devices enables the researcher not only to measure simple temporal variables but also to achieve greater

Table 1. Background Characteristics of the Participants

Variable	Healthy ($n = 41$)	MCI ($n = 31$)	Mild AD ($n = 22$)	F Test
Mean age (*SD*)	75.8 (6.4)	76.8 (6.5)	79.9 (6.5)	—
Female (%)	53.7	41.9	50.0	—
Mean years of education (*SD*)	13.6 (2.6)[b]	13.0 (2.7)	11.7 (2.5)	3.5*
Mean MMSE (*SD*)	28.7 (1.1)[a,b]	26.6 (2.4)[c]	23.7 (2.8)	37.1**

Notes: MCI = mild cognitive impairment; AD = Alzheimer's disease. A dash indicates that the results were not significant.

[a]Denotes a statistically significant difference between healthy and MCI participants.

[b]Denotes a statistically significant difference between healthy and mild AD participants.

[c]Denotes a statistically significant difference between MCI and mild AD participants.

*$p < .05$; **$p < .001$.

precision or detail in the temporal and spatial dimensions (e.g., the amount of time that a person holds her or his pen above the writing surface or on the writing surface, or the ratio between the two). In addition, the researcher can monitor other variables, such as the pressure exerted on the writing surface and the angle with which the pen is held. Because the digitizing tablet and a laptop computer are portable, the researcher can obtain these measures either in the writer's natural everyday environment (e.g., at home) or in a medical center. Finally, as a result of the automation of the data-collection and analysis procedures, it is feasible for a researcher to collect relatively large numbers of handwriting samples in a single experimental session, and to follow up with participants performing similar tasks under the same conditions.

Kinematic Assessment of Handwriting in AD

The majority of the studies assessing kinematic characteristics of handwriting were performed in children (Rosenblum, Weiss, & Parush, 2003) and normal adults (Van Galen & Morasso, 1998). We were able to find only two studies examining written language in AD that were based on kinematic analysis. Slavin and colleagues (1999), in a study of motor control, requested participants to write on a computer graphics tablet the simple cursive letter "L," with varying levels of visual feedback. Another recent study found statistically significant differences in kinematic handwriting parameters between persons with MCI, patients with AD, and healthy controls who were requested to draw concentric superimposed circles (Schroter et al., 2003). More specifically, persons with MCI and patients with probable AD exhibited loss of fine motor performance and less regular movements than did healthy controls. Findings of these studies showed that, irrespective of medication or severity, patients' handwriting strokes were of significantly less consistent duration, and significantly less consistent peak velocity, than were those of healthy controls. However, the findings are limited by the fact that the tasks assessed were not functional tasks.

Because the assessment of cognitive functioning is usually precipitated by the elderly person's or family caregivers' subjective complaints about difficulties performing functional tasks (such as difficulties in writing a check or a modification of calligraphy; Croislie, 1999), the assessment of functional writing tasks may contribute to a more timely diagnosis of AD while providing a more person-centered, holistic approach. Moreover, because, as we previously stated, scientific and clinical research in the area of AD during the past few years has shifted its focus to early diagnosis, especially to the transitional phase between normal aging and dementia (i.e., MCI), there is need for researchers to examine these issues in persons with MCI as well, while trying to see if the analysis of the handwriting process allows them to differentiate between persons with MCI and those with mild AD and healthy controls, or between persons with MCI who will progress and develop dementia and those who will not.

Therefore, our three main aims in the present study were as follows: (a) to examine kinematically the handwriting process of persons with MCI, as compared with patients diagnosed with mild AD and healthy controls, on their performance of functional writing tasks while using a computerized system; (b) to assess the relative importance of kinematic measures for the differentiation of the groups; and (c) to assess the characteristics of the handwriting process across different writing tasks.

Methods

Participants

Participants included 94 elderly persons aged 65 years or older. Of these, 31 were persons diagnosed with MCI according to the criteria for MCI set forth by Petersen and associates (1999), 22 were patients diagnosed with mild AD according to the criteria for dementia set forth by the National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer's Disease and Related Disorders Association (McKhann et al., 1984), and 41 were healthy elderly persons matched by age and gender to the other groups. We recruited persons with MCI and those diagnosed with AD from two major memory clinics in the central part of Israel. We recruited healthy participants from several day care centers in the northern part of Israel.

Our inclusion criteria included the following: The person had to live in Israel for at least 20 years; be proficient in Hebrew; be right handed; have normal or corrected to normal vision and hearing ability; and have at least 8 years of education. Our exclusion criteria included the following: The person had other coexistent neurological diseases, arthritis, or hypothyroidism. Persons taking medications affecting the central nervous system were requested to refrain from taking their medication on the day before the test and the day of it.

Background characteristics of the participants are shown in Table 1. The mean age ranged from 76 to 80 years. Although, compared with the other groups, a lower percentage of participants with MCI were female, these differences were not statistically significant. A one-way analysis of variance (ANOVA) revealed significant effects of education, $F(2, 93) = 3.5$, $p < .05$, and Mini-Mental State Examination (MMSE) scores, $F(2, 93) = 37.1$, $p < .001$. Post hoc tests displayed no significant differences in education between healthy and MCI participants, and between MCI and mild AD participants, although healthy participants were significantly more educated than mild AD

Figure 1. The computerized system including laptop computer, Penmanship Objective Evaluation Tool software, and digitizing tablet.

participants. We also found significant differences in MMSE scores for all the groups.

Equipment and Tasks

Digitizing tablet and online data-collection and analysis software.—We used online, computerized handwriting evaluation, in the form of the Penmanship Objective Evaluation Tool, known as POET, to administer the stimuli and to collect and analyze the data. The tool includes two main parts: first, data collection, which is language independent and easy to use for handwriting tasks; second, data analysis, which we programmed by means of MATLAB software toolkits. We designed the data-collection part to be as user friendly as possible so as to enable clinicians and researchers to employ it in their everyday practice.

We had all writing tasks performed on A4 size, lined paper affixed to the surface of a WACOM Intuos 2 x–y digitizing tablet (Model GD 0912 [Wacom, http://www.wacom-europe.com], which has a 9 in. × 12 in., i.e., approximately 22.86 cm × 30.48 cm, recording area), which is used with a wireless electronic inking pen (Model GP-110). We sampled displacement, pressure, and pen-tip angle at 100 Hz by means of a 1300-MHz Pentium (R)M laptop computer. The computerized system enables the researcher to collect spatial, temporal, and pressure data while the individual is writing (see Figure 1). The digitizer gives an accurate temporal measure along the total writing performance, as well as when the pen is touching the tablet and when the pen is in the air.

Tasks.—Researchers asked participants to perform five functional writing tasks: copying a phone number, copying a grocery list (five words), copying the details of a check into the appropriate places, copying the alphabet sequence, and copying a paragraph (107 characters). Two underlying assumptions guided our selection of these tasks. First, they are functional tasks related to the performance of daily activities. Second, they reflect an increase in difficulty, as they are longer and involve an increased need of cognitive and motor abilities (including the Hebrew alphabet). We had all tests performed in Hebrew.

Kinematic measures.—The primary kinematic measures included temporal, spatial, and pressure measures of handwriting. The temporal measures included the time taken to complete the writing tasks, as measured in seconds, specifically for the on-paper time and the in-air time. We defined the in-air time as the time during the writing of the task that the pen was not in contact with the writing surface—meaning when the pressure was under 50 in nonscaled pressure units. We determined this cutoff point on the basis of the analysis of the written output parallel to the pressure values. We determined that no writing traces were found on the paper when pressure values were between 0 and 50. Furthermore, we calculated the mean velocity when the pen was on the paper for the whole task.

The spatial measures included on-paper length of the curve of all the written characters as measured in millimeters, that is, the mean distance from starting point to finishing point in each written letter. The pressure measure included the mean pressure implemented on the writing surface in nonscaled units from 0 to 1,024.

Regarding the spatial measure, the digitizer gives an accurate measure when the pen is touching the tablet or when the pen is lifted up to 6 mm above the digitizer. Beyond 6 mm, the spatial measurement is not reliable. Therefore, in the current study, we do not report total or in-air spatial measures. All data presented are for the global task performance for all participants. We did no filtering to the measures and excluded no data.

After we provided a complete description of the study to the participants, we obtained written informed consent from them. All participants performed the experiment under similar environmental conditions in a quiet room at the memory clinics or in their homes. Researchers presented participants with copying tasks, written in Guttman Yad-Brush font size 20, on a piece of paper that was affixed to the computer screen. This procedure was approved by the Helsinki committee of the hospital with which the clinics were affiliated.

Background Characteristics

Background characteristics included sociodemographic characteristics (gender, age, and number of years of education) and cognitive status. To assess cognitive status, we ensured that all participants were administered the Hebrew version of the MMSE (Werner, Heinik, & Mendel, 1999), an 11-item

Table 2. Means and Standard Deviations of Kinematic Measures in Healthy, MCI, and Mild AD Participants

Task	Healthy ($n = 41$)	MCI ($n = 31$)	Mild AD ($n = 22$)	F Test	η^2
Task 1: Copying a phone number (10 characters)					
On paper time	4.3 (1.1)[b]	4.6 (1.3)[c]	7.2 (5.9)[b,c]	6.9**	.13
In air time	4.5 (2.4)[b]	4.3 (2.2)[c]	7.4 (4.3)[b,c]	9.0***	.16
In air, on paper	1.0 (0.5)	1.0 (0.4)	1.2 (0.6)	ns	—
On paper length	99.6 (22.7)[b]	107.1 (21.9)	122.8 (36.7)[b]	5.5**	.11
Velocity	31.1 (7.5)	31.4 (8.1)	27.8 (7.8)	ns	—
Pressure	742.6 (177.6)[a,b]	592.9 (148.7)[a]	549.5 (167.1)[b]	12.1***	.21
Task 2: Copying the alphabet (22 characters)					
On paper time	7.2 (2.0)[a,b]	9.4 (3.3)[a]	13.5 (12.3)[b]	7.1**	.14
In air time	13.6 (8.4)[a,b]	21.3 (10.9)[a,c]	35.4 (26.4)[b,c]	14.6***	.24
In air, on paper	1.1 (0.4)[b]	1.3 (0.4)	1.5 (0.6)[b]	5.3**	.10
On paper length	192.1 (44.1)[a,b]	214.2 (46.4)[a,c]	251.7 (68.9)[b,c]	9.4***	.17
Velocity	35.7 (8.1)	32.7 (8.6)	31.4 (8.4)	ns	—
Pressure	758.8 (168.1)[a,b]	594.3 (142.8)[a]	547.8 (149.1)[b]	16.4***	.27
Task 3: Copying a grocery list (26 characters)					
On paper time	7.5 (1.8)[a,b]	8.9 (3.1)[a]	13.3 (11.6)[b]	6.7**	.13
In air time	8.4 (3.6)[a,b]	11.7 (5.6)[a,c]	19.1 (16.6)[b,c]	10.2***	.18
In air, on paper	1.7 (0.5)[b]	2.1 (1.0)	2.6 (1.0)[b]	7.6**	.14
On paper length	215.4 (56.0)[b]	237.3 (50.1)	265.1 (67.8)[b]	5.5**	.11
Velocity	36.0 (8.2)	34.8 (8.5)	31.9 (7.9)	ns	—
Pressure	716.1 (176.1)[a,b]	558.2 (137.1)[a]	572.2 (174.2)[b]	12.8***	.22
Task 4: Copying a check (50 characters)					
On paper time	15.4 (4.9)[a,b]	17.9 (9.7)[a]	23.8 (17.6)[b]	5.4 **	.11
In air time	27.5 (15.1)[a,b]	37.9 (22.6)[a,c]	59.1 (40.3)[b,c]	11.1***	.20
In air, on paper	1.9 (0.8)[a,b]	2.3 (0.8)[a]	3.0 (1.7)[b]	7.2**	.14
On paper length	379.4 (82.4)[a,b]	403.1 (83.0)[a]	404.9 (131.9)[b]	ns	—
Velocity	34.6 (7.2)[b]	32.3 (7.9)	28.1 (7.2) [b]	ns	—
Pressure	747.2 (162.7)[a,b]	575.9 (148.3)[a]	537.6 (187.2)[b]	15.4***	.25
Task 5: Copying a paragraph (107 characters)					
On paper time	31.2 (7.4)[a,b]	36.4 (12.7)[a,c]	50.5 (27.9)[b,c]	10.5***	.19
In air time	52.9 (26.2)[a,b]	72.6 (42.6)[a,c]	109.3 (76.2)[b,c]	10.2***	.18
In air, on paper	1.7 (0.6)[b]	1.9 (0.6)	2.3 (1.4)[b]	3.4*	.07
On paper length	889.1 (208.2)[b]	942.2 (264.8)[c]	1,112.3 (275.2)[b,c]	6.1**	.12
Velocity	37.2 (8.3)[b]	34.9 (8.0)	32.9 (7.5)	ns	—
Pressure	735.6 (177.2)[a,b]	561.9 (156.9)[a]	556.5 (181.9)[b]	12.1***	.21

Notes: MCI = mild cognitive impairment; AD = Alzheimer's disease. On paper time and in air time were measured in seconds; on paper length was measured in millimeters.

[a]Statistically significant differences between healthy and MCI subjects.

[b]Statistically significant differences between healthy and mild AD subjects.

[c]Statistically significant differences between MCI and mild AD subjects.

$^*p < .05$; $^{**}p < .01$; $^{***}p < .001$.

instrument assessing cognitive functioning that has scores ranging from 0 (total cognitive deterioration) to 30 (normal cognitive functioning).

Statistical Analysis

We used descriptive statistics (means, standard deviations, and percentages) to describe the sample and the main variables. We used ANOVAs to test group differences across sociodemographic and cognitive characteristics as well as across computerized measures (e.g., on-paper time, in-air time) for each writing task. In order to examine the source of the significance, we performed Scheffé post hoc tests. We set statistical significance, after Bonferroni correction, at $p = .01$.

Finally, we conducted discriminant analyses in order to determine which variables would be the best predictors of group membership (i.e., controls, MCI, or mild AD).

Results

Differences in Kinematic Handwriting Measures Between Groups

Table 2 shows descriptive statistics for kinematic measures reflecting handwriting performance in the three groups for all functional tasks. Observing the results across groups, we found that in-air time consistently differentiated among the three groups in four out of the five tasks. Participants with MCI and with mild AD spent a significantly longer time with the pen in the air (i.e., in-air time) than did healthy participants. An example of in-air measures is presented in Figure 2.

With the exception of velocity, all kinematic measures consistently differentiated between healthy and mild AD participants (see Table 2). Pressure consistently differentiated between healthy and MCI participants. Healthy participants exerted significantly more pressure while writing than did either MCI or mild AD participants.

Measures of strength of relationship (eta-squared scores) showed that kinematic measures accounted for 10% to 27% of the total variability in the group scores.

Finding the Best Predictors to Discriminate Between Groups

In order to assess the relative importance of the different variables in classifying the dependent variable, we performed multiple discriminant analyses. The dependent variable was the three groups of participants, and the independent variables included the MMSE score and five kinematic measures (on-paper time, in-air time, on-paper length, mean velocity, and mean pressure) for each one of the tasks. In order to assess the independent effect of the MMSE score and of the kinematic measures, we examined three separate equations. In the first equation, we entered the MMSE score as the only independent variable to assess its contribution to the correct classification of the diagnostic groups. In the second equation, we performed a stepwise discriminant analysis to assess the relative contribution of the five kinematic measures assessed. Finally, in the third equation, we assessed the contribution of the MMSE score together with the kinematic variables that were found to be statistically significant predictors in the second equation. Results of the discriminant equations are displayed in Table 3.

As one can see from Table 3, 63% of the participants overall were correctly classified when the MMSE score was used by itself as a predictor. However, classification accuracy for the MCI group was extremely poor.

An examination of the second equation reveals that using two or three of the kinematic measures by themselves allowed us to correctly classify from 42% to 81% of the cases. Moreover, in three of the five tasks, overall classification accuracy was similar or higher than with the MMSE score by itself. Likewise, classification accuracy for the MCI group was considerably higher in these equations than in the first one containing the MMSE score as the only predictor. We consistently found mean pressure to be a significant predictor in all tasks.

Finally, the combination of the MMSE together with the kinematic variables that were found to be statistically significant predictors in the second equation provided us with the highest predictive classification for each one of the groups (between 45% and 85% of the cases). We found the MMSE score, in-air time, and mean pressure to be the most important predictors in all of the tasks examined.

Characteristics of Kinematic Handwriting Measures Across Different Tasks

In examining these results across tasks, we found that on-paper time, in-air time, and the proportion of in-air and on-paper time increased almost linearly for all groups as the length or difficulty of the task increased. Indeed, the results of the repeated measures ANOVAs performed for each group revealed statistically significant differences at the $p < .001$ level in all of the groups across tasks (see Table 4).

Compared with these measures, pressure and velocity remained more constant across tasks. Although we found an overall statistically significant effect in the repeated measures analysis ($p < .05$), examining the individual effects revealed

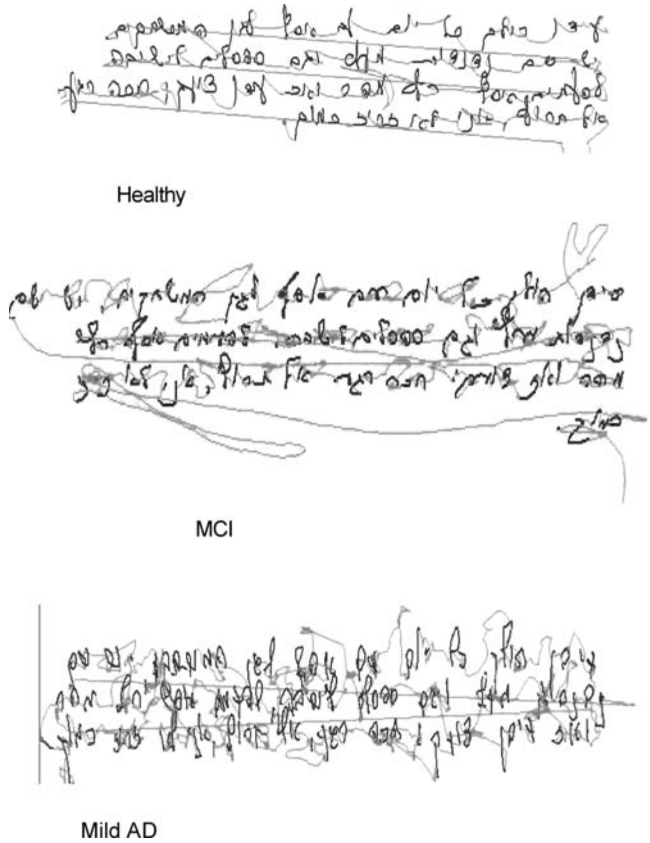

Figure 2. In-air measures for a typical participant from each group (in-air time = 20.00 s, 57.76 s, and 84.33 s for participants who are healthy, have mild cognitive impairment, and have mild Alzheimer's disease, respectively).

that there were no significant effects between Tasks 1 and 3, 1 and 4, 2 and 4, 3 and 4, and 3 and 5 for all groups.

Discussion

Summary of Findings

We examined the kinematic characteristics of the handwriting process of 94 elderly persons aged 65 and older by using several functional tasks. We summarize the results of the study according to its three main aims.

Our first aim was to examine kinematically the handwriting process of persons with MCI, patients with mild AD, and healthy controls. The results of the present study showed significant differences between the groups (MCI, mild AD, and healthy controls) in almost all kinematic measures, with the MCI group assuming, as we expected, a position between the other two groups. Temporal measures (and especially in-air time) were higher in the more cognitively deteriorated groups and may be associated with the motor behavior model presented herein.

Mean pressure was lower in more deteriorated groups. This finding contradicts the study of LaBarge and colleagues (1992), who found that mild to moderate AD patients significantly increased their handwriting thickness and pressure on the pen,

Table 3. Discriminant Analyses for Classifying the Three Diagnostic Groups

Variable	Copying a Phone Number	Copying the Alphabet	Copying a Grocery List	Copying a Check	Copying a Paragraph
Equation 1					
MMSE	.55				
% of cases classified correctly					
Overall	62.8				
Healthy group	82.9				
MCI group	22.6				
Mild AD group	81.8				
Equation 2					
Mean pressure	.81	.83	.80	.80	.81
On paper time	.67				.79
In air time	.65		.61	.75	
On paper length		.73	.60		
% of cases classified correctly					
Overall	65.6	65.6	62.8	61.7	59.6
Healthy group	73.2	75.6	78.0	80.5	75.6
MCI group	58.1	51.6	41.9	41.9	48.4
Mild AD group	61.9	66.7	63.6	54.5	45.5
Equation 3					
MMSE	.67	.56	.61	.75	.60
Mean pressure	.50	.51	.53	.55	.51
On paper time					.44
In air time	.45				
On paper length		.45	.44		
% of cases classified correctly					
Overall	71.0	72.0	70.2	69.1	71.3
Healthy group	82.9	85.4	78.0	85.4	85.4
MCI group	51.6	51.6	58.1	45.2	58.1
Mild AD group	76.2	76.2	72.7	72.7	63.6

Notes: MMSE = Mini-Mental State Exam; MCI = mild cognitive impairment; AD = Alzheimer's disease.

as compared with controls. This disparity might be related to the different writing tasks assessed in both studies or to differences in methodology, such as the way in which pressure was measured.

Despite the difference in the tasks used, our study does support the conclusions of Schroter and associates (2003) insofar as statistically significant differences were found in the kinematic characteristics of the handwriting of healthy persons, persons with MCI, and patients with AD. However, given the dearth of studies in this area, additional studies are required to elucidate the role of these measures in the process of cognitive deterioration. For example, based on the results of Slavin and colleagues (1999) regarding lack of consistency, it will be interesting to develop a measure for lack of consistency and to assess this feature for in-air time duration or for pressure levels in the writing performance of patients with AD.

Table 4. *F* Scores for Differences Across Tasks for the Different Kinematic Measures

Variable	Healthy (n = 41)	MCI (n = 31)	Mild AD (n = 22)
On paper	86.3^{***}a	63.4^{***}a	32.4^{***}a
In air	41.7^{***}a	21.7^{***}a	10.5^{***}a
Velocity	16.3^{***}b	13.5^{***}c	6.9^{**}d
Pressure	5.1^{**}e	5.3^{**}f	2.7

Notes: MCI = mild cognitive impairment; AD = Alzheimer's disease.
[a]Differences were statistically significant across all tasks.
[b]Not statistically significant differences between tasks: 2–3; 2–4; 3–4.
[c]Not statistically significant differences between tasks: 1–3; 1–4; 2–5; 3–4.
[d]Not statistically significant differences between tasks: 1–3; 2–4; 2–5; 3–4.
[e]Not statistically significant differences between tasks: 1–3; 1–4; 2–5; 3–4; 3–5.
[f]Not statistically significant differences between tasks: 1–3; 1–4; 2–3; 2–5; 3–4; 3–5.
$^{**}p < .01$; $^{***}p < .001$.

Our second aim was to assess the relative importance of kinematic measures for the differentiation of the groups. The results of the present study show that kinematic measures of the handwriting process, together with cognitive status measures (MMSE), provide an efficient way to differentiate between the groups. On the basis of discriminant analysis, we found that kinematic measures together with cognitive status measures enabled us to correctly classify between 69% and 72% of the participants, though the classification of MCI is relatively poor (from 45% to 58%). Most notably, the kinematic measures by themselves provided better classification accuracy for the MCI group than did the MMSE by itself. Recently, other researchers have also reported the low effectiveness of the MMSE alone in distinguishing between those persons with normal cognition and those with MCI, and these researchers have stressed the need to find new assessment tools to improve the classification (Nasreddine et al., 2005; Tang-Wai et al., 2003). Kinematic measures by themselves or in combination with the assessment of executive functions and attention might provide such a tool.

Among the kinematic measures, we found mean pressure to provide the best information for a correct classification of the cases. This may be the consequence of a decreased awareness among people with cognitive deterioration of the difficulties, quality, and sequence of their writing. Alternatively, pressure may reflect emotional reactions (such as stress, lack of confidence, or anxiety) among people with AD while they write, or it may be directly related to neurological dysfunction. In order to understand these findings and disentangle kinematic and emotional processes, future research should examine and visualize relationships between mistakes in spatial letter formation and in lack of consistency, using measures of pressure.

Our third aim was to assess the characteristics of the handwriting process across different writing tasks. Overall, the writing characteristics of participants in all groups showed that, although measures of velocity and pressure remained relatively stable across the different tasks, the temporal and spatial measures increased as the difficulty of the task increased. Although this finding might be obvious (especially because more difficult tasks were also longer tasks), it is interesting that the increase is reflected mainly in the in-air measures. Several explanations can be provided for this finding.

The first is associated with the unique characteristics of Hebrew writing. As shown in Figure 2, Hebrew writing differs from Latin-based scripts. It progresses from right to left; successive letters are usually not connected, even in script or cursive writing; and some letters are composed of two separate, unconnected segments. Therefore, the in-air measure contains some necessary pen lifts, which might explain the increases noted in longer tasks. It is important to note that despite the distinguishing features of Hebrew writing, individuals writing in Hebrew hold the pen in such a way that they do not occlude the trace, whether in writing letters, sentences (from right to left), or even numbers (from left to right).

However, the importance of these measures (also as a significant predictor of the differences between the three groups) leads us to hypothesize that its relevance goes beyond the features of Hebrew writing. In order to write legibly and efficiently, a person must transcode abstract linguistic representations into concrete motor instructions to specific effector muscles (Rapcsak, 1997). Therefore, it can be hypothesized that more complex tasks increase the time of these transmissions and thus the amount of time the pen is held in the air.

An alternative explanation should also be considered. According to the theoretical model of motor behavior by Van Galen and Teulings (1983), three distinct stages are identified in the preparation of a writing response: first, motor pattern retrieval or motor programming; second, parameter setting; and third, motor initiation (i.e., "the generation of nerve impulses for specific muscles dependent on the actual anatomical and biomechanical context"; see Van Galen & Teulings, p. 11). Based on this model, it may be that the amount of time the pen is held in the air represents programming deficits among AD patients, who take longer to initiate movements (Bellgrove et al., 1997).

However, this effect may be compounded by the effects of visual inspection (Van Galen & Teulings, 1983). Visual inspection may be different among AD participants in terms of deficits in the visual system, which may be the earliest and most prominent signs of AD (Cogan, 1985). Another option may be that in-air time stems from the visuospatial deficits found among AD patients (e.g., Johnson, Morris, & Galvin, 2005). Focusing on the kinds of tasks for which in-air time best discriminates may reinforce the latter explanation. In all three tasks (i.e., copying a phone number, copying a grocery list, and copying details from a check), especially the check writing (in which the discriminant value was .75), there was no option to rely on a well-known writing sequence, as was possible with the alphabet letters or with the paragraph-copying tasks.

Study Limitations

Several limitations must be recognized regarding this study. The first relates to the potential explanation that the differences in the kinematic measures among the groups might be a reflection of memory problems. Although the tasks were developed to be as independent as possible from memory functioning (such as relying on copy tasks rather than on dictating tasks, and leaving the source of the stimuli constantly in front of the participant), we cannot totally neutralize the effects of memory performance on the completion of the writing tasks, and consequently on the kinematic measures. However, it should be noted that the tasks presented to the participants were not memory tasks but rather tasks involving attention and copying ability. These cognitive domains usually do not differentiate healthy elderly persons from persons with MCI and even mild AD. In fact, neuropsychological tests measuring these domains (such as digit span forward, Wechsler Memory Scale mental control, Benton copy D) failed to separate these clinical groups (Caccappolo-Van Vliet et al., 2003; Morris, Storand, Miller, & McKeel, 2001), making our results more reliable in being independent of memory. Moreover, as we stated in the introduction, handwriting, like most motor skills, imply an unbreakable combination of perceptual (implicit) memory and knowledge (Kandel, Schwartz, & Jessel, 2000).

We designed the study carefully to exclude participants with diseases that might heavily affect motor functioning. However, we cannot rule out the possibility that minor motor impairments have influenced the writing performance of the participants.

As a result of participants' needs, some of the participants performed the handwriting evaluation in their homes and some performed it at the clinics. Moreover, some of the participants performed the tasks while their spouse was present. These conditions were not previously planned and are recognized as being less than ideal. Future studies should provide identical environmental conditions to all participants.

Finally, a limitation exists regarding the equipment used in the current study, namely, the WACOM Intuos 2 digitizer. Although, as we previously stated, there are some limitations regarding the accuracy of the measurements with this equipment (especially with respect to pen pressure), it should be noticed that the research in the field of kinematic measurement is very pioneering. Indeed, there are very few laboratory centers worldwide that are able to assess with great accuracy and precision the pressure that a participant creates while writing. Moreover, the increased accuracy obtained in such laboratories is limited by the fact that the assessments are not completed in the participant's natural environment. Using the Intuos 2 digitizer, we were able to obtain our measurements at participants' homes or at the clinic. Despite these reservations, it is our feeling that the results of the present study convincingly show some preliminary patterns, which should be replicated and validated in future studies by using a more perfected pressure measurement technique.

In sum, despite its limitations, the present study is unique in that it allows researchers to assess ordinary everyday activities (such as writing tasks) by using objective measurements. Moreover, it has important implications for the timely diagnosis of AD and for the study of kinematic measures of handwriting.

The Timely Diagnosis of AD

As we previously stated, during the past few years, scientific and clinical research in the area of AD has shifted its focus to early diagnosis and especially to the transitional phase between normal aging and dementia (i.e., MCI). At the personal level, early evaluation and management of AD could improve the functional and self-care abilities of the elderly person suffering from the disease; it could delay the deterioration of cognitive functioning; and it could enhance the elderly person's and the caregiver's quality of life (Doraiswamy, Stefens, Pitchumoni, & Tabrizi, 1998). At the public level, early detection of the disease could be associated with cost savings (Ernst, Hay, Fenn, Tinklenberg, & Yesavage, 1997).

Despite these benefits, there is still a considerable lag between the appearance of the first symptoms of cognitive and memory deterioration and the timing of diagnosis. Several studies have attributed this lag to low levels of ascertainment by primary care physicians (Callahan, Hendrie, & Tierney, 1995; Eefsting, Boersma, Van den Brink, & Van Tilburg, 1996; O'Connor et al., 1988); others have contributed it to the difficulty experienced by elderly persons themselves and by their family caregivers in differentiating memory problems that are part of normal aging from those that are predictors of AD (Knopman, Donohue, & Gutterman, 2000; Werner, 2003, 2004). Thus, finding a sensitive tool based on the performance of everyday functional tasks that will allow clinicians to differentiate between normal age-related decline in cognitive functioning and abnormal deterioration, while providing a nonthreatening test for elderly persons, is of utmost importance.

Results from our study show that kinematic analysis might provide such a tool. The information gathered about the kinematic characteristics of the handwriting process, together with self-reported information about cognitive functioning and writing difficulties, allowed us to classify over three fourths of the participants correctly. Moreover, the fact that we had no refusals to participate in the study supports the feasibility of performing a nonthreatening task and the feasibility of administering it even by a thoroughly trained research assistant.

Future studies should expand on the results of our study. The contribution of adding neuropsychological tests to the use of the MMSE and the kinematic measures should be explored, as well as the relative importance of individual items in the MMSE (such as the immediate or delayed recall items).

Kinematic Assessment of Handwriting

The results of our preliminary study show that the computerized system may be appropriate for use with different pathologies that may influence handwriting, such as Anyotrophic Laterak Sclerosis, Parkinson's disease, and the like. Moreover, the findings highlight the importance of combining reports on participants' everyday handwriting deficiencies with objective measures, and they underline the significance of a client-centered approach to evaluation and intervention plans.

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