Clinical features of incidental mild cognitive impairment and dementia in a population-based study

Nozomi Hishikawa,[1] Yusuke Fukui, [1] Kota Sato, [1] Toru Yamashita, [1] Yasuyuki Ohta,[1] and Koji Abe[1]

[1]Department of Neurology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

Correspondence: Professor Koji Abe, Department of Neurology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences 2-5-1 Shikatacho Kitaku, Okayama 700-8558, Japan

Tel.: +81-86-235-7365

Fax: +81-86-235-7368

E-mail: nozomi-hishikawa@okayama-u.ac.jp

Running title: Features of incidental MCI and dementia

AUTHOR CONTRIBUTIONS

Nozomi Hishikawa and Koji Abe were involved in the concept and design of this study. Nozomi Hishikawa, Yusuke Fukui, Kota Sato, Toru Yamashita, Yasuyuki Ohta, and Koji Abe collected the data and did the analyses. Toru Yamashita and Yasuyuki Ohta advised this study. Nozomi Hishikawa wrote the first draft of the paper. Koji Abe supervised the project, and made critical adjustments to the manuscript.

ABSTRACT

Aims: The number of people with dementia is rapidly increasing as populations around the world age. It is important to grasp the characteristic features of mild cognitive impairment (MCI) for early detection and prevention of dementia.

Methods: We examined 408 individuals recruited from health checkup for metabolic syndrome, which comprised 3 groups: normal (n = 325), MCI (n = 55), and apparent cognitive decline (ACD, n = 28). We compared cognitive/affective functions and exercise/hobby habits with assessments of vascular risk factors and results from computerized touch-panel tests.

Results: Among the 408 individuals, 93.1% showed normal scores on the Mini Mental State Examination (MMSE), and 6.9% had ACD. Among the normal MMSE participants, 14.5% had MCI (13.5% of all participants). The three groups of participants showed significant differences in age, education, systolic blood pressure, glycosylated hemoglobin, and high-density lipoprotein cholesterol level. Even within the normal range, those in the MCI group exhibited significantly lower cognitive function than those in the normal group. Scores on the geriatric depression scale were greater in the MCI group and “day-night reversal” was worse in the ACD group. Scores on touch-panel screening tests were significantly worse in the MCI and ACD groups than in the normal group. Participants showed better cognitive and affective function if they exercised regularly or had hobbies.

Conclusions: Incidental MCI and ACD had prevalences of 13.5% and 6.9%, respectively in the population-based study. Participants with these conditions showed cognitive/affective decline and impairment on computerized touch-panel tests in relation to VRFs and exercise/hobbies.

Keywords: apparent cognitive decline, cognitive/affective functions, general population, mild

cognitive impairment, risk factors

Introduction

The world is facing a problem as populations age and the number of people with dementia increases. In 2010, the number of patients with dementia worldwide was 35.6 million, and this number is estimated to increase to 65.7 million by 2030 and 115.4 million by 2050.[1] Alzheimer's disease (AD) and vascular dementia (VaD) are the two leading cause of dementia. Life-style related diseases such as hypertension (HT), hyperlipidemia (HL), diabetes mellitus (DM), and metabolic syndrome are the most important vascular risk factors (VRFs) for cerebrovascular diseases, and are known to be risk factors for AD.[2]

Population-based studies have reported that in addition to medicated hypertension, midlife elevated serum cholesterol, high diastolic blood pressure, older age, the apolipoprotein E4 ε4 allele, lower education, depression, cortical atrophy, brain infarcts, and white matter hyperintensities are risk factors for cognitive impairment in dementia-free individuals. [3-7] Furthermore, our recent study showed that the risk of mild cognitive impairment (MCI) changing into AD is influenced by low education, low baseline Mini-Mental State Examination (MMSE) scores, cerebral white matter lesions, and parahippocampal gyrus volume.[8] Early detection of MCI and treatment of VRFs could lower the risk of those with MCI developing dementias such as AD and VaD.

In the present study, we examined cognitive/affective functions and exercise/hobby habits in a local community population who had a health check for metabolic syndrome. We assessed their VRFs and scores on computerized touch-panel tests, and compared the results from normal participants

with those from patients with MCI or apparent cognitive decline (ACD).

Methods

Participants

Their medical records of 604 participants were reviewed, who had received a health check for metabolic syndrome conducted by the city government, and the 408 patients (158 male and 250 female) were selected who were given both the Clinical Dementia rating (CDR) scale[9] and the MMSE examined in this cross-sectional study. Average age was 66.2 ± 12.5 years (mean ± SD); 20s (n = 5), 30s (n = 10), 40s (n = 30), 50s (n = 61), 60s (n = 102), 70s (n = 157), 80s (n = 42), and 90s (n = 1). Cognitive and affective functions and physical data were examined along with serological tests on the same day (during the morning). The 408 participants were divided 3 groups according to the criteria proposed by the Japanese Alzheimer's disease neuroimaging initiative (J-ADNI). [8, 10, 11] The 3 groups were: normal (CDR = 0 and MMSE ≥ 24, n = 325), MCI (CDR = 0.5 and MMSE ≥ 24, n = 55), an ACD (MMSE ≤ 23, n = 28). Clinical data and medical records were analyzed. We checked whether they had exercise habits (at least 3 days a week) and/or hobbies (at least one days a week) or not, by filling in the interview sheet. In this study, the kinds and amount of time on the exercise and/or hobby did not matter. We excluded those who had already received medical treatment for dementia, or who had any past or present central nervous system disease or psychiatric disorder.

All participants gave written informed consent, and the study protocol was approved by

the Ethics Committee on Epidemiological Studies of the Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences (approval #694).

Cognitive and affective functions

Participants were evaluated with neurological examinations, the CDR, and the following cognitive tests: MMSE, Hasegawa dementia score-revised (HDS-R), frontal assessment battery (FAB), the Montreal cognitive assessment (MoCA), and a computerized touch-panel test called "Ryokansan" (Ohtsu Computer Corp., Otsu, Japan). The Ryokansan program was performed according to our previous reports,[12-14] which included the times (sec) to complete the flipping-card, finding-the-mistakes, and picture-arrangement games, and the accuracy (%) on the beat-the-devils game. The flipping-card game assesses the time to find 6 matching pairs of cards. The finding-the-mistakes game measures the time to find 3 mistakes between 2 similar but different picture panels. The picture-arrangement game assesses the time to arrange 4 scenes from a famous Japanese fairy tale in the correct order. The beat-the-devils game asks participants to distinguish between the emergence of heroes and devils, and assesses accuracy in exterminating only devils during a 30-sec period. The flipping-the-card game reflects recent memory and concentration, the finding-the-mistakes game reflects the ability to discriminate and attention, the picture-arrangement game reflects the ability to long-term memory and logical thinking, and the beat-the-devil game reflects the ability of quick judgment and inhibitory control.[12-14] Depression, apathy, and behavioral and psychological symptoms of dementia (BPSD)

were evaluated with the geriatric depression scale (GDS), apathy scale (AS), and Abe's BPSD score (ABS), respectively.[15]

Serological laboratory tests

Serological laboratory data for glycosylated hemoglobin (HbA1c), low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), and triglycerides (TG) were obtained from 264 of 408 participants (normal, n = 177; MCI, n = 63; ACD, n = 24).

Statistical analysis

Statistical analysis was carried out using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). After checking normality, Kruskal–Wallis tests were performed to compare the demographic data (age, education, waist circumference, body mass index [BMI], blood pressure, and serological data) between the normal, MCI, and ACD groups. Kruskal–Wallis tests were also used to compare each cognitive and affective functional assessment, subscales of cognitive functional tests (MMSE, HDS-R, FAB, and MoCA), and the ABS across the 3 groups. We evaluated the dichotic subscales of the cognitive functional tests using the Pearson χ^2 test. Additionally, we performed Kruskal–Wallis tests to compare cognitive and affective assessments between those who exercised regularly and those who did not, and between those who had hobbies and those who did not. *P*-values less than 0.05 were considered to be significant.

Results

The demographic and characteristic data of the 408 participants are shown in Table 1. Of the 408 participants, 93.1% (n = 380) had normal-ranged MMSE (> 23), and 6.9% (n = 28) showed cognitive decline (ACD) (≤ 23). Among 380 subjects with normal MMSE, 85.5% (n = 325, 79.6% of all participants) were considered normal (CDR = 0) and 14.5% (n = 55, 13.5% of all participants) had MCI (CDR = 0.5). Analysis showed significant differences among the three groups in age (normal 64.7 ± 12.7 vs. MCI 69.9 ± 10.4 and ACD 76.5 ± 7.5, $p < 0.01$), education (normal 12.5 ± 2.3 vs. MCI 11.4 ± 1.6, $p < 0.05$; and ACD 10.1 ± 1.8, $p < 0.01$), systolic blood pressure (normal 130.9 ± 19.2 vs. ACD 142.8 ± 18.5, $p < 0.05$; MCI 130.2 ± 19.7 vs. ACD 142.8 ± 18.5, $p < 0.05$), HbA1c level (normal 5.7 ± 0.7 vs. MCI 5.9 ± 0.6, $p < 0.01$; normal vs. ACD 6.1 ± 0.9, $p < 0.05$), and HDL level (normal 62.1 ± 15.8 vs. MCI 56.4 ± 13.3, $p < 0.05$). There were more underweight individuals (BMI < 18.5) in the ACD and MCI groups than in the normal group, but the difference was not significant.

The top of the Figure 1 shows the cognitive and affective functions of the three groups (white bars: normal; dotted bars: MCI; gray bars: ACD). Each mean MMSE, HDS-R, FAB, and MoCA score in the ACD group (21.6 ± 1.9, 22.8 ± 3.7, 14.4 ± 2.4, and 18.1 ± 5.4, respectively) was significantly lower than what was observed in the normal group (28.5 ± 1.7, 28.6 ± 1.5, 16.3 ± 1.6, and 25.8 ± 2.5, respectively; $p < 0.05$). Additionally, each mean MMSE, HDS-R, and MoCA score in the MCI group (26.8 ± 1.9, 27.3 ± 2.2, and 21.8 ± 3.4, respectively) was significantly lower than the corresponding

score in the normal group ($p < 0.05$) (Fig. 1A). Affective functions also differed in some cases. Mean GDS scores for the MCI group (4.4 ± 4.2) and mean ABS scores for the ACD group (0.7 ± 1.0) were significantly higher ($p < 0.05$) than the corresponding scores in the normal group (GDS 3.0 ± 3.2, ABS 0.2 ± 0.8). In contrast, AS scores did not differ across groups (Fig. 1B). In the MCI group, 37.8% were identified as being in a depressive state (GDS: 5–9), and 9.8% exhibited depression (GDS: 10−15) (Fig. 1C). Apathy (AS: 16−42) was found in 17.9% of the normal group, 36.8% of the MCI group, and 26.1% of the ACD group (Fig. 1D). Mild ABS was found in 33.3%, of the ACD group, but only in 6.6% of the normal group and 17.7% of the MCI group (mild + moderate) (Fig. 1E).

Subscale analyses of these cognitive tests among 3 groups were generally worse in ACD group than in the MCI or normal groups (Fig. 2A-D). In contrast, scores on the following MMSE subscales were significantly lower in the MCI group than in the normal group: calculation (normal 4.3 ± 1.2, MCI 3.6 ± 1.6; $^{**}p<0.01$), recall (2.7 ± 0.6, 2.3 ± 0.8; $^{**}p<0.01$), and sentence repetition (0.9 ± 0.3, 0.7 ± 0.5; $^{**}p<0.01$) (Fig. 2A). Similarly results were found for HDS-R subscales of calculation (1.9 ± 0.3, 1.7 ± 0.5; $^{**}p<0.01$), and recall (5.5 ± 0.9, 5.0 ± 1.4; $^{**}p<0.01$) (Fig. 2B), the FAB subscale of forced grasping (3.0 ± 0.2, 2.9 ± 0.6; $^{**}p<0.01$) (Fig. 2C), and the MoCA subscales of copy cube (0.9 ± 0.2, 0.7 ± 0.4; $^{**}p<0.01$), clock drawing (2.6 ± 0.2, 0.7 ± 0.4; $^{*}p<0.05$), read list digits (1.8 ± 0.5, 1.5 ± 0.7; $^{*}p<0.05$), subtraction (2.7 ± 0.6, 2.3 ± 0.8; $^{**}p<0.01$), repeat (1.2 ± 0.6, 0.8 ± 0.6; $^{**}p<0.01$), fluency (0.6 ±0.5, 0.3 ±0.5; $^{**}p<0.01$), abstraction (2.0 ±0.1, 1.8 ±0.5; $^{**}p<0.01$), and delayed recall (3.2 ± 1.6, 1.9 ± 1.8; $^{**}p<0.01$) (Fig. 2D).

Subscale analysis of the ABS revealed that “day-night reversal” scores for the ACD group were significantly higher than for the normal group (normal: 0.04 ± 0.42; ACD: 0.33 ± 0.78; $p < 0.05$, Fig. 2E).

Additionally, individuals in the MCI and ACD groups took significantly more time to finish the touch-panel tests (Fig. 3, left): flipping-card (normal: 17.6 ± 10.8 s; MCI: 23.4 ± 14.7 s; ACD: 31.7 ± 18.9 s), finding-the-mistakes (39.5 ± 32.3 s; 47.1 ± 34.5 s; 64.3 ± 40.5 s), and picture-arrangement (14.9 ± 10.2 s; 24.3 ± 25.4 s; 42.1 ± 22.6 s). MCI (87.3% ± 21.9%) and ACD (73.5% ± 24.0%) groups were less accurate than the normal group (95.6% ± 7.3%) on the beat-the-devil game (Fig. 3, right).

In the community of this study, the most common exercise habits was walking (52%), followed by jogging (9%), training gym (9%), and golf (9%). Their hobbies were various; gardening (14%), karaoke (11%), handicrafts (8%) and so on. Figure 4A and 4C show that cognitive scores (MMSE, HDS-R, and MoCA) were all higher in people who exercised regularly or who had hobbies than in those who did not, and reached significance for HDS-R scores in people with hobbies (hobbies: 28.7 ± 1.3; no hobbies: 26.8 ± 3.2; $p < 0.05$, Fig. 4C). The affective scores (GDS, AS, and ABS) were all better in people who exercised regularly or who had hobbies than in those who did not (Fig. 4B, D), and reached significance for GDS in people with hobbies (hobbies: 2.1 ± 2.9; no hobbies: 4.2 ± 3.7, $p < 0.05$) (Fig. 4D).

Discussion

The present study examined the cognitive and affective functions of normal participants and those who had MCI and ACD, who had received a health check for metabolic syndrome conducted by the city by the city government. There were about 20% subject who were suspected MCI (13.5%) or ACD (6.9%) in this study. In 2012, the Ministry of Health, Labour and Welfare estimated that about 25% of senior people (over 65 years old) had MCI or dementia. Our study shows a slightly lower level of dementia or MCI, because our subjects might be more conscious of their health, and their average age was younger (66.2 ± 12.5 years).

Compared with the normal group, total scores on the MMSE, HDS-R, and FAB were significantly worse in the MCI group (Fig. 1A), and subscale analyses revealed declines in “calculation”, “recall”, “sentence repetition”, “copy cube”, “clock drawing test”, “read list digits”, “letter fluency”, and “abstraction” (Fig. 2), suggesting that people with MCI suffered from impairments in the resent memory, working memory, executive function, attention, and constructive apraxia. Additionally, performance on all four touch-panel screening tests was significantly worse in the MCI and ACD groups than in the normal group (Fig. 3), which was in accordance with our recent study that examined behavioral measures for distinguishing people with MCI from those without.[13] Studies using single photon emission computed tomography (SPECT) have reported that cerebral blood flow in the temporal, parietal, and prefrontal cortexes, as well as the posterior cingulate gyrus and precuneus is lower in people with MCI.[16, 17] The present study supports these findings by showing that people with MCI and ADC exhibited declines in abilities associated with frontal,

temporal, and parietal lobe activity (Fig. 3).

Several studies have identified risk factors for cognitive impairment in dementia-free local communities. These include no/less social or mental activity, older age, low education, being African American, apolipoprotein E ε4 allele, medicated hypertension, midlife elevated serum cholesterol, high diastolic blood pressure, cortical atrophy, brain infarcts, and white matter hyperintensities.[3-7] Insulin resistance, hyperinsulinemia, and HbA1c level are also associated with cognitive dysfunction and depression,[18-23] perhaps because insulin resistance and hyperinsulinemia can promote pathological degeneration related to AD.[24] In the present study, we found significant differences among the three groups in age, education, systolic blood pressure, HbA1c level, and HDL level (Table 1), and these factors are suspected to be risks for dementia. Similar to a previous report (baseline agitation and nighttime behaviors),[25] our present study showed a higher "day-night reversal" score in the ACD group (Fig. 2E).

Other studies have reported that depression and apathy are associated with cognitive dysfunction and are additional risk factors for dementia, [3, 4, 26-29] and exercise habits and hobbies might be important factors for deceleration of cognitive decline.[30] GDS scores for those with MCI and ABS scores for those with ACD were significantly worse than corresponding scores in the normal group (Fig. 1B). Declines in these affective measures were more frequent in the MCI and ACD groups than in the normal group (Fig. 1C-E). Moreover, both of the cognitive and affective scores were all better in people who exercised regularly or who had hobbies than in those who did not, especially in having

hobbies subjects, although we did not check the kinds and amount of time hobbies in this study (Fig. 4).

There are limitations to our study; small sample size and selection bias especially female preponderance of this study population. And there could be many participants who were high interest in their health and cognitive functions. Thus, a lager and comprehensive sample is required.

In summary, the present study examined cognitive and affective functions in the population who had received a health check for metabolic syndrome. In fact, our subjects could be highly conscious about their health and cognitive functions, and we evaluated the cognitive and affective functions based on restricted tests. Regardless of such limitations to this study, scores on the MMSE showed that 6.9% of the participants had ACD, and even for those with MMSE scores within the normal range, 13.5% of the participants had suspected MCI based on their CDR scores. Characteristic of MCI include cognitive declines in recent memory, working memory, executive function, attention, and constructive apraxia, as well as being more depressive and having day-night reversal, lower exercise habits and fewer hobbies. Our result could be subservient to the early detection of MCI or dementia.

Acknowledgements

This work was partly supported by a Grant-in-Aid for Scientific Research (B) 2529320216, (C) 24591263 and Challenging Research 24659651, and by Grants-in-Aid from the Research Committees

(Mizusawa H, Nakashima K, Nishizawa M, Sasaki H, and Aoki M) from the Ministry of Health, Labour and Welfare of Japan.

Disclosure statement

The authors declare no conflicts of interest.

References

1. World Health Organization and Alzheimer's Disease International. Dementia: A Public Health Priority. Geneva: *World Health Organization*; 2012; 92-93. http://www.who.int/mental_health/publications/dementia_report_2012/en/

2. Vanhanen M, Koivisto K, Moilanen L, et al. Association of metabolic syndrome with Alzheimer disease: a population-based study. Neurology. 2006; 67: 843-847.

3. Lopez OL, Jagust WJ, Dulberg C, et al. Risk factors for mild cognitive impairment in the Cardiovascular Health Study Cognition Study: part 2. Arch Neurol. 2003; 60: 1394-1399.

4. Monastero R, Palmer K, Qiu C, Winblad B, Fratiglioni L. Heterogeneity in risk factors for cognitive impairment, no dementia: population-based longitudinal study from the Kungsholmen Project. Am J Geriatr Psychiatry. 2007; 15: 60-69.

5. DeCarli C, Miller BL, Swan GE, Reed T, Wolf PA, Carmelli D. Cerebrovascular and brain morphologic correlates of mild cognitive impairment in the National Heart, Lung, and Blood Institute Twin Study. Arch Neurol. 2001; 58: 643-647.

6. Kivipelto M, Helkala EL, Hänninen T, et al. Midlife vascular risk factors and late-life mild

cognitive impairment: A population-based study. Neurology. 2001; 56: 1683-1689.

7. Tervo S, Kivipelto M, Hänninen T, et al. Incidence and risk factors for mild cognitive impairment: a population-based three-year follow-up study of cognitively healthy elderly subjects. Dement Geriatr Cogn Disord. 2004; 17: 196-203.

8. Tokuchi R, Hishikawa N, Kurata T, et al. Clinical and demographic predictors of mild cognitive impairment for converting to Alzheimer's disease and reverting to normal cognition. J Neurol Sci. 2014; 346: 288-292.

9. Morris JC. The Clinical Dementia Rating (CDR): current version and scoring rules. Neurology. 1993; 43: 2412-2414.

10. Iwatsubo T. Japanese Alzheimer's Disease Neuroimaging Initiative: present status and future. Alzheimers Dement. 2010; 6: 297-299.

11. Mueller SG, Weiner MW, Thal LJ, et al. Ways toward an early diagnosis in Alzheimer's disease: the Alzheimer's Disease Neuroimaging Initiative (ADNI). Alzheimers Dement. 2005; 1: 55-66.

12. Deguchi K, Kono S, Deguchi S, et al. A novel useful tool of computerized touch panel-type screening test for evaluating cognitive function of chronic ischemic stroke patients. J Stroke Cerebrovasc Dis. 2013; 22: 197-206.

13. Fukui Y, Yamashita T, Hishikawa N, et al. Computerized Touch-panel Screening Tests for Detecting Mild Cognitive Impairment and Alzheimer's Disease. Intern Med. 2015; 54: 895-902.

14. Kawahara Y, Ikeda Y, Deguchi K, et al. Simultaneous assessment of cognitive and affective functions in multiple system atrophy and cortical cerebellar atrophy in relation to computerized touch-panel screening tests. J Neurol Sci. 2015; 351: 24-30.

15. Abe K, Yamashita T, Hishikawa N, et al. A new simple score (ABS) for assessing behavioral and psychological symptoms of dementia. J Neurol Sci. 2015; 350: 14-17.

16. Alegret M, Cuberas-Borrós G, Espinosa A, et al. Cognitive, genetic, and brain perfusion factors associated with four year incidence of Alzheimer's disease from mild cognitive impairment. J Alzheimers Dis. 2014; 41: 739-748.

17. Hirao K, Ohnishi T, Hirata Y, et al. The prediction of rapid conversion to Alzheimer's disease in mild cognitive impairment using regional cerebral blood flow SPECT. Neuroimage. 2005; 28: 1014-1021.

18. Austin AW, Gordon JL, Lavoie KL, Arsenault A, Dasgupta K, Bacon SL. Differential association of insulin resistance with cognitive and somatic symptoms of depression. Diabet Med. 2014; 31: 994-1000.

19. Gao L, Matthews FE, Sargeant LA, Brayne C, MRC CFAS. An investigation of the population impact of variation in HbA1c levels in older people in England and Wales: from a population based multi-centre longitudinal study. BMC Public Health. 2008; 11: 54.

20. Hishikawa N, Yamashita T, Deguchi K, et al. Cognitive and affective functions in diabetic patients associated with diabetes-related factors, white matter abnormality and aging. Eur J Neurol. 2015; 22: 313-321.

21. Peila R, Rodriguez BL, White LR, Launer LJ. Fasting insulin and incident dementia in an elderly population of Japanese-American men. Neurology. 2004; 63: 228-233.

22. Willette AA, Xu G, Johnson SC, et al. Insulin resistance, brain atrophy, and cognitive performance in late middle-aged adults. Diabetes Care. 2013; 36: 443-449

23. Yaffe K, Falvey C, Hamilton N, et al. Diabetes, glucose control, and 9-year cognitive decline

among older adults without dementia. Arch Neurol. 2012; 69: 1170-1175.

24. Biessels GJ, Staekenborg S, Brunner E, Brayne C, Scheltens P. Risk of dementia in diabetes mellitus: a systematic review. Lancet Neurol. 2006; 5:64-74.

25. Peters ME, Rosenberg PB, Steinberg M, et al. Neuropsychiatric symptoms as risk factors for progression from CIND to dementia: the Cache County Study. Am J Geriatr Psychiatry. 2013; 21: 1116-1124.

26. Ikeda M, Fukuhara R, Shigenobu K, et al. Dementia associated mental and behavioural disturbances in elderly people in the community: findings from the first Nakayama study. J Neurol Neurosurg Psychiatry. 2004; 75: 146-148.

27. Köhler S, Buntinx F, Palmer K, van den Akker M. Depression, vascular factors, and risk of dementia in primary care: a retrospective cohort study. J Am Geriatr Soc. 2015; 63: 692-698.

28. Lyketsos CG, Lopez O, Jones B, Fitzpatrick AL, Breitner J, DeKosky S. Prevalence of neuropsychiatric symptoms in dementia and mild cognitive impairment: results from the cardiovascular health study. JAMA. 2002; 288: 1475-1483.

29. Palmer K, Berger AK, Monastero R, Winblad B, Bäckman L, Fratiglioni L. Predictors of progression from mild cognitive impairment to Alzheimer disease. Neurology. 2007; 68: 1596-1602.

30. Hughes TF, Chang CC, Vander Bilt J, Gainguli M. Engagement in reading and hobbies and risk of incident dementia: the MoVIES project. Am J Alzheimers Dis Other Demen. 2010; 25:432-438.

Figure legends

Figure 1. Comparison of cognitive and affective scores among the three groups: normal (white bars), MCI (dotted bars), and ACD (gray bars) (A, B). Note the significant differences among the three groups (*$p < 0.05$). Affective scores are shown as percentages of normal and disease conditions for the three groups: GDS (C), AS (D), and ABS (E). The columns show mean value.

Figure 2. Comparison of subscale analysis of cognitive tests (A-D) among 3 subgroups: normal (white bars), MCI (dotted bars), and ACD (gray bars). The results are expressed as percentages of full scores. The columns show mean value. Note significant differences among 3 subgroups (*p <0.05, **p <0.01). Subscale analysis of ABS scores among the three groups (E). Note, “day-night reversal” in the ACD group is significantly worse that in the normal group (*$p < 0.05$). The columns show mean value and bars mean one standard deviation.

Figure 3. Touch panel test performance for the three groups: normal (white bars), MCI (dotted bars), and ACD (gray bars). The columns show mean value. Note the significant differences between the normal group and the MCI or ACD groups (*$p < 0.05$).

Figure 4. Cognitive (A, C) and affective (B, D) scores for those with and without habits or hobbies. The columns show mean value. Note significant differences in HDS-R and GDS scores between people with hobbies and without ones (*$p < 0.05$) (C, D).

Figure 1

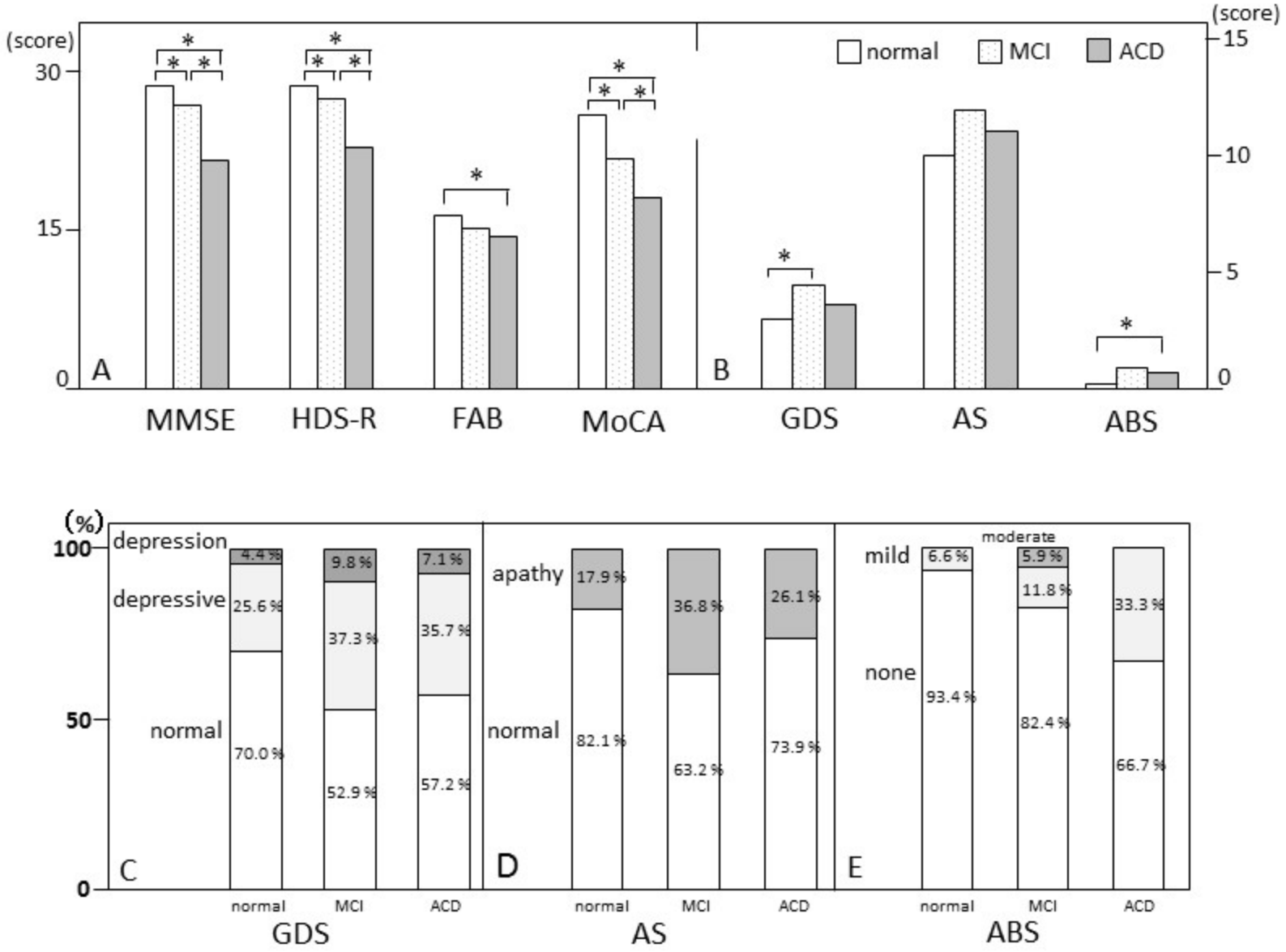
(score)
30
15
0
A
MMSE
HDS-R
FAB
MoCA
normal
MCI
ACD
(score)
15
10
5
0
B
GDS
AS
ABS
(%)
100
50
0
depression
depressive
normal
4.4 %
25.6 %
70.0 %
9.8 %
37.3 %
52.9 %
7.1 %
35.7 %
57.2 %
C
normal
MCI
ACD
GDS
apathy
normal
17.9 %
82.1 %
36.8 %
63.2 %
26.1 %
73.9 %
D
normal
MCI
ACD
AS
mild
moderate
none
6.6 %
93.4 %
5.9 %
11.8 %
82.4 %
33.3 %
66.7 %
E
normal
MCI
ACD
ABS

Figure 2

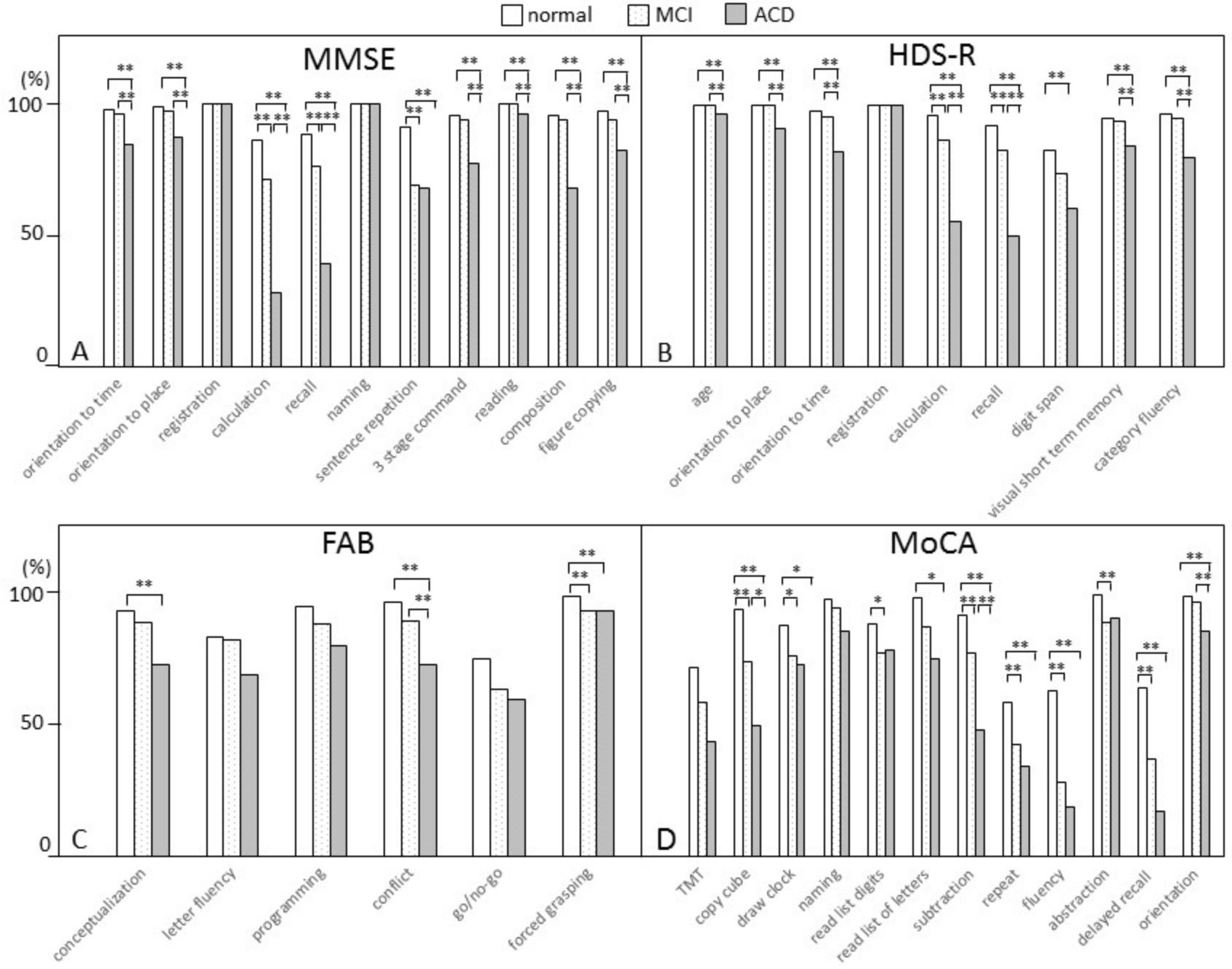
normal
MCI
ACD
MMSE
HDS-R
(%)
100
50
0
A
B
orientation to time
orientation to place
registration
calculation
recall
naming
sentence repetition
3 stage command
reading
composition
figure copying
age
orientation to place
orientation to time
registration
calculation
recall
digit span
visual short term memory
category fluency
FAB
MoCA
C
D
conceptualization
letter fluency
programming
conflict
go/no-go
forced grasping
TMT
copy cube
draw clock
naming
read list digits
read list of letters
subtraction
repeat
fluency
abstraction
delayed recall
orientation

Figure 2

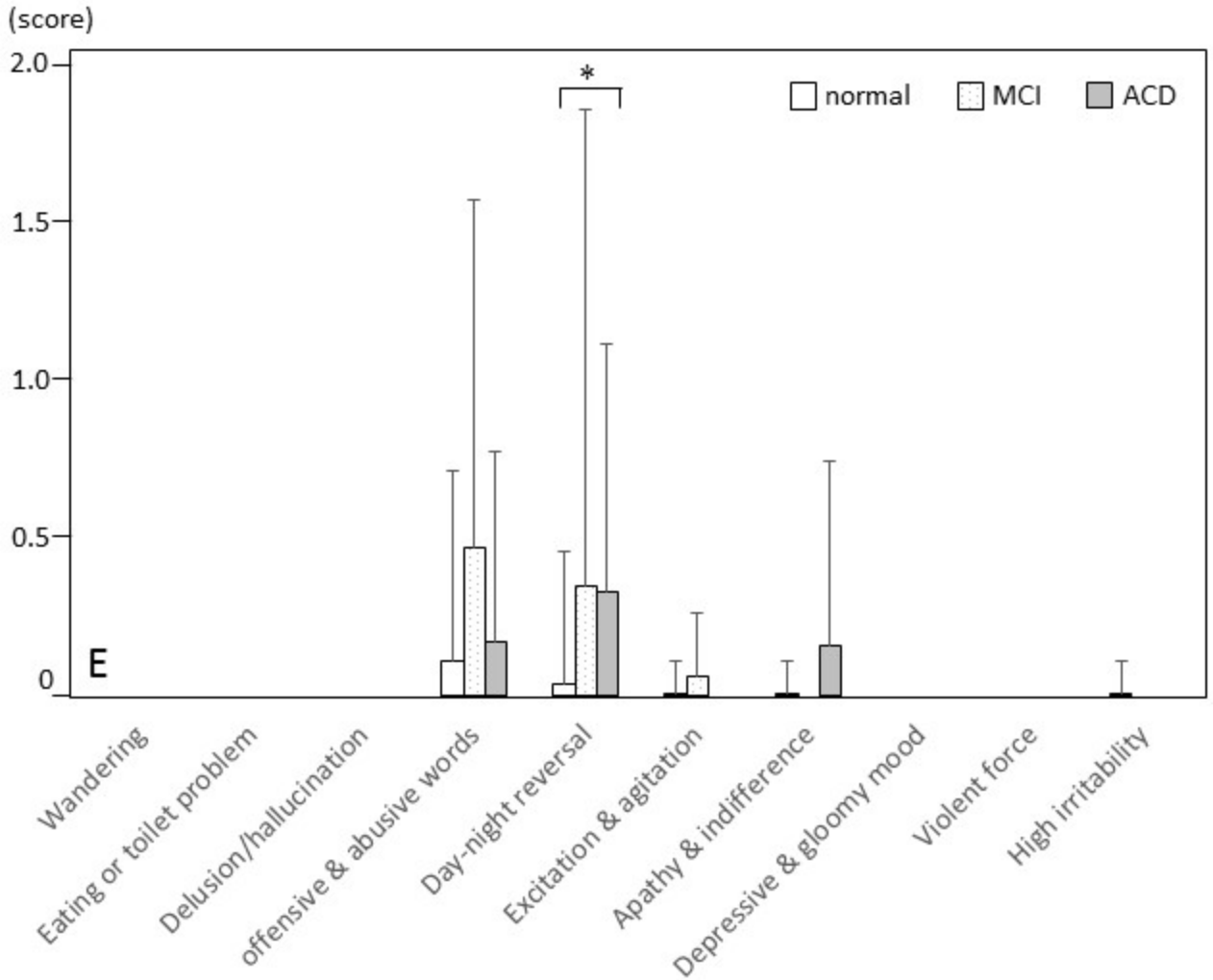
(score)
2.0
1.5
1.0
0.5
0
*
normal
MCI
ACD
E
Wandering
Eating or toilet problem
Delusion/hallucination
offensive & abusive words
Day-night reversal
Excitation & agitation
Apathy & indifference
Depressive & gloomy mood
Violent force
High irritability

Figure 3

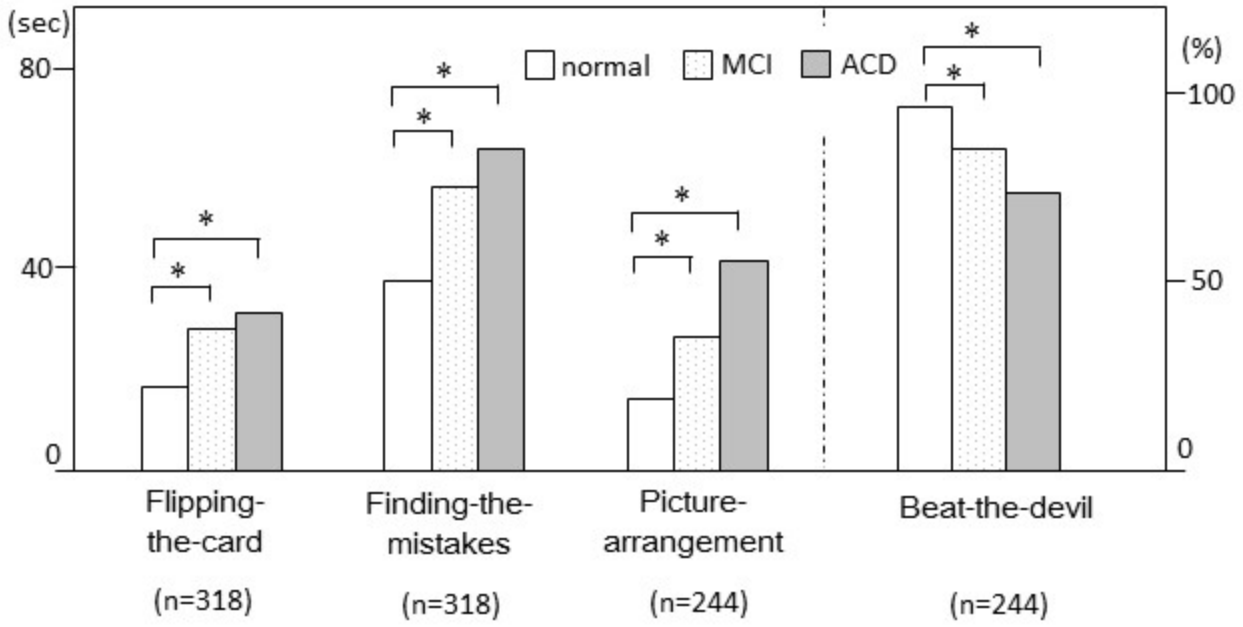
(sec)
80
40
0
normal
MCI
ACD
(%)
100
50
0
*
Flipping-the-card
(n=318)
Finding-the-mistakes
(n=318)
Picture-arrangement
(n=244)
Beat-the-devil
(n=244)

Figure 4

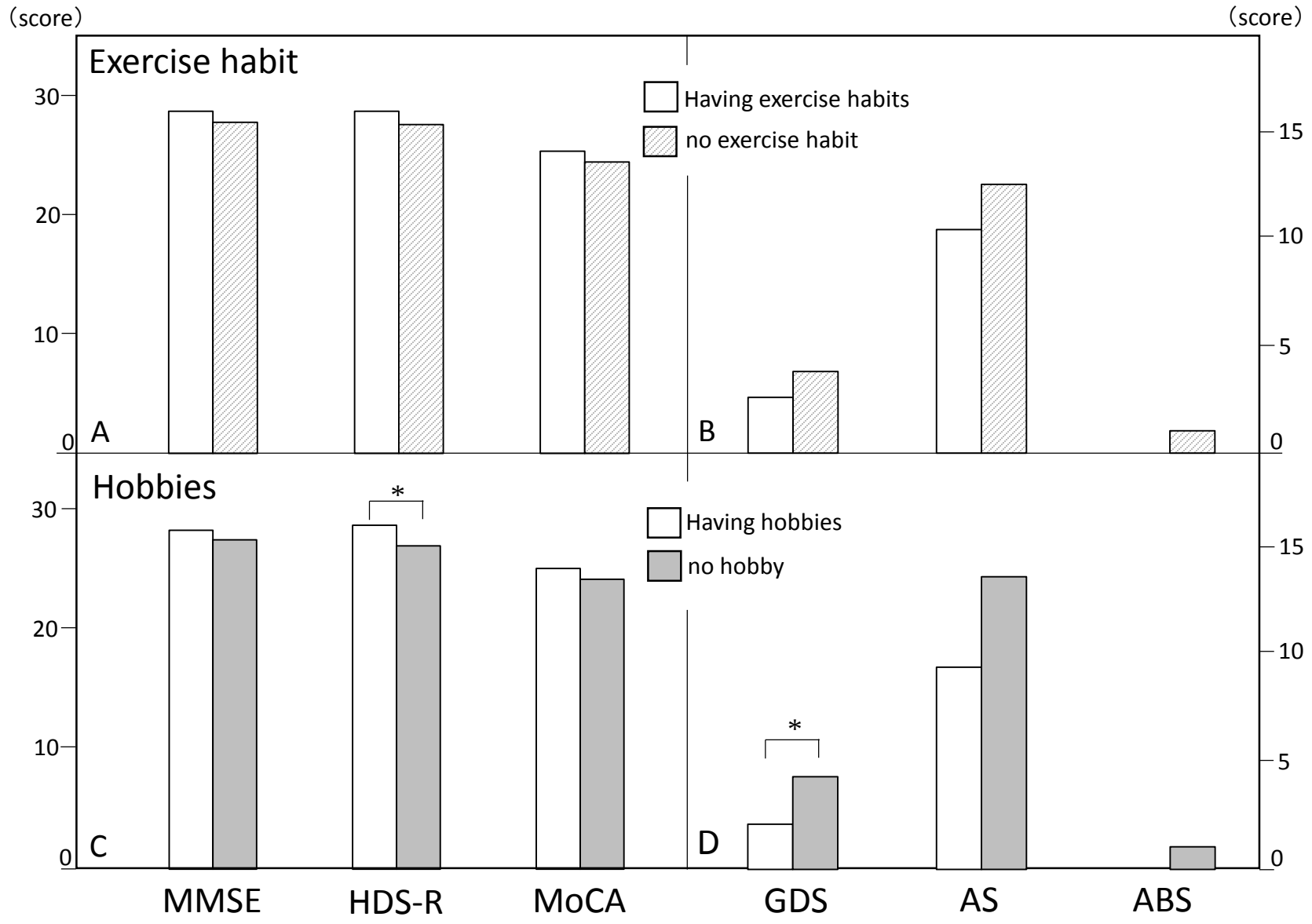
(score)
(score)
Exercise habit
Having exercise habits
no exercise habit
30
20
10
0
15
10
5
0
A
B
Hobbies
Having hobbies
no hobby
*
*
C
D
MMSE
HDS-R
MoCA
GDS
AS
ABS

Table 1. The demographic and characteristic data of the 408 subjects divided into 3 subgroups (normal, MCI, and ACD).

	normal	mild cognitive impairment (MCI)	apparent cognitive decline (ACD)
	24≦MMSE (n=380)		MMSE≦23 (n=28)
	CDR=0 (n=325)	CDR=0.5 (n=55)	
age (years old)	64.7±12.7	69.9±10.4**	76.5±7.5**
M:F	124:201	20:35	14:14
education (years)	12.5±2.3	11.4±1.6*	10.1±1.8**
smoking (%)	17.9	31.6	16.6
waist circumference (cm)			
male	86.3±7.8	85.6±9.1	81.9±6.3
female	83.3±9.2	81.0±9.7	84.2±8.7
body mass index (BMI)	23.1±3.3	23.0±3.4	22.3±3.6
BMI<18.5 (%)	7.1	10.7	21.1
25.0≤BMI (%)	27.2	25.0	26.3
systolic blood pressure (mmHg)	130.9±19.2	130.2±19.7	142.8±18.5**, #
diastolic blood pressure (mmHg)	76.4±10.3	71.9±11.1	75.8±16.7
HbA1c	5.7±0.7	5.9±0.6**	6.1±0.9*
LDL (mg/dl)	133.2±34.4	129.2±30.2	125.9±33.4
HDL (mg/dl)	62.1±15.8	56.4±13.3#	54.8±14.0
TG (mg/dl)	122.9±62.0	113.3±63.2	118.4±60.7

p <0.05 vs Group A, ***p* <0.01 vs Group A, #*p* <0.05 vs Group B, ##*p* <0.01 vs Group B