PSYCHOGERIATRICS
The Official Journal of the Japanese Psychogeriatric Society
doi:10.1111/psyg.12289 PSYCHOGERIATRICS 2018; 18: 98–105

ORIGINAL ARTICLE

Triple test, a diagnostic observation, can detect cognitive impairment in older adults

Ahmet T. ISIK,[1] Pinar SOYSAL ,[2] Derya KAYA[1] and Cansu USAREL[1]

[1]Unit for Aging Brain and Dementia, Department of Geriatric Medicine, Faculty of Medicine, Dokuz Eylul University, Izmir and [2]Department of Geriatric Medicine, Geriatric Center, Kayseri Education and Research Hospital, Kayseri, Turkey

Correspondence: Professor Ahmet T. Isik MD, Yaşlanan Beyin ve Demans Ünitesi, Geriatri BD, Dokuz Eylul Üniversitesi Tıp Fakültesi, 35340 Izmir, Turkey. Email: atisik@yahoo.com

Disclosure: The authors have no conflicts of interest to disclose.

Received 17 April 2017; revision received 13 June 2017; accepted 17 July 2017.

Abstract

Background: A simple, quick, and efficient screening tool for detecting mild cognitive impairment (MCI) and Alzheimer's disease (AD) is essential, especially in the primary care setting. In this study, we examined the neuropsychological profiles of elderly patients and aimed to assess the diagnostic value of the triple test, comprised of the attended alone sign (AAS), head-turning sign, and applause sign (AS), for detecting MCI and AD.

Method: Comprehensive geriatric assessment was performed in 354 elderly outpatients, and the presence or absence of AS, AAS and HTS was investigated.

Results: Of the 354 patients, 93 patients were considered to be cognitively impaired (MCI: 30; AD: 63); the remaining 261 were cognitively healthy. Relative to those without AS, patients with AS had significantly lower scores on the Mini–Mental State Examination, the clock-drawing test, Instrumental Activities of Daily Living Scale, and Basic Activities of Daily Living Scale ($P < 0.001$, for each). Similar significant differences were found between patients who were positive and negative for the HTS ($P < 0.001$) and between those who attended the clinic alone and those who were accompanied ($P < 0.001$). The sensitivity of the triple test for identifying cognitively impairment (CI), MCI, and AD was 0.61, 0.30, and 0.72, respectively; the specificity was 0.85, 0.68, and 0.83, respectively; and the positive and negative predictive values were 0.69, 0.09, and 0.59, respectively, and 0.79, 0.90, and 0.89, respectively.

Conclusions: The present study suggests that the triple test is a simple, quick, and efficient screening tool for detecting cognitive impairment, and the results may reflect deterioration in patients' activities of daily living. Additionally, it could be advantageous in clinical practice because educational level does not affect the test outcome. Therefore, it may be an appropriate test to screen for cognitive impairment in the elderly, both as a bedside diagnostic test and in daily clinical practice, especially in the primary care setting.

Key words: *applause sign, attended alone sign, dementia, elderly, head-turning sign, triple test.*

INTRODUCTION

In day-to-day clinical practice, especially in a primary care setting or when providing consultations for hospitalized elderly patients, looking for evidence for underlying cognitive impairment (CI) indicative of a neurodegenerative disorder requires long, time-consuming cognitive tests and sophisticated evaluations. However, this can be difficult to manage during a busy clinical day in part because of a lack of professionals to conduct neuropsychological testing and the related expense. Therefore, less time-consuming, cheaper, and more reliable clinical approaches are needed to accurately diagnose patients with CI. This may also help primary care professionals or physicians determine whether it is necessary to refer a patient to a tertiary care physician or a medical centre for cognitive diseases.

Some clinical signs of neurodegenerative diseases that may lead to dementia could have a crucial role in the diagnostic process. They may affect treatment decisions and help identify high-risk individuals. The attended alone sign (AAS), head-turning sign (HTS), and applause sign (AS) have separately been reported as evidence of CI or underlying neurodegenerative diseases.[1–7]

AAS (i.e. attending the clinic alone) is one reported to be an indication of the absence of dementia[3] regardless of the patient's gender and age.[4] However, data about AAS have consistently come from one cognitive function clinic in the UK. Therefore, there is no information as to whether AAS is affected by cultural factors. HTS (i.e. the patient turning to a caregiver when asked a question)[8] is another sign that has been reported to be reliably absent in those without CI. In a heterogeneous patient cohort from the clinic in the UK, which included 26 cases with Alzheimer's disease (AD) or mixed AD/cerebrovascular disease, 28 with amnestic minimal cognitive impairment (MCI), 8 with frontotemporal lobar degenerations, 7 with dementia with Lewy bodies (DLB), 2 with subcortical ischaemic vascular dementia, and 11 with miscellaneous others, HTS was shown to have a sensitivity of 0.63 and specificity of 0.95 for the presence of CI. HTS was found in 39% of the whole cohort.[9] In 2011, Fukui *et al*. reported HTS in 42% of patients with AD, 15% of DLB patients, 25% of amnestic MCI patients, 25% of progressive supranuclear palsy (PSP), and 17% of patients with vascular dementia; the significance of these findings differed among the groups in post-hoc analysis. The authors concluded that HTS was more prevalent in AD and amnestic MCI than in related non-AD groups, such as DLB, PSP, and vascular dementia. The study, which was performed in Japan, found that HTS occurred more frequently in female patients, independent of the epidemiological fact that AD is more prevalent in women.[2]

Finally, AS (i.e. a tendency to clap more than three times in response to the demonstration of clapping only three times)[1] was present in various neurodegenerative diseases, such as PSP, Parkinson's disease,[10–12] corticobasal syndrome,[13] multisystem atrophy, cortical dementias (e.g. AD and behavioural variant of frontotemporal dementia),[6] and amyotrophic lateral sclerosis.[14] AS is considered a consequence of perseveration due to frontal lobe impairment,[5] a part of dysexecutive syndrome.[11] This sign is the one that would be least likely to be affected by cultural features. AS may be also seen in non-neurodegenerative conditions, and it can be reversible, as observed in a lymphomatous meningitis case with central nervous system involvement.[15] In 2011, Walsh *et al.* reported another transient positive AS case with acute bilateral lentiform infarction and postulated that the AS was the result of basal ganglia-frontal disconnection syndrome.[16]

Each of these signs has been previously evaluated in a limited number of studies, but the effectiveness of using these signs in combination in a large number of older adults with or without CI has not been evaluated.[1,5–8,11] Moreover, these signs have not been studied in different locations and cultures. In the present study, we aimed to assess the value of each sign, alone and in combination, to screen for CI. We also sought to analyze the relationship among these signs and the cognitive status of older adults. To the best of our knowledge, this is one of the first studies to investigate all three of the clinically observed signs.

MATERIALS AND METHODS

Patients

We recruited consecutive outpatients, aged 60 years and older, between September 2014 and September 2015 from the memory centre at the Department of Geriatric Medicine at Dokuz Eylul University, Faculty of Medicine. We investigators evaluated each patient during a routine clinic visit. For each patient, a comprehensive geriatric assessment, including complete physical and mental examinations, was performed, and laboratory findings were reviewed.[17] Patients were assessed based on the Mini-Mental State Examination (MMSE),[18] Geriatric Depression Scale (GDS),[19,20] Basic Activities of Daily Living Scale (BADL), Instrumental Activities of Daily Living (IADL),[21,22] clock-drawing test, and Clinical Dementia Rating. Further evaluations that are needed for the differential diagnosis of CI, such as laboratory tests and brain imaging for patients with CI, were also performed.

Dementia was diagnosed according to the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (text revision) criteria.[23] The diagnosis of CI, including MCI and AD, was established based on the

criteria of Petersen *et al.*,[24] a Clinical Dementia Rating of at least 0.5,[25] and the National Institute on Aging and the Alzheimer's Association Workgroup's criteria.[26] The cognitively healthy group consisted of patients who were forgetful but had normal cognitive assessments and those who attended to our geriatric outpatient clinic for clinical or prevention programmes because of other medical problems. All the patients and their relatives gave their written informed consent, and the local ethics committee approved the study.

The present study's exclusion criteria were as follows: (i) a GDS score higher than 7; (ii) a recent or current acute confusional state, psychotic attack (e.g. schizoaffective disorder), or treatment-resistant major depressive disorder during evaluation; (iii) reversible CI related to vitamin B12 or folic acid deficiency, hypothyroidism, subdural haematoma, hyponatraemia, medications (e.g. corticosteroids, antipsychotics, benzodiazepines); (iv) irreversible CI unrelated to AD; (v) diseases that could seriously impair the individual's general health such as acute cerebrovascular event, gastrointestinal bleeding, sepsis, acute renal insufficiency, acute coronary syndrome, acute hepatic insufficiency, and acute respiratory failure; (vi) substance abuse problems; (vii) the inability to speak Turkish; (viii) institutionalization; and (ix) unilateral hearing impairment or deafness.

Evaluation of the signs

The signs were assessed by one physician (P.S.) who was blinded to the diagnosis of the patients. Presence or absence of AS, AAS, and HTS was investigated.

AS—also called the clapping test, three-clap test, or signe d'applause—was detected as described previously.[1,4] The patient was asked to clap three times as quickly as possible after the examiner had performed a demonstration. If the patient clapped three times, they were deemed negative for AS; if the patient clapped more than three times, they were considered positive for AS (PAS). Patients who clapped fewer less than three times were considered as pathologic and having PAS, as reported previously.[6,27]

As previously described in the literature,[2,4] HTS was assessed while the patient's caregiver sat quietly at a 45° angle, approximately 1 m behind the patient. The patient was engaged in a conversation about their cognitive function history. If the patient looked to the caregiver for help, the patient was considered to be positive for HTS (PHTS); if the patient did not seek help, they were considered negative for HTS (NHTS).

AAS was evaluated based on whether the patient attended the clinic with a caregiver, family member, or friend. If the patient was accompanied, they were considered negative for attended alone sign (NAAS).[4]

Statistical analyses

SPSS version 15 software for Windows (SPSS, Chicago, IL, USA) was used for statistical analyses. The percentages of subjects with PAS, NAAS and PHTS were reported, and sensitivity, specificity, and positive and negative predictive values of each sign were calculated individually and in combination. The combinations were assessed when all three were present (PAS + NAAS + PHTS), and the individual signs were evaluated when any single one was present (i.e. PAS, NAAS, or PHTS). The *t*-test was used for continuous data (age, MMSE, CDT, GDS, BADL and IADL scores, education), and the χ^2 test for categorical data (gender; the presence of HTS, AAS, AS). One-way ANOVA was used to analyze the differences among group means.

RESULTS

A total of 354 outpatients (120 men, 234 women) with a median age of 74 years were assessed. Of those, 93 patients (42 men, 51 women) were diagnosed with CI, and 261 (78 men, 183 women) were diagnosed as cognitively healthy. A greater proportion of female patients were cognitively healthy than cognitively impaired ($P = 0.008$). As expected, patients with CI were older (76.4 $\pm$ 8.3 vs 73.3 $\pm$ 8.2; $P = 0.002$) than the cognitively healthy patients; there was no difference between the two groups in terms of years of education (7.1 $\pm$ 4.6 vs 7.8 $\pm$ 4.6 years; $P = 0.190$).

Ninety-three patients were considered to have CI (MCI: 30; AD: 63); the remaining 261 were cognitively healthy. Among all the patients, there was no significant difference in years of educational or GDS score, but there were significant differences with regard to age, gender, MMSE, clock-drawing test, BADL, and IADL scores among the groups (Table 1).

A total of 233 patients (65.8%) attended the clinic with a caregiver, family member, or friend; this includes 84 of the 93 cognitively impaired patients.

Table 1 Characteristics of the participants

	Cognitive impairment (n = 93)			
	AD (n = 63)	MCI (n = 30)	Cognitively healthy (n = 261)	P-value
Age (years)	77.1 ± 8.6	75.0 ± 7.6	73.3 ± 8.2	0.004†
M/F (n)	23/40	19/11	78/183	0.001‡
Education (years)	6.6 ± 5.0	8.0 ± 3.7	7.8 ± 4.6	0.164†
MMSE	15.6 ± 7.4	25.5 ± 2.9	26.2 ± 4.8	<0.001§
GDS	3.3 ± 3.6	2.4 ± 2.6	3.2 ± 3.5	0.447§
CDT	2.1 ± 1.5	4.1 ± 1.2	4.3 ± 1.2	<0.001§
BADL	79.7 ± 21.2	95.5 ± 8.0	92.6 ± 14.5	<0.001§
IADL	5.7 ± 4.2	12.7 ± 2.5	13.0 ± 4.4	<0.001§
PAS, n (%)	45 (71.4)	8 (26.7)	32 (12.3)	<0.001‡
PHTS, n (%)§	58 (95.1)	13 (56.5)	71 (47.7)	<0.001‡
NAAS, n (%)	61 (96.8)	23 (76.7)	149 (57.1)	<0.001‡

† One-way ANOVA.
‡ χ^2 test.
§ Total number of points for PHTS is 233 (23 MCI + 61 AD + 149 cognitively healthy).
AD, Alzheimer's disease; BADL, Basic Activities of Daily Living; CDT, clock-drawing; GDS, Geriatric Depression Scale; IADL, Instrumental Activities of Daily Living; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; one sign;NAAS, negative for attended alone sign; PAS, positive for applause sign; PHTS, positive for head-turning sign.
Score range for each of the assessments: BADL, 0–100; CDT, 0–5; GDS, 0–15; IADL, 0–17; MMSE, 0–30. In all cases, the lower the score, the greater the cognitive impairment.
All data are means ± SD.

Only nine patients with CI (MCI: 7; AD: 2) attended alone; all lived very close to the clinic and had a Clinical Dementia Rating of 1 (Table 2). A larger proportion of women (67.9%) than men (61.7%) were NAAS (P = 0.238).

Of the 233 patients who were NAAS, 142 (60.9%) were PHTS, including 71 (50%) who had CI. A larger proportion of women (67.3%) than men (47.3%) were PHTS (P = 0.004).

A total of 85 patients (24.0%) were PAS and applauded more than three times; this included 26.1% of the female patients and 20.0% of male patients (P = 0.206). Fifty-three PAS patients (62.4%) suffered from CI.

Of the 93 patients with CI, 57.0% were PAS, 76.3% were PHTS, and 90.3% were NAAS; in contrast, the presence of these signs was significantly lower in the cognitively healthy patients (PAS: 12.3%; PHTS: 47.7%; NAAS, 57.1%; $P < 0.001$ for each test). The presence of AS, HTS, and AAS in each group is shown in Table 1.

Table 2 AAS status in all patients

	AD (n)	MCI (n)	Cognitively healthy (n)	Total (n)
NAAS	61	23	149	233
AAS	2	7	112	121
Total	63	30	261	354

AD, Alzheimer's disease; MCI, mild cognitive impairment; NAAS, negative for attended alone sign; PAAS, positive for attended alone sign.

Patients' neuropsychological profiles were assessed based on the presence or absence of these signs (Table 3). Patients who were PAS had significantly lower scores on the MMSE, clock-drawing test, IADL, and BADL than those who were NAS ($P < 0.001$ for each test). Similar significant differences were also found between patients who were PHTS and NHTS ($P < 0.001$) and between those who were NAAS and positive for AAS (PAAS) ($P < 0.001$).

Diagnostic values of the signs with regard to the diagnoses are shown in Table 4. Area under the receiver–operator curve analysis is shown in Figure 1.

DISCUSSION

This study demonstrated that the presence or absence of AS, AAS, or HTS, alone or in combination, is a practical and easy way to detect possible CI, in particular AD, in older adults.

Diagnosing CI, such as MCI and AD, in older adults is difficult, especially in the early stages.[28] To make a differential diagnosis, it is highly important for physicians to consider the early clinical signs of specific neurodegenerative diseases as evidence of dementia. Signs that would help a physician decide to perform further investigations or to refer a patient to a specialized memory centre are critical to clinical practice. Therefore, we investigated whether to diagnose patients with CI based on AS, AAS, and HTS.

Table 3 Neuropsychological profile and applause sign, head-turning sign, and attended alone sign

	PAS (n = 85)	NAS (n = 269)	P-value†	PHTS (n = 142)	NHTS (n = 91)	P-value†	PAAS (n = 121)	NAAS (n = 233)	P-value†
MMSE	16.6 ± 7.9	26.7 ± 3.7	<0.001	19.6 ± 7.7	26.5 ± 3.8	<0.001	28.0 ± 2.2	22.3 ± 7.3	<0.001
CDT	2.3 ± 1.6	4.3 ± 1.1	<0.001	3.0 ± 1.7	4.3 ± 1.2	<0.001	4.5 ± 0.9	3.6 ± 1.6	<0.001
IADL	6.7 ± 5.2	13.2 ± 3.8	<0.001	7.8 ± 4.8	12.6 ± 4.1	<0.001	15.4 ± 1.6	9.7 ± 5.1	<0.001
BADL	77.5 ± 24.9	94.7 ± 9.1	<0.001	82.9 ± 21.2	92.5 ± 12.7	<0.001	97.9 ± 2.7	86.6 ± 18.9	<0.001

† *t*-test.

BADL, Basic Activities of Daily Living; CDT, clock-drawing test; IADL, Instrumental Activities of Daily Living; MMSE, Mini-Mental State Examination; NAS, negative for applause sign; NAAS, negative for attended alone sign; PHTS, positive for head-turning sign; PAAS, positive for attended alone sign; PAS, positive for applause sign; PHTS, positive for head-turning sign.

Score range for each of the assessments: BADL, 0–100; CDT, 0–5; IADL, 0–17; MMSE, 0–30. In all cases, the lower the score, the greater the cognitive impairment.

All data are means ± SD.

In the current study, AS was found to have a specificity of 0.88 and a low sensitivity of 0.57 in the detection of CI. In a 2016 study, Bonello and Larner demonstrated that AS had a sensitivity of 0.39 and a specificity of 0.89 for identifying patients with any CI (dementia, MCI); this sensitivity was lower than that for identifying patients with subjective memory complaints, and the specificity was comparable. Their study involved 71 patients with MCI, 52 with dementia, and 152 with subjective memory complaints. However, the control group in the Bonello and Larner study consisted of patients with unidentified forms of dementia cases and subjective memory complaints.[29]

In 2013, Isella *et al.* reported that PAS had a sensitivity of 0.39 and a specificity of 0.90 in discriminating between patients with cortical dementia (20 AD + 10 posterior cortical atrophy (PCA)) and cortical-subcortical dementia (20 LBD + 16 corticobasal syndrome), indicating that PAS was found more frequently in patients with cortical-subcortical dementia than in those with cortical ones.[27] In another 2013 study, Luzzi *et al.* detected PAS detected in 43.8% of 105 patients with AD.[29] In the present study, PAS frequency in AD patients was higher than that found in the studies by Isella *et al.* (71.4% vs 10%) and Luzzi *et al.* (71.4% vs 43.8%).[27,29,30]

PAAS may be indicative of preserved executive function in the domain of transferring in activities of daily living.[21,22,31] It also suggests preserved non-cognitive functions in the same domain, such as mobility, gait, and balance. In the present study, 90.3% of demented patients were NAAS compared to 57.1% of non-demented patients, results similar to those in Larner's 2009 study.[31] This emphasizes that the both cognitive and non-cognitive functions are important for elderly patients to attend the clinic alone. It should be noted that the relatively high rate of non-demented patients attending the clinic with a caregiver, family member or friend may be because of sociological features of Turkish society: generally speaking, not accompanying a patient, especially an older one, is frowned upon. AAS needs to be studied in different social and cultural contexts because other existing reports are from one cognitive function clinic in the UK. Reports from that clinic indicated that around 59% of 312 non-demented patients were accompanied to the clinic.[31] However, those patients received a letter asking them to be accompanied by a caregiver, family member, or friend when coming to the clinic.

HTS, which could be indicative of memory impairment and dependency, may be more severe in AD patients than in DLB, PSP, or vascular dementia patients.[2] In the present study, 76.3% of CI patients were PHTS compared to 47.7% of non-demented patients. The proportion of PHTS patients with AD was higher in this study than in that of Fukui *et al.* (95.1% vs 42%).[2] However, both studies found that more women were PHTS. The higher frequency of PHTS among elderly women could be a reflection of their low confidence due to patriarchal social structures.

Until now, the diagnostic value of these signs had been evaluated only separately; they had not been assessed in combination in elderly patients. Therefore, this is the first study to examine the triple test, which encompasses all three signs. With a specificity of 0.83 (i.e. the presence of all the three signs), the triple test has a diagnostic value comparable to common tools such as the Turkish version of the MMSE (specificity: 0.95),[18] the Montreal Cognitive Assessment (specificity: 0.78),[32] Saint Louis University

Table 4 Assessment of diagnostic value of the each sign individually and in combination

	PAS (*n* = 85)			NAAS (*n* = 233)			PHTS (*n* = 142)			PAS, NAAS, and PHTS (*n* = 74)			PAS, NAAS, or PHTS (*n* = 233)		
	CI	MCI	AD	CI	MCI	AD	CI	MCI	AD	CI	MCI	AD	CI	MCI	AD
n (%)	53 (62.4)	8 (9.4)	45 (52.9)	84 (36.1)	23 (9.9)	61 (26.2)	71 (50)	13 (9.2)	58 (40.8)	51 (68.9)	7 (9.5)	44 (59.5)	73 (49)	14 (9.4)	59 (39.6)
PPV	62.4	9.4	52.9	36.1	9.9	26.2	50	9.2	40.8	68.9	9.5	59.5	49	9.4	39.6
NPV	85.1	91.8	86.3	92.6	94.2	98.3	85.7	89	96.7	79.2	89.9	89.3	86.9	89.3	97.6
Sensitivity	57	26.7	71.4	90.3	76.7	96.8	84.5	56.5	95.1	60.7	30.4	72.1	86.9	60.9	96.7
Specificity	87.7	76.2	70.9	42.9	35.2	40.9	52.3	38.6	51.2	84.6	68.1	82.6	49	35.7	47.7

AD, Alzheimer's disease; CI, cognitive impairment; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; NAAS, negative for attended alone sign; NPV, negative predictive value; PAS, positive for applause sign; PHTS, positive for head-turning sign; PPV, positive predictive value.

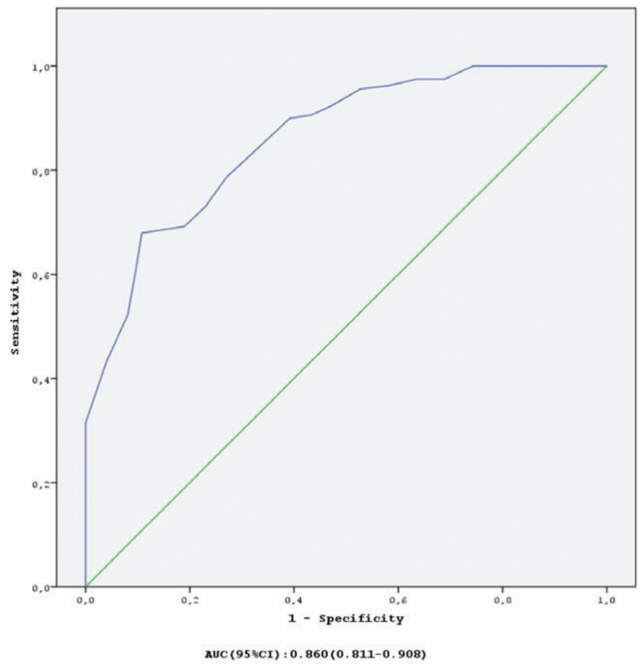

Figure 1 Receiver–operating characteristic test of triple test for all participants. Area under curve (AUC) (95%CI): 0.860 (0.811–0.908). CI, Confidence interval.

Mental Status Examination (specificity: 0.87),[33] and Cognitive State Test (specificity: 0.87).[34] As such, the triple test could be considered as a screening test for AD in older adults.

The triple test reflects deterioration in activities of daily living, one of the predictors of dementia in older adults,[31] while being unaffected by educational level. Moreover, the test is a simple, brief, time-effective, and sensitive tool to screen for CI in geriatric outpatient clinics. We believe that if all the triple test components are present, this test has the power to identify CI; however, its relatively low sensitivity means that it may miss approximately 39% of CI cases. Any component of the triple test has the power to catch CI, but it lacks a high level of specificity. Nevertheless, we believe that the chief utility of the triple test resides in its support of CI diagnoses and as an indicator of the need for further investigation, especially in primary care settings. Additionally, the accuracy values of the triple test for AD, but not for MCI, are good enough; the test can also be used as a tool to decide which patients should be referred to a medical centre for cognitive diseases.

The present study has several strengths. It was the first to include only older patients whose lone

complaint was forgetfulness. In addition, the diagnostic value of AAS, AS, and HTS was evaluated only in patients with CI, such as MCI and AD.

This study also has some limitations. This study was conducted at a memory centre; therefore, our results might not be generalizable for a wider population. Also, it would be better if the AS were scored based on the number of claps instead of evaluated as positive or negative. Finally, evaluating HTS requires a patient to be accompanied to the clinic, so someone who is PAAS will be, in most cases, NHTS because of circumstance. Nevertheless, because PAAS is a good marker for being cognitively healthy, patients who could not be evaluated for HTS may be considered cognitively healthy.

In conclusion, the present study suggests that the triple test is a simple, quick, and efficient screening tool for detecting CI that reflects deterioration in activities of daily living. Moreover, the results are unaffected by a patient's education level. Therefore, the triple test may be an appropriate test to screen for CI in the elderly, both as a bedside diagnostic test and in daily clinical practice, especially in the primary care setting.

ACKNOWLEDGMENT

We thank Dr Hulya Ellıdokuz for providing help in statistically evaluating the data for the study.

REFERENCES

1 Dubois B, Slachevsky A, Pillon B, Beato R, Villalponda JM, Liyvan I. 'Applause sign' helps to discriminate PSP from FTD and PD. *Neurology* 2005; **64**: 2132–2133.
2 Fukui T, Yamazaki T, Kinno R. Can the 'head-turning sign' be a clinical marker of Alzheimer's disease? *Dement Geriatr Cogn Dis Extra* 2011; **1**: 310–317.
3 Larner AJ. 'Who came with you?' A diagnostic observation in patients with memory problems? *J Neurol Neurosurg Psychiatry* 2005; **76**: 1739.
4 Larner AJ. History and neurological examination. In: Larner AJ, ed. *Dementia in Clinical Practice: A Neurological Perspective*, 2nd edn. London: Springer-Verlag, 2014; 41–64.
5 Luzzi S, Fabi K, Pesallaccia M, Silvestrini M, Provinciali L. Applause sign: is it really specific for parkinsonian disorders? Evidence from cortical dementias. *J Neurol Neurosurg Psychiatry* 2015; **82**: 830–833.
6 Wu LJ, Sitburana O, Davidson A, Jankovic J. Applause sign in Parkinsonian disorders and Huntington's disease. *Mov Disord* 2008; **23**: 2307–2311.
7 Soysal P, Usarel C, Ispirli G, Isik AT. Attended with and head-turning sign can be clinical markers of cognitive impairment in older adults. *Int Psychogeriatr* 2017; **29**: 1–7.
8 Bouchard RW, Rossor MN. Typical clinical features. In: Gauthier S, ed. *Clinical Diagnosis and Management of Alzheimer's Disease*. London: M. Dunitz, 1996; 35–50.
9 Larner AJ. Head turning sign: Pragmatic utility in clinical diagnosis of cognitive impairment. *J Neurol Neurosurg Psychiatry* 2012; **83**: 852–853.
10 Somme J, Gomez-Esteban JC, Tijero B, Berganzo K, Lezcano E, Zarranz JJ. The applause sign and neuropsychological profile in progressive supranuclear palsy and Parkinson's disease. *Clin Neurol Neurosurg* 2013; **115**: 1230–1233.
11 Tomic S, Vladetic M, Solic K, Misevic S, Soldo SB. The applause sign in Parkinson's disease patients is related to dysexecutive syndrome. *J Clin Neurosci* 2013; **20**: 1734–1736.
12 Weerkamp NJ, Tissingh G, Poels PJ *et al*. Applause sign in advanced Parkinson's disease. *Parkinsonism Relat Disord* 2014; **20**: 1268–1269.
13 Arkadir D, Greene PE, Waters CH, Moskowitz CB, Sharp ME. Applause sign in clinically overlapping diseases: a case of TDP-43 proteinopathy. *Parkinsonism Relat Disord* 2013; **19**: 774–775.
14 Anneser JM, Krzovska M, Borasio GD, Danek A. Occurrence of the 'applause sign' in patients with amyotrophic lateral sclerosis. *Clin Neurol Neurosurg* 2015; **137**: 8–10.
15 Gallagher DA, Schott JM, Childerhouse A, Wilhelm T, Gale AN, Schrag A. Reversible 'applause sign' secondary to diffuse large B cell lymphoma. *Mov Disord* 2008; **23**: 2426–2428.
16 Walsh RA, Duggan J, Lynch T. Localisation of the applause sign in a patient with acute bilateral lenticular infarction. *J Neurol* 2011; **258**: 1180–1182.
17 Isik AT, Bozoglu E, Yay A, Soysal P, Ateskan U. Which cholinesterase inhibitor is the safest for heart in elderly patients with Alzheimer's disease? *Am J Alzheimers Dis Other Demen* 2012; **27**: 171–174.
18 Güngen C, Ertan T, Eker E, Yaşar R, Engin F. Reliability and validity of the standardized Mini Mental State Examination in the diagnosis of mild dementia in Turkish population. *Turk Psikiyatri Derg* 2002; **13**: 273–281 (in Turkish).
19 Sheikh JI, Yesavage JA. Geriatric Depression Scale (GDS): recent evidence and development of a shorter version. *Clin Gerontol* 1986; **5**: 165–173.
20 Ertan T, Eker E. Reliability, validity, and factor structure of the geriatric depression scale in Turkish elderly: are there different factor structures for different cultures? *Int Psychogeriatr* 2000; **12**: 163–172.
21 Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist* 1969; **9**: 179–186.
22 Mahoney FI, Barthel D. Functional evaluation: the Barthel Index. *Md State Med J* 1965; **14**: 56–61.
23 American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 4th edn., text revision edn. Washington, DC: American Psychiatric Association, 2000.
24 Petersen RC, Smith GE, Waring SC, Ivnik RJ, Kokmen E, Tangelos EG. Aging, memory, and mild cognitive impairment. *Int Psychogeriatr* 1997; **9**: 65–69.
25 Chang YL, Bondi MW, McEvoy LK *et al*. Global Clinical Dementia Rating of 0.5 in MCI masks variability related to level of function. *Neurology* 2011; **76**: 652–659.
26 McKhann GM, Knoppman DS, Chertkow H *et al*. The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association Workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement* 2011; **7**: 263–269.

27 Isella V, Rucci F, Traficante D, Mapelli C, Ferri F, Appollonio IM. The applause sign in cortical and cortical-subcortical dementia. *J Neurol* 2013; **260**: 1099–1103.
28 Bradford A, Kunik M, Schulz P, Williams SP, Singh H. Missed and delayed diagnosis of dementia in primary care: prevalence and contributing factors. *Alzheimer Dis Assoc Disord* 2009; **23**: 306–313.
29 Bonello M, Larner AJ. Applause sign: screening utility for dementia and cognitive impairment. *Postgrad Med* 2016; **128**: 250–253.
30 Luzzi S, Fabi K, Pesallaccia M, Silvestrini M, Provinciali L. Applause sign in Alzheimer's disease: relationships to cognitive profile and severity of illness. *J Neurol* 2013; **260**: 172–175.
31 Larner AJ. 'Attended alone' sign: validity and reliability for the exclusion of dementia. *Age Ageing* 2009; **38**: 476–478.
32 Selekler K, Cangöz B, Uluç S. Montreal Bilişsel Değerlendirme Ölçeği'nin (MOBİD) hafif bilişsel bozukluk ve Alzheimer hastalarını ayırt edebilme gücünün incelenmesi. *Turk J Geriatr* 2010; **13**: 166–171.
33 Kaya D, Isik AT, Usarel C, Soysal P, Ellidokuz H, Grossberg GT. The Saint Louis University Mental Status Examination is better than the Mini-Mental State Examination to determine the cognitive impairment in Turkish elderly people. *J Am Med Dir Assoc* 2016; **17**: 370.e11–e15.
34 Babacan-Yildiz G, Isik AT, Ur E *et al*. COST: Cognitive state test, a brief screening battery for Alzheimer disease in illiterate and literate patients. *Int Psychogeriatr* 2013; **25**: 403–412.