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ORIGINAL ARTICLE

Predictors of probable attention deficit hyperactivity disorder in elderly patients with mild cognitive impairment visiting a memory clinic

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Abstract

Aim: Characteristics of attention deficit hyperactivity disorder (ADHD) that persist into old age are often confused with symptoms of mild cognitive impairment (MCI), and the actual rate of probable ADHD in people with MCI is unknown. This study estimated the proportion of MCI patients with probable ADHD and investigated the factors to identify MCI patients with probable ADHD.

Methods: We recruited 36 elderly patients (11 males, 25 females, mean age 72.4 ± 7.6 years) who met the MCI criteria. The MCI patients were classified as those with [MCI/ADHD (+)] and without [MCI/ADHD (−)] probable ADHD, according to the Wender Utah Rating Scale scores. The autism features, inattention, and hyperactivity features during childhood and current periods, estimated intelligence quotient, and demographic data were compared between the groups. Multiple logistic regression analysis was performed to identify factors of MCI/ADHD (+) patients.

Results: Nine (25.0%) and 27 patients were added into the MCI/ADHD (+) and MCI/ADHD (−) groups, respectively. The MCI/ADHD (+) group mostly comprised men, those who visited the clinic at a younger age, had more years of schooling, and had strong autism spectrum disorder tendencies. Multiple logistic regression analysis indicated male sex and current hyperactivity as significant predictors of probable ADHD in MCI patients.

Conclusion: A quarter of the patients with MCI had probable ADHD. Male sex and hyperactivity at the time of MCI diagnosis might help in predicting probable ADHD in MCI patients. However, these results were obtained from a single-center, small-case study and should be confirmed via longitudinal studies with a large number of cases.

KEYWORDS

attention deficit hyperactivity disorder, memory clinic, mild cognitive impairment, predictor

INTRODUCTION

Mild cognitive impairment (MCI) is a condition in which memory is impaired but daily activities are unaffected. Petersen et al.[1] proposed MCI and initially positioned it as a precursor to Alzheimer's disease (AD). Conversely, MCI was later thought to include various causes other than AD.[2,3] Because MCI conditions vary, it is important to identify the causes of MCI and distinguish between MCI in the early stages of AD and other MCIs.

Attention deficit hyperactivity disorder (ADHD) is an innate disorder characterized by inattention, hyperactivity, and impulsivity, whose signs and symptoms typically begin in early childhood.[4] However, impaired working memory in people with ADHD is known to persist even into old age.[5] ADHD features that persist into old age are often mistaken for MCI, with patients misdiagnosed with a neurodegenerative disease.[6] Recent studies have pointed out that patients with undiagnosed features of ADHD into adulthood may be classified among patients with MCI.[7] However, no previous studies have examined the actual rate of probable ADHD in people with MCI.

A recent study compared neuropsychological test results between adults with ADHD and MCI, and healthy adults.[8] The authors found no significant differences between people with MCI and those with ADHD, and concluded that neuropsychological tests could not differentiate between these disorders. Consequently, these findings suggest that it would be difficult to distinguish between patients with old-age ADHD and those with predementia among people with MCI. Furthermore, diagnosing adult ADHD requires collecting information regarding individual ADHD features in childhood, yet many adults would not have another person to rely on for gathering information about themselves in early childhood. In such situations, age is a useful criterion for diagnosing this condition. For example, one of the diagnostic criteria of ADHD, according to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5), is onset by 12 years,[4] which can be problematic for diagnosis in the abovementioned cases. This criterion makes it difficult to decide due to problems such as age in the exclusion criteria. In addition, at the time of MCI diagnosis, it would be clinically useful to estimate the number of persons with MCI who had ADHD symptoms as children; however, such a study has not been conducted. The prevalence of ADHD in MCI is still under investigation. There are methodological limitations in estimating ADHD in persons with MCI because ADHD symptoms (DSM-5)[4] overlap with MCI, and there are reports that neuropsychological tests have failed to differentiate between adult ADHD and MCI.

An assessment that can easily infer the presence or absence of probable ADHD in the elderly would therefore be helpful in the differential diagnosis of MCI caused by a wide variety of background diseases, as well as for implementing the appropriate subsequent treatment approach and clinical response.

In this study, we used the Wender Utah Rating Scale (WURS)[9,10] to determine the proportion of patients with probable ADHD among older adults with MCI who visited an outpatient memory clinic and met the criteria for MCI. We then examined the proportion of patients with probable ADHD among adults with MCI. In addition, we attempted to identify factors that could be used to infer individuals with probable ADHD in childhood at the time of MCI diagnosis.

METHODS

Participants

The participants for this study were recruited from 222 consecutive patients who visited the memory clinic in the department of neuropsychiatry at Kochi University Medical Hospital for memory complaints and whose age was ≥50 years from June 2015 to October 2017. The inclusion criteria of the participants of this study were as follows:[1] patients who had a normal general cognitive function: Mini-Mental State Examination (MMSE) ≥24;[2,11] patients who had normal capacities for the activities of daily living, including domestic chores and work; and[3] patients diagnosed as not having dementia, and who met the criteria for MCI with a Clinical Dementia Rating of 0.5.[12] Patients were excluded if the disease causing the MCI was identified as traumatic brain injury and normal pressure hydrocephalus or if they were currently under psychiatric therapy for complaints other than memory disturbances, such as psychiatric or neurological symptoms, including delirium, schizophrenia, depression, anxiety disorder, and autism spectrum disorder[4] (Figure 1).

Assessment

The following scales were used to evaluate the patients' neuropsychiatric state.

1) Childhood ADHD features

We used the Japanese version[13] of the WURS[9,10] to retrospectively detect childhood ADHD cases without using parental/guardian information. Originally, WURS had 61 items that focused on various behavioral problems, but it now has 25 items that show significant differences between people with and without childhood ADHD. The questions are answered on a five-level scale, varying from “very rare” (0 points), “mildly” (1 point), “moderately” (2 points), “quite a bit” (3 points), to “very much” (4 points), and it has a maximum score of 100 points. Concerning the WURS cutoff value, 30-point,[14] 36-point, and 46-point scores[9] have been studied. Since our participants were of advanced age, it was presumed that individuals with ADHD might underestimate their difficulties. Consequently, we used a cutoff of 30 points, which was similar to the cutoff value used in a study based on the prevalence of ADHD among adult psychiatric outpatients in Sweden to detect borderline cases[14] and classify MCI patients with probable ADHD (MCI/ADHD [+]). In contrast, patients scoring less than 30 points were classified as MCI patients without probable ADHD (MCI/ADHD [−]).[14]

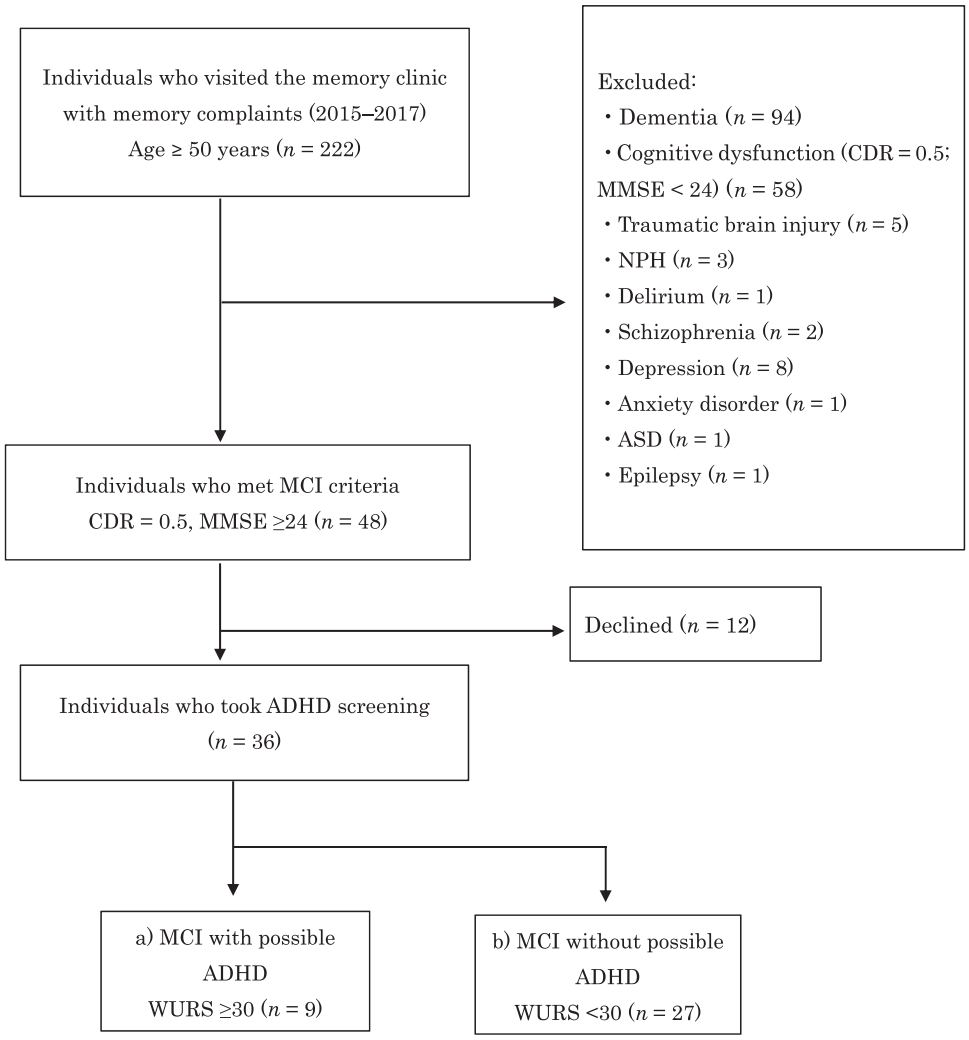

FIGURE 1 Flow chart of participants. ADHD, attention deficit hyperactivity disorder; CDR, Clinical Dementia Rating; MCI, mild cognitive impairment; NPH, normal pressure hydrocephalus; MMSE, Mini-Mental State Examination; WURS, Wender Utah Rating Scale.

2) Inattention and impulsivity in childhood (12 years) and adulthood (current)

The ADHD Rating Scale-IV (ADHD RS-IV)[15–17] is a questionnaire based on the DSM-IV diagnostic criteria assessing inattention, hyperactivity, and impulsivity, the prominent ADHD features. This questionnaire can be used to screen, diagnose, and treat ADHD. The ADHD RS-IV in this study was used to evaluate inattention and impulsivity during childhood (under 12 years) and adulthood (current). Although the ADHD RS-IV was originally intended for ages 5–18 years, behavioral characteristics described in the DSM-5,[4] which are also found in adults, were added to the ADHD RS-IV in this study to allow assessment at ages 50 and older (e.g., Question 1. Fails to give close attention to details or makes careless mistakes in schoolwork.⇒ Fails to give close attention to details or makes careless mistakes in schoolwork, *at work, or with other activities*; Question 6. Runs about or climbs excessively in situations in which it is inappropriate.⇒ Runs about or climbs in situations where it is not appropriate *[adolescents or adults may be limited to feeling restless]*). In addition, the ADHD RS-IV scale is usually evaluated by a parent/teacher, but in this study the participants were over 50 years old, the parents were deceased and absent, there were no teachers, and the participants themselves evaluated the scale because MCI does not impair remote memory or cognitive functions.

3) Autism spectrum disorder features

The Japanese version[18] of the Autism Spectrum Quotient (AQ) was used to detect autism spectrum disorder (ASD) features of participants. AQ is a widely used questionnaire designed to assess ASD features in adults via subjective self-assessments. It comprises 50 items that are answered on a four-level scale, and a score of 32 or more indicates clinically significant levels of autistic traits.[19]

4) Estimated intelligence quotient (IQ)

The Wechsler Adult Intelligence Scale, 3rd edition (WAIS-III) Short Form (2nd item) Matrix Reasoning/Knowledge was used to estimate the IQ of patients. Although there are many ways to perform the WAIS-III Short Form test, we administered it as recommended by the WAIS-III Japanese Version Publication Committee.[20]

Statistical analysis

First, the demographic data and scale scores between the MCI/ADHD (+) and MCI/ADHD (−) groups were compared using the *t*-test, Mann–Whitney *U* test, or Fisher's exact test. Second, multiple logistic regression analysis (stepwise method) was performed to predict patients with probable ADHD in childhood at the time of MCI. The response variable was whether the patients were classified into the MCI/ADHD (+) group or MCI/ADHD (−) group. The explanatory variables were age, sex, each of the four ADHD RS-IV scores (childhood inattention, childhood hyperactivity, current inattention, and current hyperactivity), AQ, and estimated IQ. Statistical analyses were performed using the Statistical Package for the Social Sciences Program (SPSS version 27). The statistical significance level was set at 5%.

RESULTS

Demographic data and MMSE, AQ, ADHD RS-IV, and estimated IQ

Demographic data and the results of MMSE, AQ, ADHD RS-IV, and the estimated IQ of participants are shown in Table 1. Nine (25.0%) and 27 (75.0%) patients with MCI were classified into MCI/ADHD (+) and MCI/ADHD (−), respectively.

Compared to the MCI/ADHD (−) group, the MCI/ADHD (+) group had more males, were younger at consultation, and had more years of education, higher AQ total scores, and higher ADHD RS-IV inattention and hyperactivity scores both in childhood and current (Table 1). We could not find a significant difference between the groups in MMSE and estimated IQ.

Predictors of ADHD features

Multiple logistic regression analysis in MCI patients with WURS scores of <30 or ≥30 points as the dependent variable showed that male sex and the ADHD RS-IV current hyperactivity score were significant predictive factors (Table 2).

DISCUSSION

We found that 25% of the 36 MCI patients who visited the outpatient memory clinic of our university hospital had probable ADHD as determined by WURS. Participants with probable ADHD were males, younger at the time of consultation, had more years of education, and had a higher ASD tendency measured with AQ than those without probable ADHD. In addition, the multiple logistic regression analysis showed that being male and the ADHD RS-IV current hyperactivity score would be useful for predicting probable ADHD in MCI patients.

To the best of our knowledge, this study is the first to demonstrate the proportion of probable ADHD and related variables in patients with MCI. The proportion of patients with MCI with probable ADHD (25%) was higher in this study than in the previous epidemiological studies.

In this study, we considered the cutoff value of the WURS to be 30 points because this study included elderly patients, and this cutoff value ensured that ADHD characteristics were not missed or underestimated. Nylander et al.,[14] who used the same cutoff value of 30, reported that more than 50% of patients who were diagnosed with ADHD using DSM-IV belonged in the low-score group having 30–45 points, and the possibility of contamination due to false

TABLE 1 Comparison of evaluations between MCI/ADHD (+) and MCI/ADHD (−) groups.

	Total (*n* = 36)	MCI/ADHD (+) (*n* = 9)	MCI/ADHD (−) (*n* = 27)	Group comparison (P-value)
Sex (male/female)	11/25	6/3	5/22	0.012*
Age at consultation	72.4 ± 7.6	65.9 ± 9.9	74.5 ± 5.3	0.033
Education (years)	12.3 ± 2.6	14.4 ± 2.6	11.7 ± 2.2	0.008
MMSE	26.9 ± 2.0	27.2 ± 2.2	26.8 ± 1.9	0.568
AQ total	18.9 ± 5.7	21.7 ± 3.6	18.0 ± 6.1	0.038
ADHD RS-IV childhood inattention	3.9 ± 3.7	7.4 ± 3.9	2.7 ± 3.9	0.001
ADHD RS-IV childhood hyperactivity	2.1 ± 3.2	5.0 ± 4.6	1.1 ± 1.7	0.037
ADHD RS-IV current inattention	3.1 ± 4.0	7.9 ± 5.9	2.7 ± 3.0	0.002
ADHD RS-IV current hyperactivity	2.6 ± 3.5	4.2 ± 3.2	1.0 ± 1.3	0.016
Estimated IQ	89.3 ± 19.3	85.0 ± 20.7	90.7 ± 19.0	0.447
Total WURS score	19.8 ± 15.5	41.2 ± 10.0	12.5 ± 8.0	0.000

Abbreviations: ADHD, attention deficit hyperactivity disorder; ADHD RS-IV, ADHD Rating Scale-IV; AQ, Autism Spectrum Quotient Test; IQ, intelligence quotient; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; WURS, Wender Utah Rating Scale.

*Fisher exact test others; *t*-test

TABLE 2 Multiple logistic regression analysis (stepwise) results.

	Odds ratio	95% CI	P-value
Sex	22.3	1.5–325.5	0.023
ADHD RS-IV current hyperactivity	2.8	1.2–6.9	0.023

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; ADHD RS-IV, ADHD Rating Scale-IV; CI, confidence interval.

positives was considered low. In addition, as shown in Table 1, statistically significant differences were found in many items between the two groups that were categorized using the cutoff value of 30 points, suggesting that the cutoff value of 30 points was appropriate for this study.

ADHD is commonly thought to be a childhood disorder, but it is now recognized that symptoms can persist into adulthood and old age. This condition, in particular, persists in 40%–60% of pediatric cases[21,22] and affects approximately 2%–4%[17,21,23,24] and 3%–4% of older adults.[25,26] Guldberg-Kjär and Johansson[27] used a self-administered scale to conduct epidemiological studies on older adults with ADHD in Sweden and found that approximately 3% of individuals aged ≥65 years had ADHD, indicating that the disorder is not limited to younger individuals. Furthermore, Deberdt et al.[28] reported that 17.4% of adult patients seeking care in general psychiatric institutions have ADHD, implying that psychiatric outpatient clinics may have more adults with ADHD than the community. The signs and symptoms of MCI and ADHD are very similar, which could explain the high proportion of probable ADHD in patients with MCI in our sample. For example, the diagnostic criteria of ADHD, such as "Prone to forgetting items necessary for tasks and activities," "Prone to forgetting daily activities," or "Fails to complete tasks such as homework," could be interpreted as forgetfulness in daily life and memory impairments in people with MCI.

In our sample, male sex was a strong predictor of probable ADHD, with six out of 11 male patients classified as MCI/ADHD (+), while only three out of 25 female patients were classified in the same category. Because males make up a larger portion of the general population with ADHD,[4] the higher proportion of males in the MCI/ADHD (+) group in this study could simply reflect gender differences in ADHD prevalence. However, current research findings on gender differences in the prevalence and influencing factors of MCI remain inconsistent. Although some studies found no gender difference in the prevalence of MCI,[29–31] other studies found that the prevalence of MCI was higher in females than in males.[32,33] Furthermore, the rate of progression to AD in patients with MCI is higher in females than in males,[34,35] and females with MCI may be more likely to have pre-dementia. Our participants revealed that approximately half of the male MCI patients were classified as having probable ADHD, thus the male sex indicates probable ADHD among the MCI group.

Current hyperactivity was another strong predictor of probable ADHD. There are several possible explanations for this result. First, noticeable hyperactivity in early childhood generally tends to decrease with growth in people with ADHD,[36–38] and those who have residual hyperactivity in adulthood might have stronger ADHD features. Therefore, current hyperactivity may have more power in diagnosing ADHD than hyperactivity in childhood. Second, there are people with hyperactive tendencies in early childhood, even in the absence of ADHD,[39] which may undermine the strength of the predictive power. Third, ADHD inattention in late adolescence and adulthood tends to persist throughout life,[40] and it may persist further into old age to the extent that it can be diagnosed as ADHD. Since inattention is a possible feature of AD, the power of current inattention in differentiating between ADHD and AD may be weak. Fourth, the accuracy with which individuals recall memories of their early childhood is unclear. Consequently, current hyperactivity in male patients can be obtained reliably, leading to clinical effectiveness for differentiating elderly patients with ADHD features from people with MCI.

Compared to the MCI/ADHD (−) group, patients in the MCI/ADHD (+) group were younger at consultation in this study. As for the age at which individuals tend to seek medical consultation, people with pre-dementia, who accounted for most of the MCI/ADHD (−), are more likely to visit a healthcare facility at or slightly before the common age of dementia onset.[41] Meanwhile, adult ADHD may be linked to deteriorating brain function with age, and this decline may reach disorder levels in presenium,[40,42,43] thereby forcing these individuals to seek medical attention at a slightly earlier age.

Higher ASD traits in the MCI/ADHD (+) group compared with the MCI/ADHD (−) group in this study could be explained by the high ADHD and ASD comorbidity rates. In fact, 20%–50% of children with ADHD also meet the ASD criteria.[44] Adults are also affected by this comorbidity.[45] Another explanation could be that individuals in the early stages of frontotemporal dementia (FTD) were included in the MCI/ADHD (+) group. FTD has symptoms similar to ADHD and ASD.[46–48] To illustrate, the two primary characteristics of FTD, namely, social interaction loss and impaired self-control, overlap with those of ASD. Furthermore, FTD symptoms, such as inattentiveness and distractibility, loss of planning ability, and disorganization,[49] are shared with those of ADHD.

This study has several limitations. First, the sample size was small. A multicenter or epidemiological study should be conducted to determine more precisely the rate of ADHD in MCI patients. Second, this study did not make a definitive ADHD diagnosis; rather, it assessed probable ADHD in patients with MCI. Future clinical studies involving multidisciplinary experts, such as pediatric and geriatric psychiatrists, and using standardized interviews and biomarkers are warranted. Third, this was a cross-sectional study. Neither of the groups was followed up to examine patients' long-term clinical course and compare cases that remained ADHD and MCI patients who progressed into dementia. Fourth, the reliability of the WURS in patients with MCI has not been confirmed in this study, therefore further studies are warranted to determine ADHD tendencies in patients with MCI using WURS.

Despite these limitations, this study revealed that a high proportion of people with MCI who had visited a memory clinic

exhibited probable ADHD, and male sex and hyperactivity at the time of diagnosis were effective factors for differentiating between people with early-stage dementia and those who meet the MCI diagnostic criteria and have probable ADHD. These clinically useful findings should be tested in more detail in a future longitudinal study.

CONCLUSION

A high percentage (25%) of people with MCI had probable ADHD. Among them, it was clear that being male and hyperactive at the time of diagnosis were important factors in differentiating these patients from individuals in the pre-dementia stage.

AUTHOR CONTRIBUTIONS

N.S. and K.N. designed the study. K.N. and S.S. supervised the data collection. N.S., K.H., S.N., T.H., and K.N. assisted in data analysis. N.S. was responsible for the statistical design and analysis and wrote the first manuscript draft. All authors were involved in the interpretation and presentation of the data, reviewed and revised the initial draft and subsequent versions of the manuscript, and approved the submitted version.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The availability of the data in this study is not open access due to the provisions of the ethics committee and the extent of participants' consent. If readers wish to apply for the use of the data, they must contact the corresponding author and consult the Ethics Committee of Kochi Medical School, Kochi University.

ETHICS APPROVAL STATEMENT

This study was approved by the Ethics Review Board of the Kochi Medical School, Kochi University (Approval no.: ERB-107198) and it complies with the Declaration of Helsinki and the Japanese Ethical Guidelines for Medical and Health Research Involving Human Subjects.

PATIENT CONSENT STATEMENT

Written informed consent was obtained from the study participants. Participants in the study were not compensated.

CLINICAL TRIAL REGISTRATION

N/A.

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