The Ege Agraphia Test Battery for Identifying Writing Disorders in Cases of Mild Cognitive Impairment and Alzheimer's Disease

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SUMMARY

Objective: The purpose of this study was to create an agraphia test battery specific to the Turkish language, to obtain normative data for the performance and error types of this test, and to demonstrate its success in detecting cognitive disorders in cases of Mild Cognitive Impairment (MCI), which cannot be diagnosed by formal neuropsychological tests due to the fact that writing is a complex function.

Method: For this purpose, 20 healthy control (HC) subjects, 20 MCI patients and 20 Alzheimer's Disease (AD) patients with a Clinical Dementia Rating (CDR) of 1 were evaluated with the Ege Agraphia Test Battery.

Results: Significant differences were found between the performance scores and error types of HC subjects, MCI cases, and AD patients. As the cognitive impairment of the subjects in the study got worse, writing skills also became worse, resulting in lower test scores. In addition, some statistically significant differences between the error types of MCI cases and AD patients were found.

Conclusion: The Ege Agraphia Test Battery is not only a practical test, but also the first defined agraphia test specific to the Turkish language. Writing disorders in cases of MCI support the view that MCI is a transition period for AD. Further studies are required to increase the test data and make any necessary adjustments to the test battery.

Keywords: Agraphia, Alzheimer Disease, Mild Cognitive

INTRODUCTION

Mild Cognitive Impairment (MCI) is considered a transition period between normal age-related cognitive changes and Alzheimer's Disease (AD). In patients diagnosed with MCI, there is more forgetfulness than would be expected according to their age, but these cases do not meet the criteria for a diagnosis of AD. The prevalence of MCI among those in the over 65-age group has been found to be 3% - 19% (Petersen et al. 2009). The current criteria for a diagnosis of MCI are as follows (Petersen 2004):

Forgetfulness confirmed by a patient's relative

Objectively demonstrated memory impairment according to age and education

General cognitive functions largely preserved

Daily activities largely unimpaired

Dementia not found

Medical history taken from the patient and patient's relative and results of neuropsychological evaluation are valuable for diagnosis. Mild Cognitive Impairment or AD cannot be diagnosed only by looking at the results of neuropsychological tests. However, these tests are useful in diagnosing dementia in the early phase.

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Loss or disorders of the ability to write resulting from acquired brain abnormalities are known as "agraphia". In addition, the present use of this term includes disturbances in the ability to use proper grammatical rules (Cummings and Mega 2003). Disorders may be seen at any level in the production of written language, including the sentence and paragraph level (Benson and Cummings 1985, Cummings and Mega 2003, Kirshner 2004, Rapcsak and Beeson 2002, Roeltgen 1997).

When the literature is reviewed, it can be seen that studies investigating language disorders in cases of dementia often evaluate spoken language or language as a whole; however, there has been less work on written language, which allows earlier diagnosis (Blair et al. 2007, Bruni 2010, Carthery et al. 2005, Croisile et al. 1996a, Croisile et al. 1996b, Dijkstraa et al. 2004, Forbes-McKay and Venneri 2005, Glosser et al. 1999, Groves-Wright et al. 2004, Mendez et al. 2003, Marczinski 2006, Murdoch et al. 1987, Ortiz and Bertolucci 2005). An examination of studies on the concurrence of agraphia and dementia reveals that patient populations have been limited to those diagnosed with AD (Forbes et al. 2004, Henderson et al. 1992, Horner et al. 1988, Hughes et al. 1997, Kemper et al. 1993, Kumar and Giacobini 1990, LaBarge et al. 1992, Lambert et al. 1996, Lambert et al. 2007, Luzzatti et al. 2003, Neils et al. 1989, Neils et al. 1995, Platel et al. 1993, Silveri et al. 2007). Apart from some kinematic analyses (examinations of the geometric direction of movement) (Schröter et al. 2003, Werner et al. 2006), there have been no studies evaluating the written language of MCI patients. Moreover, studies on Alzheimer's patients have examined writing disorders at the word or paragraph level only; there has been no comprehensive evaluation also examining handwriting or types of mistakes, which could clarify the writing process.

The main aim of the present study was to assess the applicability of and produce preliminary normative data for the Ege Agraphia Test Battery, which is a detailed test designed to examine all aspects of writing disorders in the Turkish language, which is phonologically regular, i.e. has high phoneme to grapheme correspondence. The other main aims were to evaluate a complex process such as writing in MCI patients and by doing this, to demonstrate the unexpected presence of writing disorders as well as memory disorders in these patients, and to compare the writing disorders of MCI and AD patients.

METHOD

Sampling

Individuals aged over 60 with at least primary education who had applied to the Ege University Medical Faculty Neurology Department polyclinic complaining of forgetfulness were included in the study. First, patients were given a detailed neurological examination and those with extrapyramidal, pyramidal, or cerebellar symptoms were excluded. Individuals with a history of stroke, epilepsy, neuroleptic drug use, positive psychiatric disorders, or drug or alcohol abuse were also excluded from the study. The complete blood counts, liver function tests, kidney function tests, levels of vitamin B12 and folic acid, and thyroid function tests of the patients were evaluated. Those with pathology identified on these tests were excluded from the study. Subsequently, a cranial computerised tomography (CT) scan or magnetic resonance imaging (MRI) scan was conducted on all patients. Those patients with stuctural or ventricular pathologies that could explain their symptoms were excluded from the study. The presence of depression among individuals complaining of forgetfulness was excluded by administering the Geriatric Depression Scale (GDS) (Ertan et al. 1997).

Data Collection Instruments

After these tests, individuals complaining of forgetfulness who were suitable for inclusion in the study were given a detailed neuropsychological assessment. First, a detailed history was taken from patients and their relatives. Then, patients were administered the Mini Mental State Examination (MMSE, Güngen et al. 2002), Verbal Memory Processes Test (Tanör 2011), Visual Memory Subtest of the Wechsler Memory Scale and Stroop Test (Karakaş 2004), Clock Drawing Test (Cangöz et al. 2006), Boston Naming Test (Kafadar et al. 2002), Rey Complex Figure Test (Dinn and Dinn 2012), Luria's Alternating Sequences and Proverbs Interpretation Tests (Öktem 2004) and the Frontal Behavioural Inventory (Akça-Kalem et al. 2005). Patients identified as having only verbal memory cognitive impairment on the tests and who met the other Petersen (2004) diagnostic criteria were given a diagnosis of amnestic MCI. Meanwhile, the Clinical Dementia Rating scale (CDR) (Morris 1993) was administered to patients who showed impairment in more than one cognitive area and were diagnosed with possible AD according to the NINCDS-ADRDA (National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association) diagnostic criteria (McKhann et al. 1984) to determine the stage of their dementia. Dementia patients with a CDR level of 1 and individuals diagnosed with amnestic MCI (CDR level 0.5) were included in the study and were assessed with the Ege Agraphia Test Battery.

The healthy control (HC) group consisted of healthy volunteers selected from the population, who had no history of neurological or psychiatric disorders, and were matched in terms of age and educational level with the patient groups. The MMSE and GDS were administered to these participants, who had no memory complaints, as a screening measure. Thus, cognitive loss and the presence of depression were

excluded. Subsequently, the Ege Agraphia Test Battery was administered to those individuals who were suitable.

The Ege Agraphia Test Battery was created with reference to Benson and Cummings' (1985) classic taxonomy and the test batteries of Groves-Wright et al. (2004) and Silveri et al. (2007). In terms of Turkish parts of speech, only nouns and adjectives were used as words to be written. Various written sources were used in the selection of words and sentences; both short and long words were chosen according to number of syllables.

In the sentence writing test, there was also a balance of short and long sentences, based on number of words. In the generation of meaningless words, a large number of syllables taken from texts were put together randomly and those that could be pronounced were recorded as meaningless words.

The sections included in the Ege Agraphia Test Battery are Signing a Signature, Evaluation of Spontaneous Writing, Evaluation of Dictated Writing and Evaluation of Copying. During the spontaneous writing, participants were required to write their name and address, the numbers 1-10, the first 10 letters of the alphabet, the names of three objects in the examination room, and spontaneous sentences about a topic and a picture. During the dictation and copying, participants were required to write letters, numbers, words (real, meaningless and abstract), and sentences. During the dictation and copying, participants were given instructions to write freely, or in upper or lower case letters according to the plan of the test. There was no time limit.

Following this, information was gathered from the relatives of MCI and mild AD patients about whether there had been a deterioration in their signatures and general writing formation compared to the past.

A scoring system generated scores on the subtests. For the spontaneous writing, dictation, and copying tests, test scores were calculated by giving one point for each correctly written item (word or sentence). The subtests of spontaneous writing involving writing about a topic and a picture were evaluated separately; the mean number of words in a sentence, mean number of conjunctions, mean information units, and rate of conciseness were found.

Mistakes made during writing were categorised as central errors (semantic, orthographic, syntax, and grammatical) and peripheral errors (graphomotor, allographic, and perseveration), and, for each error type, total error scores were calculated from the spontaneous writing, dictation, and copying (see Appendices 1 and 2 for presentation of the Ege Agraphia Test Battery, its application, and scoring).

The study protocol was approved by the Ege University Medical Faculty Ethics Committee. Participants were given detailed information about the study and written consent was obtained from patients and their relatives.

Data Evaluation

SPSS (Statistical Package for Social Sciences) 18.0 for Windows was used for the statistical analysis. Mean agraphia test scores and standard deviations (SD) were calculated for the HC, MCI, and AD groups. The X^2 test was used to compare the HC, MCI, and AD groups in terms of signatures and disorders of writing formation. The Kruskal-Wallis test was used to compare the test scores of the HC, MCI, and AD groups. Post-hoc tests were used to find the group from which the significance resulted. The Mann-Whitney U test with Bonferroni correction was used for post-hoc tests. As three groups were to be compared, the Bonferroni adjusted level of significance was determined to be 0.05/3=0.0167. The results of the Mann-Whitney U test paired comparisons were then evaluated.

RESULTS

The study included 20 participants diagnosed with MCI according to the Petersen criteria, 20 patients meeting the NINCDS-ADRDA criteria for possible AD at level 1 according to the CDR, and a HC group of 20 participants matched in age and educational level to the other groups.

The participants in the Mild Cognitive Impairment group were aged from 64-79 (mean=73.7, SD=6.17), the CDR-1 AH group from 63-79 (mean=71.63, SD=5.56), and the HC group from 65-77 (mean=70, SD=5.98). Length of education was 5-16 years (mean=11, SD= 3.67) in the MCI group, 5-13 years (mean=9.6, SD=4.21) in the AD group, and 5-15 years (mean=10.35, SD=3.09) in the HC group. There was no statistically significant difference between the groups in terms of age or length of education ($p>0.05$).

Minimum and maximum, means, and standard deviations of scores of the HC, MCI, and AD groups on the parameters evaluated on the agraphia test are shown in Table 1. Time taken to complete the test ranged from 30-45 minutes.

A comparison of the HC, MCI, and AD groups in terms of defects of writing and signature formation revealed statistically significant differences in writing formation ($X^2=15.372$, $p<0.001$) and signature formation ($X^2=6.871$, $p<0.05$) between the groups according to diagnosis. In other words, a relationship was found between increasing levels of CDR and increasing defects in writing and signature formation. In the MCI group, the rate of writing formation defects was 35% and rate of signature formation defects was 30%. Meanwhile, in the Alzheimer group, there was a 64% rate of writing formation defects and 81% rate of signature formation defects.

Table 1. Scores of the HC, MCI, and AD groups on the Ege Agraphia Test Battery parameters, total time taken to complete the test and the results of the Kruskal-Wallis test comparisons and post-hoc analyses

	HC Mean-SD Min-Max	MCI Mean-SD Min-Max	AD Mean-SD Min-Max	p	Post-hoc		
					HC-AD	MCI-AD	HC-MCI
Sp Name Surname Address	5.80±0.410 (5-6)	5.15±0.745 (4-6)	4.55±0.688 (4-6)	p=0.001	*	-	*
Sp Number	10±0 (10-10)	9.95±0.224 (9-10)	9.91±0.302 (9-10)	p=0.444	-	-	-
Sp Letter	9.05±0.686 (8-10)	8.05±1.234 (6-10)	7.45±2.252 (4-10)	p=0.019	-	-	*
Sp Object	2.90±0.308 (2-3)	2.75±0.444 (2-3)	2.36±0.674 (1-3)	p=0.210	-	-	-
Sp Sent Word	6.925±2.318 (3-12)	5.395±1.870 (2-9)	3.471±1.307 (0-4.5)	p=0.001	*	*	-
Sp Sent Conj	1.170±0.705 (0.4-3.3)	0.697±0.551 (0-2.0)	0.230±0.219 (0-0.7)	p=0.001	*	*	-
Sp Sent Unit	1.735±0.497 (1-3)	1.510±0.510 (1-2.5)	1.090±0.536 (0-2.0)	p=0.012	*	-	-
Sp Sent Concise	0.268±0.066 (0.13-0.44)	0.283±0.580 (0.14-0.40)	0.286±0.121 (0-0.46)	p=0.317	-	-	-
Sp Pict Topic	4.25±0.967 (3-6)	2.45±1.050 (1-5)	1.36±1.027 (0-3)	p=0.001	*	*	*
Sp Pict Effect	2.65±0.489 (2-3)	1.55±0.686 (1-3)	1.0±0.632 (0-2)	p=0.001	*	-	*
Sp Pict Unit	6.3±2.755 (3-15)	4.35±2.852 (1-13)	2.09±1.758 (0-5)	p=0.001	*	*	*
Sp Pict Concise	0.277±0.071 (0.18-0.47)	0.293±0.084 (0.11-0.43)	0.163±0.118 (0-0.33)	p=0.008	-	*	-
Dict Letter	5.85±0.366 (5-6)	5.80±0.523 (4-6)	5.45±0.522 (5-6)	p=0.033	-	-	-
Dict Number	15.50±1.573 (10-16)	15.45±1.276 (12-16)	13.0±3.795 (8-16)	p=0.013	-	-	-
Dict Word Real Free	5.70±0.571 (4-6)	5.60±0.503 (5-6)	3.64±1.362 (2-6)	p=0.001	*	*	-
Dict Word Real Capital	5.50±1.395 (0-6)	4.55±2.089 (0-6)	4.18±1.834 (0-6)	p=0.012	*	-	-
Dict Word Meaningless Free	4.80±1.056 (2-6)	3.95±1.146 (2-6)	2.00±1.483 (0-4)	p=0.001	*	*	-
Dict Word Meaningless Capital	4.55±1.849 (0-6)	2.90±2.22 (0-6)	2.91±1.868 (0-5)	p=0.011	*	-	*
Dict Word Abstract	5.50±0.827 (3-6)	4.90±1.119 (3-6)	3.18±1.328 (1-6)	p=0.001	*	*	-
Dict Sent	5.60±0.503 (5-6)	4.50±0.946 (3-6)	1.55±1.440 (0-5)	p=0.001	*	*	*
Copy Letter	11.90±0.308 (11-12)	11.35±1.26 (7-12)	11.09±0.944 (9-12)	p=0.008	*	-	-
Copy Number	16±0 (16-16)	15.9±0.308 (15-16)	14.91±1.30 (12-16)	p=0.001	*	-	-
Copy Word Real Seen	5.55±0.759 (4-6)	4.30±1.559 (0-6)	3.09±1.578 (0-6)	p=0.001	*	-	*
Copy Word Real Case	4.20±2.118 (0-6)	3.0±2.406 (0-6)	2.91±1.578 (1-5)	p=0.118	-	-	-
Copy Word Meaningless Seen	5.50±0.761 (4-6)	4.05±1.877 (0-6)	3.55±1.508 (1-6)	p=0.001	*	-	*
Copy Word Meaningless Case	3.90±2.125 (0-6)	3.15±1.755 (0-6)	2.09±1.640 (0-5)	p=0.026	-	-	-
Copy Word Abstract	4.75±1.773 (0-6)	3.10±2.337 (0-6)	2.73±1.679 (0-5)	p=0.003	*	-	*
Copy Sent Case	3.10±0.64 (2-5)	2.55±0.510 (2-3)	1.36±0.674 (0-2)	p=0.001	*	*	-

Table 1 (Continued).

	HC Mean-SD Min-Max	MCI Mean-SD Min-Max	AD Mean-SD Min-Max	p	Post-hoc		
					HC-AD	MCI-AD	HC-MCI
Sem Spon	0±0.009 (0-0)	0.1±0.2 (0-0)	0.1±0.35 (0-0)	p=0.466	-	-	-
Sem Dict	0.45±0.605 (0-2)	1.50±1.395 (0-5)	2.91±2.468 (0-8)	p=0.001	*	-	*
Sem Copy	0.35±0.671 (0-2)	0.90±1.021 (0-3)	1.36±1.748 (0-5)	p=0.085	-	-	-
Ortho Spon	0.411±0.577 (0.0-2.12)	1.44±1.299 (0-3.98)	3.19±2.32 (0.41-9.13)	p=0.001	*	*	*
Ortho Dict	4.75±4.115 (0-13)	8.10±3.892 (1-16)	18.09±8.006 (4-29)	p=0.001	*	*	*
Ortho Copy	3.20±3.72 (0-15)	7.40±6.54 (0-22)	11.45±6.593 (1-21)	p=0.002	*	-	*
Syntax	0.116±0.236 (0-0.91)	0.478±0.631 (0-2.0)	0.88±0.26 (0.33-1.25)	p=0.001	*	*	-
Gram	0.15±0.29 (0-1.1)	0.66±0.83 (0-2.5)	1.04±0.69 (0.3-2.0)	p=0.001	*	-	-
Graph Spon	0.82±0.94 (0-3.40)	4.06±3.07 (0.25-9.97)	7.53±3.22 (1.63-13.49)	p=0.001	*	*	*
Graph Dict	5.45±3.87 (0-12)	18.7±7.65 (4-33)	31.55±9.98 (10-44)	p=0.001	*	*	*
Graph Copy	7.55±5.36 (0-20)	20.85±7.81 (8-35)	31.64±11.45 (15-54)	p=0.001	*	*	*
Allog Spon	0.58±0.76 (0-2.73)	1.50±1.18 (0-3.83)	4.62±3.39 (0.09-9.20)	p=0.001	*	*	*
Allog Dict	5.10±5.92 (0-17)	10.30±6.48 (1-24)	15.82±6.41 (5-24)	p=0.001	*	-	*
Allog Copy	19.70±6.96 (0-33)	24.55±6.76 (15-38)	22.82±11.51 (3-40)	p=0.130	-	-	-
Persev Spon	0.14±0.31 (0-1)	0.36±0.66 (0-2)	1.51±1.79 (0-5)	p=0.002	*	*	-
Persev Dict	0.05±0.22 (0-1)	0.25±0.44 (0-1)	1.18±2.18 (0-7)	p=0.060	-	-	-
Persev Copy	0.10±0.30 (0-1)	0.70±2.25 (0-10)	2.0±1.67 (0-5)	p=0.001	*	*	-
Frag Spon	0±0 (0-0)	0±0 (0-0)	0.28±0.90 (0-3)	p=0.024	-	-	-
Frag Dict	0±0 (0-0)	0.10±0.30 (0-1)	0.27±0.64 (0-2)	p=0.176	-	-	-
Frag Copy	0±0 (0-0)	0.05±0.22 (0-1)	0.45±1.21 (0-4)	p=0.117	-	-	-
Null Spon	2.81±2.98 (0-11)	3.0±2.42 (0-11)	3.37±2.51 (0-7)	p=0.489	-	-	-
Null Dict	1.20±5.36 (0-24)	1.90±5.67 (0-25)	6.18±12.54 (0-38)	p=0.034	-	-	-
Null Copy	0.80±2.66 (0-12)	1.55±3.48 (0-15)	8.45±14.22 (0-39)	p=0.020	*	-	-
Unnec Sp	2.06±2.25 (0-9)	2.12±1.55 (0-4)	3.46±1.37 (2-5)	p=0.033	*	-	-
Unnec Dict	0.15±0.36 (0-1)	0.05±0.22 (0-1)	1.09±1.81 (0-5)	p=0.049	-	-	-
Unnec Copy	0±0 (0-0)	0.45±1.79 (0-8)	1.55±1.96 (0-5)	p=0.002	-	-	-
Total Test Time	32.25±1.83 (30-35)	34.85±2.05 (32-38)	43.50±1.35 (40-45)	p=0.001	*	*	*

See "Abbreviations" section for abbreviations of table and test parameters.
* groups found to create significant differences on the post hoc tests
- groups not found to create significant differences on the post hoc tests

ABBREVIATIONS

AD = Alzheimer's Disease

Allog Copy = Allographic error in copied writing

Allog Dict = Allographic error in dictated writing

Allog Spon = Allographic error in spontaneous writing

Copy Letter = Copying of capital and small letters shown on cards as they are seen

Copy Number = Copying of 1, 2, 3, and 4 digit numbers shown on cards

Copy Sent Case = Copied writing of sentences shown on cards in either upper or lower case letters according to instructions

Copy Word Abstract = Copying of abstract words shown on cards as they are seen

Copy Word Meaningless Case = Copied writing of meaningless words shown on cards in either upper or lower case letters according to instructions

Copy Word Meaningless Seen = Copying meaningless words shown on cards as they are seen

Copy Word Real Case = Copied writing of real words shown on cards in either upper or lower case letters according to instructions

Copy Word Real Seen = Copying of real words shown on cards as they are seen

Dict Letter = Writing of dictated letters

Dict Number = Writing of dictated 1, 2, 3, and 4 digit numbers

Dict Sent = Free writing of dictated sentences

Dict Word Abstract = Free writing of dictated abstract words

Dict Word Meaningless Capital = Writing of dictated meaningless words in capital letters

Dict Word Meaningless Free = Free writing of dictated meaningless words

Dict Word Real Capital = Writing of dictated real words in capital letters

Dict Word Real Free = Free writing of dictated real words

Frag Copy = Fragmented writing during copying

Frag Dict = Fragmented writing during dictation

Frag Spon = Fragmented spontaneous writing

Gram = Grammatical errors

Graph Copy = Graphomotor errors in copied writing

Graph Dict = Graphomotor errors in dictated writing

Graph Spon = Graphomotor errors in spontaneous writing

HC = Healthy Control

Max = Maximum

MCI = Mild Cognitive Impairment

Min = Minimum

Null Copy = Null response in copied writing

Null Dict = Null response in dicated writing

Null Spon = Null response in spontaneous writing

Ortho Copy = Orthographic error in copied writing

Ortho Dict = Orthographic error in dictated writing

Ortho Spon = Orthographic error in spontaneous writing

Persev Copy = Perseveration errors in copied writing

Persev Dict = Perseveration errors in dictated writing

Persev Spon = Perseveration errors in spontaneous writing

SD = Standard deviation

Sem Copy = Semantic error in copied writing

Sem Dict = Semantic error in dictated writing

Sem Spon = Semantic error in spontaneous writing

Sp Letter = Writing the first 10 letters of the Turkish alphabet in order

Sp Number = Writing the numbers 1 to 10 as figures

Sp Name Surname Address = Writing name, surname and address

Sp Object = Writing the names of 3 objects seen in the room

Sp Pict Concise = Rate of conciseness in writing about pictures shown

Sp Pict Effect = Assessment of communication effectiveness in written descriptions of pictures shown

Sp Pict Topic = Number of defined topics in writing about pictures shown

Sp Pict Unit = Number of information units in writing about pictures shown

Sp Sent Concise = Rate of conciseness in sentences in spontaneous writing

Sp Sent Conj = Mean number of conjunctions in sentences in spontaneous writing

Sp Sent Unit = Mean number of information units in sentences in spontaneous writing

Sp Sent Word = Mean number of words in sentences in spontaneous writing

Syntax = Errors in word order, syntax errors

Unnec Copy = Unnecessary writing during copying

Unnec Dict = Unnecessary writing during dictation

Unnec Sp = Unnecessary spontaneous writing

Test scores of the HC, MCI, and AD participants on the Ege Agraphia Test and their total test administration times were compared using the Kruskal-Wallis test, and results with $p<0.05$ were accepted as statistically significant. Post-hoc analyses showed from which group the differences originated (Table 1). Statistically significant differences between the three groups were found on all agraphia subtests except for spontaneous writing of numbers, spontaneous writing of object names, rate of conciseness in spontaneously written sentences, and letter case transformation in copying real words. A significant relationship was found between diagnosis and test scores; as cognitive impairment and CDR levels rose, test scores decreased and writing defects increased. Furthermore, statistically significant differences were found between the error scores of the three groups on all subtests except for semantic errors in spontaneous writing and copying, allographic errors in copying, perseveration in dictation, fragmented writing in dictation and copying, and null response in spontaneous writing. As level of cognitive impairment and CDR increased, error scores also increased.

Significant differences were found between the HC and MCI participants on the spontaneous writing, dictation, and copying subtests. It was observed that for the MCI group, writing defects were concentrated in the spontaneous writing subtests. Statistically significant differences were also found between the error scores of these two groups; these differences resulted from orthographic, graphomotor, and allographic errors in particular.

Statistically significant differences were also found between the HC and AD groups on the spontaneous writing, dictation,

and copying subtests; writing disorders had a large effect on all subtests. Regarding error scores, there was a statistically significant difference between the HC and AD groups regarding error types similar to those of the MCI group. However, for the AD group, differences in grammatical errors, perseveration errors and examples of unnecessary writing were also statistically significant.

A comparison of the AD and MCI groups revealed performance differences, especially on the spontaneous writing and dictation subtests. Regarding error scores, statistically significant differences were found between the AD and MCI groups in terms of orthographic, syntax, graphomotor, allographic, and perseveration errors.

Examples of writing defects from MCI and AD participants are shown in Figures 1-6.

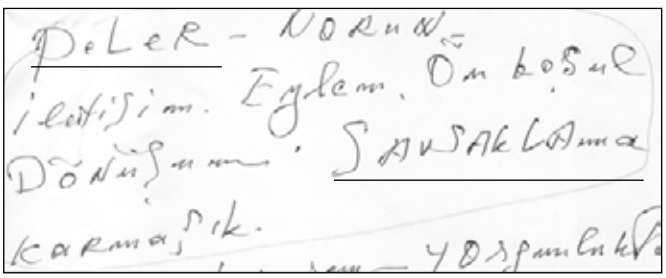

Figure 1. Participant with Mild Cognitive Impairment. Allographic errors identified in writing of words dictated to be written in capital letters.

Figure 2. Participant with Mild Cognitive Impairment. Example of fragmentation in the writing of the sentence 'İşleri elimizden geldiği kadar gevşek tutuyoruz'.

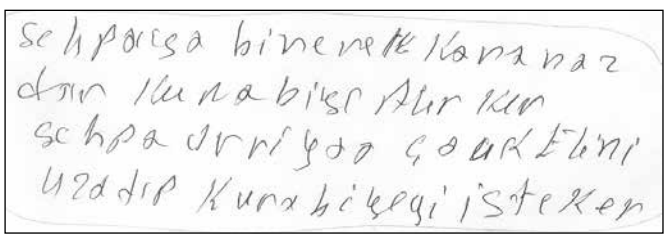

Figure 3. Participant with CDR-1 AD. Syntax errors in spontaneous writing.

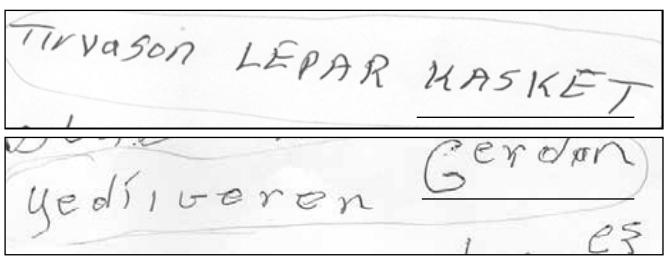

Figure 4. Participant with CDR-1 AD. Semantic errors in dictation and copying (participant had been asked to write "katpet" and "gergedan").

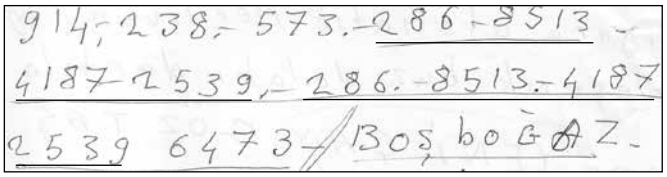

Figure 5. Participant with CDR-1 AD. Example of perseveration while copying.

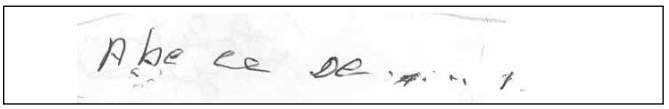

Figure 6. Participant with CDR-1 AD. Example of fragmentation in spontaneous writing.

DISCUSSION

Writing is a skill that has been acquired more recently than other cognitive skills with the evolution of the brain, involves quite complex mechanisms, and is used less than other cognitive skills (Rapcsak and Beeson 2002). This is why writing is generally very sensitive to the effects of acquired brain lesions and in cases involving pervasive cerebral effects, such as degenerative dementia, writing may be the language function which shows the most deterioration (Benson and Cummings 1985, Cummings and Mega 2003, Kirshner 2004, Roeltgen 1997).

When the literature is reviewed, it can be seen that assessments of the relationship between dementia and agraphia have concentrated on AD, that writing disorders in cases of MCI have only been studied in relation to kinematics, and that, in the assessment of agraphia, frequently used methods are picture description, naming, or writing down what is heard (Blair et al. 2007, Croisile et al. 1996a, Croisile et al. 1996b, Forbes et al. 2004, Groves-Wright et al. 2004, Luzzatti et al. 2003, Neils-Strunjas et al. 2006, Schröter et al. 2003, Werner et al. 2006). The Ege Agraphia Test Battery, which evaluates all aspects of writing skills, constitutes the first agraphia assessment scale for Turkish language which has been created with the sole aim of examining writing disorders in detail.

In pioneering research into the development of agraphia in cases of AD, it has been proposed that at first, a central writing disorder appears, with errors predominantly in the semantic, and to a lesser extent phonological processes, and that as the disease progresses, peripheral writing abnormalities such as defects in letter formation and the positioning of lines are added to the central agraphia (Forbes et al. 2004, Neils-Strunjas et al. 2006, Rapcsak et al. 1989).

The evaluation of agraphia in the present study, however, has revealed that peripheral agraphic errors may be seen from the first stages in AD patients, and even MCI patients, as defects in writing and signature formation. This suggests that peripheral writing mechanisms deteriorate early, and that the development of agraphia in cases of AD does not follow a

uniform pattern. Peripheral level disorders, disorders of apraxic type agraphia, are related to damage to the superior parietal lobe, angular, and supramarginal girus (Rapcsak and Beeson 2002). These areas are closely related to the central processes of writing (Penniello et al. 1995). Damage to the association areas is usual in AD, but it is interesting that peripheral-type language disorders were also found in the MCI group in the present study. Defects in writing and signature formation and peripheral-type writing disorders characterised by graphomotor and allographic errors were seen in patients with amnestic MCI. This supports the view that in amnestic MCI, the pathology is not limited to the hippocampus, and the pervasive cerebral effects seen in AD begin years before. Werner et al. (2006) conducted a kinematic assessment of the handwriting processes of a control group, MCI group, and mild AD group; they identified an intermediate level of disorder in the MCI group. Schröter et al. (2003) also demonstrated defects in writing skills in MCI and AD patients associated with loss of fine motor skills. In light of the present findings, it may be proposed that the monitoring of agraphic disorders in cases of MCI may be valuable in determining their transition into AD.

The statistically significant differences between the MCI and HC group found in the present study also provide some interesting data regarding central writing disorders. It was found that, compared to the control group, patients with MCI demonstrated poorer performance on spontaneous name-surname and letter writing, choosing a topic on the picture description test, and regarding effective communication and number of information units. Furthermore, there were also problems with dictation and copying in the MCI group. Regarding error types, there were statistically significant differences between the MCI and control group in terms of semantic and orthographic-type central errors.

Semantic errors, which are among the central-type errors, appear when the lexical-semantic route is affected; this route is anatomically localised in the left temporal-parietal-occipital junction. Meanwhile, orthographic errors, another central-type error, are closely connected to working memory, storing memory, and attention spans; these functions are considered a product of the fronto-parietal cortical network (Forbes et al. 2004). The central-type errors seen in the results of the present study also indicate a pervasive cerebral pathology in the MCI group and signal that there is an early effect on the association areas of the brain. Thus, the assessment of writing skills, which include many cognitive functions such as attention, memory, and executive functions, is useful both in revealing a complex cognitive disorder and as a possible practical measure for identifying and monitoring cases of MCI that have the possibility of transitioning into AD. In a retrospective study, Balestrino et al. (2012) reported a significant connection between features and errors of writing and cognitive losses. In summary, they asserted that cognitive status was reflected in the evaluation of handwriting. The significant relationships found in the present study between diagnosis and agraphia test parameters provide similar evidence. Further studies are planned to increase the data in this area.

A comparison between the AD and MCI groups in the present study identified significant differences, especially in terms of syntax, orthographic, graphomotor, and allographic errors and perseverative responses. The interpretation of these results may be that increasing central-type errors are seen with the increase in cognitive impairment and pathology in AD; allographic errors occur due to a decrease in semantic and working memory capacity; attention and inhibition deficits result in the impairment of error control, leading to perseveration. These results demonstrate that all kinds of writing errors may occur as the degeneration progresses, that both central and peripheral errors may be observed together even in the early stages of AD, and that from the early stages onwards, the lexical-semantic and phonological systems are affected together.

In conclusion, no practical problems were encountered with the administration of the Ege Agraphia Test Battery in this study, which aimed to create an agraphia test battery for the phonologically regular Turkish language, gather normative data for this test, and, based on the fact that writing has a complex nature and is a cognitive function sensitive to pervasive cerebral disorders, to develop an assessment scale which may provide clues about cognitive loss, particularly in cases of MCI. Statistically significant differences were found between the MCI and AD groups and the HC group. The most important finding of the present study was the observation of writing disorders in MCI patients using the Ege Agraphia Test. The data obtained demonstrate the possibility of identifying disorders relating to the semantic and phonological systems of writing in the early stages in cases of MCI. The Ege Agraphia Test Battery may be used in the monitoring of MCI patients to predict the risk of transition to AD. In particular, the appearance of certain error types and a drop in performance during monitoring may provide a warning. Although a qualitative assessment, attention should be given to writing and signature formation defects, which represent peripheral motor disorders in writing, when seen in patients with cognitive complaints in the early stages.

The data presented here must be accepted as a preliminary study. The sample size was limited by difficulties in finding patients without accompanying depression or other neurological or psychiatric disorders. In order to make adjustments to the test, it will be necessary to conduct multivariate analyses, increasing the number of participants in each group and grouping by education, as well as to gather data relating to different neurological disorders.

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