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후뇌 위축 육안평가 척도를 통한 알츠하이머병의 진행속도 예측

Association between visual rating of posterior cortical atrophy and the rate of cognitive decline in Alzheimer's disease

2017 년 2 월

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서 지 원

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지도교수 김 상 윤

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위 원 장 오창완 (인)

부위원장 김상윤 (인)

위 원 한문구 (인)

Abstract

Association between visual rating of posterior cortical atrophy and the rate of cognitive decline in Alzheimer's disease

Jee Won Suh
Graduate School of Translational Medicine
College of Medicine
The Graduate School
Seoul National University

Rate of disease progression in Alzheimer’ s disease (AD) is associated with prognosis in terms of mortality and caregiver dependency. Rapid progressive AD patients have different characteristics compared with slow progressive patients. Some researchers have found that brain morphological changes correlate

with rate of AD progression. Recent Voxel-based morphometric (VBM) analysis demonstrated that AD patients with rapid cognitive decline had a more extensive cortical atrophy than slow decliners, especially in the medial occipito-parietal areas. Nonetheless, there is a limit to apply VBM analysis in individual patients. Recently, easily applicable posterior visual rating scale is developed which can evaluate the posterior cortical atrophy. In this study we investigated the relation between visual rating scale of posterior cortical atrophy and the progression rate of disease in early stage of AD patients.

This was a retrospective cohort study from newly diagnosed AD patients who visited Seoul National University Bundang Hospital. 106 AD patients with initial MMSE score 21 to 26 were followed up for 1 year. We measured posterior atrophy scale and one-year follow-up MMSE score to see whether brain atrophy according to posterior atrophy scale is associated with rapid cognitive decline after one year.

Rapid cognitive decline ($\geq$3 score drop in MMSE test) at one year follow-up occurred in 27 subjects (25.5%). In logistic regression analysis, posterior atrophy in brain MRI was associated with rapid

cognitive decline in one-year follow-up (regression coefficient 2.79, 95% CI 1.16 to 6.97, p=0.028). While, medial temporal lobe atrophy or frontal atrophy showed no significant association with rapid cognitive decline.

This study showed that an easily measurable posterior visual rating scale can predict the rate of disease progression in early AD patients.

Keywords: Alzheimer's disease, Rapid cognitive decline, Posterior cortical atrophy, Visual rating score

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Introduction

Among the patients diagnosed with Alzheimer's disease (AD), the rate of disease progression varies between individuals. The prevalence of rapid cognitive decline in AD is approximately 30%.[1-3] Compared with the slowly progressive AD patients, rapidly progressive AD patients have higher rate of mortality and caregiver dependency.[4,5] Prediction of disease progression rate among AD patients can provide important information in planning treatment strategies for the physicians and caregivers.

Previously several researches were done comparing the characteristics between rapidly progressive and slowly progressive AD patients. The disease progression rate is usually rapid among the patients with younger-onset, high education level, poor nutritional status, and prominent behavioral and psychological symptoms.[6-8]

Recent investigation with voxel-based morphometry (VBM) analysis showed that brain morphological changes, especially atrophies of the parietal and occipital lobe are also associated with the rate of AD progression.[9] Nonetheless, there is a limitation in

applying VBM analysis to individual patients because it requires additional data analyzing process. Recently, easily applicable posterior visual rating scale is developed.[10] Visual rating scale has advantage over VBM analysis in that it can be used directly in clinical settings.

In this study, we investigated the association between visual rating scale of the posterior cortical atrophy and the progression rate of disease in early stage of AD patients. The newly diagnosed AD patients were followed for one year and treated with acetylcholinesterase inhibitor. We investigated whether the quantitative parieto-occipital area atrophy measured by visual rating scale can predict the rate of AD progression.

Methods

Subject

This was a retrospective cohort study of patients with newly diagnosed AD. A consecutive series of patients who visited Seoul National University Bungdang Hospital from August 2012 to July 2014 and newly diagnosed as probable Alzheimer's disease by National Institute of Neurological and Communicative Disorders and Stroke – Alzheimer's Disease and Related Disorders Association (NINCDS–ADRDA) criteria[11] were identified from the registry database. The patients have started acetylcholinesterase inhibitor medication and were followed up for a year.

Procedures

Demographic data and clinical information were obtained from the database. Acquired information included onset age, final diagnosis, education year, history of stroke, presence of comorbid diseases (hyperlipidemia, hypertension, diabetes mellitus, ischemic heart disease), clinical dementia rating (CDR), Barthel activity of daily

living (B-ADL) scale, Korean instrumental activity of daily living (K-IADL) scale and the type of acetylcholinesterase inhibitor treated. In case of education year, we dichotomized the patients into less-educated (0-6 year) and more-educated (> 6-year education) groups. For the neurocognitive function, we use MMSE score. We did initial MMSE test at the time of diagnosis. Follow up MMSE scores were measured at 355 to 395 days after the initial test. Rapidly progressive AD patients were defined as the patients with decline of MMSE score more than 3 points over one year.[6]

Patients were included on the basis of the following criteria: (i) initial MMSE score from 16 to 26 point (ii) CDR score of 0.5 or 1 (iii) Brain MRI was performed at the time of diagnosis of AD. Inclusion criteria for initial cognitive function was established as MMSE score from 16 to 26 to exclude severe AD patients. We excluded the patients if they did not have Brain MRI scans of axial, sagittal, and coronal plane because these three views on the MRI scans were needed for visual rating. We also excluded the patients without follow up MMSE score after one year of diagnosis.

MRI acquisition

Brain MRI was performed at the time of diagnosis of AD on either a 1.5-Tesla unit or a 3-Tesla unit. The scanning protocol included T1- and T2-weighted sequences of three dimensional planes of axial, coronal and sagittal planes.

Visual rating scale

Posterior atrophy (PA) was assessed according to a previously described scale using sagittal, axial and coronal plane of MRI images.[10] PA score is based on posterior cingulate sulcus, parieto-occipital sulcus, parietal lobe and precuneus atrophy and consists of 4-point scale. In sagittal orientation, widening of the posterior cingulate and parieto-occipital sulcus and atrophy of the precuneus were evaluated. In axial orientation, widening of the posterior cingulate sulcus and sulcal dilatation in parietal lobes were rated and in coronal orientation, widening of the posterior cingulate sulcus and parietal lobes were rated.

We also measure the atrophy of medial temporal lobe and frontal lobe as control regions to assess the specificity of PA as an imaging

marker. Medial temporal atrophy (MTA) was assessed using a standardized scale developed by Scheltens et al.[12] It rates atrophy based on the height of hippocampal formation, width of the choroidal fissure and the temporal horn at the coronal plane image. It consists of 5-point scale. (0 = absent, 1 = minimal, 2 = mild, 3 = moderate, 4 = severe)

Frontal atrophy (FA) was assessed with the frontal sub-scale of the global cortical atrophy scale (GCA-F) on T1-weighted images.[13,14] GCA-F visual rating scale is evaluated by frontal sulcal dilatation. (0 = absent, 1 = mild, 2 = moderate, 3 = severe) The visual rating of three brain regions are summarized in Table 1.

All MRI images were assessed independently by three neurologists experienced in visual rating blinded to clinical information. Three raters measure the atrophy scales for the left and right hemispheres, respectively. In case of discrepancy between the raters, the final score was determined by discussion among the raters. For the analysis, average atrophy score of the left and right hemisphere were used. MTA, PA and GCA-F scores were dichotomized into normal and atrophy group for further analysis.

Statistical analysis

The baseline characteristics among the rapidly progressive AD patients and the slowly progressive ones were compared using Student t test for continuous variables and Pearson's chi-square test for categorical variables.

To examine the association of the progression rate of AD with posterior atrophy scores, univariate logistic regression analysis was performed. PA of average 1.5 or more score was considered as atrophied.[15] We also analyze the association of disease progression rate of AD with MTA and FA as control regions. MTA of average 2 or more and GCA-F of average 1 or more were considered as atrophied.[16] To identify covariate factors, multiple logistic regression analysis was performed. PA, MTA and GCA-F scores, age, sex, onset age, education level, past medical history, CDR were simultaneously entered into the logistic regression model. We then performed multiple logistic regression with backward stepwise analysis using an entry probability of .05 and a removal probability of .10.

All statistical analysis was performed using SPSS version 19

(SPSS Inc., Chicago, Illinois). The study protocol was approved by the Institutional Review Board of Seoul National University Bundang Hospital.

Results

Total 379 patients were identified as probable AD from the data base. Total 190 patients were identified as mild AD and met the inclusion criteria. 78 patients were excluded because they do not have follow up MMSE score. 5 patients were excluded because they lack part of the three planes of brain MRI. (Figure 1) One patient was excluded because of significant change in medical condition in the follow up period. After excluding 84 patients inappropriate for analysis, the total study population consisted of 106 patients. (Figure 1)

After one year of follow-up period, 27 patients showed rapid progression of disease, while 79 patients were not. The baseline characteristic differences between two groups showed in table 2. There are no statistically significant different characteristics between two groups. Rapid progression groups showed 4.3-point decline of MMSE score in one-year follow-up while slow progression groups showed 0.3-point decline of MMSE score in the equal period. Among 106 patients, 51 patients had PA atrophy

(48.1%) and 79 patients had MTA atrophy (72.5%). According to the GCA-F score, 66 patients (62.3%) have frontal atrophy. The distribution of visual rating scores showed that rapid decliners have higher distribution of PA, MTA and GCA-F scores. (Figure 2) Patients with rapid cognitive decline showed higher distribution of visual rating scores regardless of the region of atrophy compared with non-rapid cognitive decline group.

Univariate analyses of PA showed significant correlation with rapid progression. (regression coefficient 0.788, 95% CI 1.115 to 6.972, p=0.028). In multiple logistic regression analysis, posterior atrophy in brain MRI was associated with rapid cognitive decline in one-year follow-up (regression coefficient 4.372, 95% CI 1.396 to 13.686, p=0.011). After the backward stepwise analysis, female sex, higher score of initial MMSE, low education level, CDR scores, and MTA showed significant association with rapid progression of AD. However, FA showed no significant correlation with rapid progression of AD (Table3). We analyzed for multicollinearity by assessing correlation between covariates. There is no multicollinearity among the covariates. (Variance inflation factors from 1.049 to 1.771)

Discussion

This study demonstrates that the posterior atrophy was associated with rapid progression of AD, as well as medial temporal atrophy. The frontal atrophy showed no significant correlation with rapid progression of AD. Previous researches showed that the posterior atrophy assessed by visual rating is associated with progression to dementia in patients with mild cognitive impairment.[17-19] However, there has been no previous report about the correlation between posterior cortical atrophy assessed by visual rating and the progression rate of disease in the patients already diagnosed as AD. This study showed the usefulness of visual rating scoring system. In newly diagnosed early AD patients, visual assessment of brain atrophy in posterior and medial temporal cortex can provide information about the disease course and the progression rate of cognitive decline. Prediction of disease progression rate can be used in settlement of a long term treatment plan including nursing management.

Medial temporal atrophy is one of well-known characteristic

findings of AD.[12,20] The medial temporal atrophy is significantly correlated with progression to AD in MCI patients[17] or rapid cognitive decline in AD.[21] Current study showed the consistent results in medial temporal atrophy, but demonstrated that the posterior atrophy also showed the significant correlation with rapid progression of AD. Posterior atrophy showed more significant correlation with disease progression rate of AD than medial temporal atrophy. The patients included in this study are in mild stage of AD, and more than 70% of patients have MTA. However, in respect of disease progression, we can predict that the AD patients with more extensive brain atrophy including especially parieto-occipital area can show more rapid cognitive decline in disease course.

Current study showed consistent result with VBM analysis conducted on the 23 AD patients[9] that PA rather than frontal atrophy showed the correlation with rapid progression in AD. Our study showed that the structural involvement in AD with rapid progression is specified to posterior region rather than frontal region. This result can be explained by the different vulnerability of intrinsic connectivity of brain network in AD. Previous studies with

connectivity data of brain MRI and FDG-PET, a posterior network including the precuneus, posterior cingulate gyrus and angular gyrus showed structural atrophy and decreased connectivity in AD compared with healthy control.[22-24] Our findings support a role of posterior network in AD. It is possible to assume that damage to the posterior network of intrinsic connectivity is related to the rapid disease progression of AD.

This assumption is connected with concept of cognitive reserve. According to the concept of cognitive reserve, individuals with higher cognitive reserve have more advanced neuropathology in the brain compared with those with lower cognitive reserve at the point of same degree of cognitive decline. Accordingly, those with higher cognitive reserve have less time to reach the point when the pathology overwhelms functions, thus have more rapid rate of cognitive decline.[25] Among individuals with the equivalent severity of disease in MCI and AD, reduced brain volume is associated with higher cognitive reserve.[26] This means that AD patients with more extensive brain atrophy in parieto-occipital area have higher cognitive reserve and will show more rapid rate of cognitive decline than patients without posterior atrophy. It is consistent with the

result of our study.

This study also demonstrates that people with female sex, higher score of initial MMSE, low education level, and CDR scores showed more rapid progression of AD after one year from diagnosis. Risk of gender and initial score of MMSE, CDR are consistent with previous findings.[27-29] Correlation of higher cognitive function and rapid progression is explained by less cognitive reserve in patients with higher cognitive test score. In respect of education level, several studies demonstrated that AD patients with higher education level experience faster cognitive decline which is also explained by cognitive reserve.[27,30-32] However, some research also demonstrated that more educated people showed slower rate of cognitive decline in AD patients.[33] The research explained that this result was because persons with higher education had more and better resources to compensate for clinical manifestations of the disease. It requires further analysis in future study to evaluate the exact effect of education in AD patients.

This study has potential limitations. First, the patients in this study were followed for a year from the initial diagnosis. Therefore, the result of current study can be applied to the early stage of AD.

It is possible to evaluate the association of visual rating scale and progression rate of AD in entire disease course if the follow up data are collected. Second, the cut-off value of visual rating in MTA and PA were established according to the previous study to evaluate the diagnosis of AD or progression to AD in MCI. The current study setting is different with mentioned previous studies in that this study population is already diagnosed as AD. Therefore, it is required to establish the different cut-off value of visual rating to evaluate the disease progression. In addition, some of demographic factors showed conflicting results in the direction of association with progression rate of AD. This requires further evaluation in another setting to evaluate the association between demographic factors and progression rate of AD.

Our study represents that posterior atrophy assessed by visual rating can provide important information for prediction of disease progression rate of AD. Posterior brain atrophy might mean that cognitive reserve is declined in parieto-occipital area and pathophysiology of disease is already progressed. Furthermore, it might represent that AD patients with more profound pathophysiology show rapid disease progression rate. Further

studies are required to evaluate the specific anatomical regions of parieto-occipital area that affect the disease progression in AD.

References

1. Dumont C, Voisin T, Nourhashemi F, Andrieu S, Koning M, Vellas B. Predictive factors for rapid loss on the mini-mental state examination in Alzheimer's disease. J Nutr Health Aging. 2005;9(3):163-7.

2. Cortes F, Nourhashemi F, Guerin O, Cantet C, Gillette-Guyonnet S, Andrieu S, et al. Prognosis of Alzheimer's disease today: a two-year prospective study in 686 patients from the REAL-FR Study. Alzheimer's & dementia : the journal of the Alzheimer's Association. 2008;4(1):22-9.

3. Aubert L, Pichierri S, Hommet C, Camus V, Berrut G, de Decker L. Association between comorbidity burden and rapid cognitive decline in individuals with mild to moderate Alzheimer's disease. J Am Geriatr Soc. 2015;63(3):543-7.

4. Hui JS, Wilson RS, Bennett DA, Bienias JL, Gilley DW, Evans DA. Rate of cognitive decline and mortality in Alzheimer's disease. Neurology. 2003;61(10):1356-61.

5. Holtzer R, Wegesin DJ, Albert SM, Marder K, Bell K, Albert M, et al. The rate of cognitive decline and risk of reaching clinical

milestones in Alzheimer disease. Arch Neurol. 2003;60(8):1137-42.

6. Soto ME, Andrieu S, Arbus C, Ceccaldi M, Couratier P, Dantoine T, et al. Rapid cognitive decline in Alzheimer' s disease. Consensus paper. The Journal of Nutrition, Health & Aging. 2008;12(10):703-13.

7. Musicco M, Palmer K, Salamone G, Lupo F, Perri R, Mosti S, et al. Predictors of progression of cognitive decline in Alzheimer's disease: the role of vascular and sociodemographic factors. Journal of neurology. 2009;256(8):1288-95.

8. Bowler JV, Munoz DG, Merskey H, Hachinski V. Factors affecting the age of onset and rate of progression of Alzheimer's disease. Journal of neurology, neurosurgery, and psychiatry. 1998;65(2):184-90.

9. Kinkingnehun S, Sarazin M, Lehericy S, Guichart-Gomez E, Hergueta T, Dubois B. VBM anticipates the rate of progression of Alzheimer disease: a 3-year longitudinal study. Neurology. 2008;70(23):2201-11.

10. Koedam EL, Lehmann M, van der Flier WM, Scheltens P, Pijnenburg YA, Fox N, et al. Visual assessment of posterior atrophy

development of a MRI rating scale. Eur Radiol. 2011;21(12):2618-25.

11. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease Report of the NINCDS-ADRDA Work Group* under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology. 1984;34(7):939-939.

12. Scheltens P, Leys D, Barkhof F, Huglo D, Weinstein HC, Vermersch P, et al. Atrophy of medial temporal lobes on MRI in "probable" Alzheimer's disease and normal ageing: diagnostic value and neuropsychological correlates. Journal of Neurology, Neurosurgery & Psychiatry. 1992;55(10):967-72.

13. Pasquier F, Leys D, Weerts JG, Mounier-Vehier F, Barkhof F, Scheltens P. Inter- and intraobserver reproducibility of cerebral atrophy assessment on MRI scans with hemispheric infarcts. European neurology. 1996;36(5):268-72.

14. Ferreira D, Cavallin L, Granberg T, Lindberg O, Aguilar C, Mecocci P, et al. Quantitative validation of a visual rating scale for frontal atrophy: associations with clinical status, APOE e4, CSF biomarkers and cognition. Eur Radiol. 2016;26(8):2597-610.

15. Lehmann M, Koedam EL, Barnes J, Bartlett JW, Ryan NS, Pijnenburg YA, et al. Posterior cerebral atrophy in the absence of medial temporal lobe atrophy in pathologically-confirmed Alzheimer's disease. Neurobiol Aging. 2012;33(3):627 e1- e12.

16. Ferreira D, Cavallin L, Larsson EM, Muehlboeck JS, Mecocci P, Vellas B, et al. Practical cut-offs for visual rating scales of medial temporal, frontal and posterior atrophy in Alzheimer's disease and mild cognitive impairment. Journal of internal medicine. 2015;278(3):277-90.

17. Korf ES, Wahlund LO, Visser PJ, Scheltens P. Medial temporal lobe atrophy on MRI predicts dementia in patients with mild cognitive impairment. Neurology. 2004;63(1):94-100.

18. Lehmann M, Koedam EL, Barnes J, Bartlett JW, Barkhof F, Wattjes MP, et al. Visual ratings of atrophy in MCI: prediction of conversion and relationship with CSF biomarkers. Neurobiol Aging. 2013;34(1):73-82.

19. Kim HR, Park YH, Jang JW, Park SY, Wang MJ, Baek MJ, et al. Visual Rating of Posterior Atrophy as a Marker of Progression to Dementia in Mild Cognitive Impairment Patients. Journal of Alzheimer's disease : JAD. 2016.

20. Jack CR, Petersen RC, Xu YC, Waring SC, O'Brien PC, Tangalos EG, et al. Medial temporal atrophy on MRI in normal aging and very mild Alzheimer's disease. Neurology. 1997;49(3):786-94.

21. Cheng Y-W, Chen T-F, Cheng T-W, Lai Y-M, Hua M-S, Chen Y-F, et al. Hippocampal atrophy but not white-matter changes predicts the long-term cognitive response to cholinesterase inhibitors in Alzheimer's disease. Alzheimer's research & therapy. 2015;7(1):72.

22. La Joie R, Landeau B, Perrotin A, Bejanin A, Egret S, Pelerin A, et al. Intrinsic connectivity identifies the hippocampus as a main crossroad between Alzheimer's and semantic dementia-targeted networks. Neuron. 2014;81(6):1417-28.

23. Damoiseaux JS, Prater KE, Miller BL, Greicius MD. Functional connectivity tracks clinical deterioration in Alzheimer's disease. Neurobiol Aging. 2012;33(4):828 e19-30.

24. Ranganath C, Ritchey M. Two cortical systems for memory-guided behaviour. Nat Rev Neurosci. 2012;13(10):713-26.

25. Stern Y. Cognitive reserve in ageing and Alzheimer's disease. The Lancet Neurology. 2012;11(11):1006-12.

26. Sole-Padulles C, Bartres-Faz D, Junque C, Vendrell P, Rami

L, Clemente IC, et al. Brain structure and function related to cognitive reserve variables in normal aging, mild cognitive impairment and Alzheimer's disease. Neurobiol Aging. 2009;30(7):1114-24.

27. Musicco M, Palmer K, Salamone G, Lupo F, Perri R, Mosti S, et al. Predictors of progression of cognitive decline in Alzheimer's disease: the role of vascular and sociodemographic factors. Journal of neurology. 2009;256(8):1288-95.

28. Doody RS, Massman P, Dunn JK. A method for estimating progression rates in Alzheimer disease. Archives of neurology. 2001;58(3):449-54.

29. Doody RS, Pavlik V, Massman P, Rountree S, Darby E, Chan W. Predicting progression of Alzheimer's disease. Alzheimer's research & therapy. 2010;2(1):1.

30. Scarmeas N, Albert S, Manly J, Stern Y. Education and rates of cognitive decline in incident Alzheimer's disease. Journal of Neurology, Neurosurgery & Psychiatry. 2006;77(3):308-16.

31. Chaves ML, Camozzato AL, Kähler C, Kaye J. Predictors of the progression of dementia severity in brazilian patients with Alzheimer's disease and vascular dementia. International Journal of

Alzheimer’s Disease. 2010;2010.

32. Ngandu T, von Strauss E, Helkala E-L, Winblad B, Nissinen A, Tuomilehto J, et al. Education and dementia What lies behind the association? Neurology. 2007;69(14):1442-50.

33. Fritsch T, McClendon MJ, Smyth KA, Lerner AJ, Chen CH, Petot GJ, et al. Effects of educational attainment on the clinical expression of Alzheimer's disease: results from a research registry. American journal of Alzheimer's disease and other dementias. 2001;16(6):369-76.

Table 1 Visual rating of three brain regions evaluated in the study

		0	1	2	3	4
PA	Widening of posterior cingulate and parieto-occipital sulcus	N	↑	↑↑	↑↑↑	
	Widening of sulcus of precuneus and parietal lobes	N	↑	↑↑	↑↑↑	
MTA	Width of choroidal fissure	N	↑	↑↑	↑↑↑	↑↑↑↑
	Width of temporal horn	N	N	↑	↑↑	↑↑↑
	Height of hippocampal formation	N	N	↓	↓↓	↓↓↓
GCA-F	Widening of frontal sulcus	N	↑	↑↑	↑↑↑	

↑, increase; ↓, decrease; N, normal.

PA, posterior atrophy; MTA, middle temporal atrophy; GCA-F, frontal subscale of global cortical atrophy

Table 2 Demographic characteristics of rapid decliner and non-rapid decliner

Characteristics	Rapid decliner	Non-rapid decliner	*P* value*
Number of subjects	27	79	
Gender (M/F)	9/18	37/42	0.222
Age, mean (SD)	75.6 (8.07)	76.6 (7.38)	0.548
Disease onset age, mean (SD)	73.7 (8.85)	74.5 (7.86)	0.668
Year of education, mean (SD)	8.6 (4.65)	10.1 (5.53)	0.211
More-educated (>6yr)	13 (48.1%)	51 (64.6%)	0.132
CDR (n)			0.622
0.5	16 (59.3%)	51 (64.6%)	
1	11 (40.7%)	28 (35.4%)	
Initial MMSE score, mean (SD)	22.2 (2.97)	21.06 (2.85)	0.080
f/u MMSE score, mean (SD)	17.9 (3.02)	21.4 (3.30)	<0.001

B- ADL (SD)	19.6 (1.39)	19.32 (1.90)	0.498
K-IADL (SD)	0.77 (0.71)	0.68 (0.24)	0.441
Hypertension (n)	15 (55.6%)	51 (64.6%)	0.405
Diabetes (n)	10 (37.0%)	17 (21.5%)	0.110
Hyperlipidemia (n)	7 (25.9%)	18 (22.8%)	0.740
Ischemic heart disease (n)	1 (3.7%)	13 (16.5%)	0.091
Prior stroke (n)	0 (0%)	2 (2.5%)	1.000
Acetylcholine receptor inhibitor (n)			
Donepezil	19 (70.4%)	51 (64.6%)	
Rivastigmine	8 (29.6%)	22 (27.8%)	
Galantamine	1 (3.7%)	3 (3.8%)	
Memantine	2 (7.4%)	7 (8.9%)	

CDR, Clinical dementia rating scale; MMSE, mini-mental state examination; B-ADL, Barthel activity of daily living scale; K-IADL, Korean instrumental activity of daily living scale; SD, standard deviation.

*P values were obtained using Student t test or Pearson chi-square test as appropriate.

Table 3 Regression coefficients (95% CI) and significance level for associations with rapid progression in multiple logistic regression analysis

	Regression coefficients	*p*
PA	4.372 (1.396−13.686)	0.011
MTA	4.734 (1.151−19.465)	0.031
GCA−F	0.945 (0.194−4.606)	0.944
Male	0.145 (0.039−0.540)	0.004
Initial MMSE	1.636 (1.227−2.180)	0.001
High education	0.299 (0.093−0.967)	0.044
CDR	7.056 (1.595−31.212)	0.010

PA, posterior atrophy scale; MTA, medial temporal atrophy scale; GCA−F: frontal subscale of global cortical atrophy; CDR, clinical dementia rating scale.

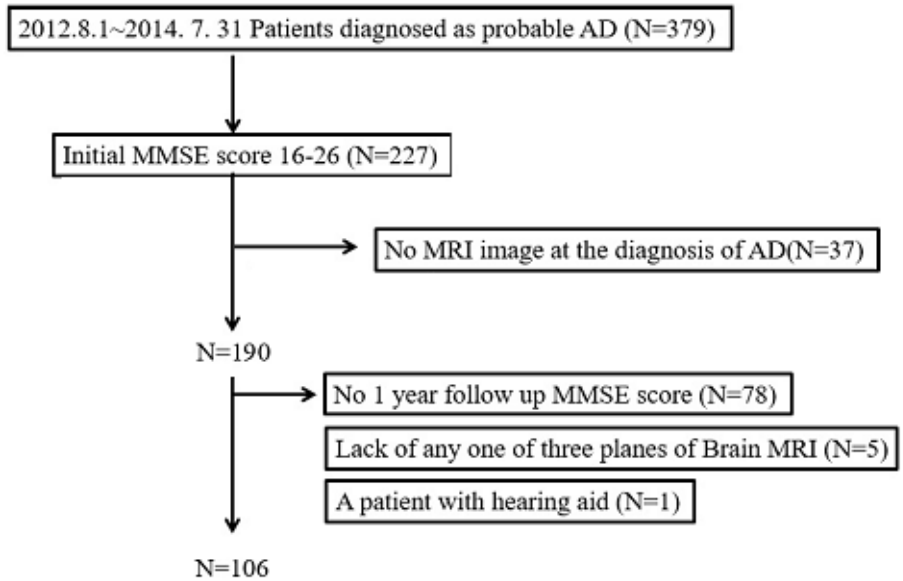

Figure 1 Overview of subjects included for the analysis

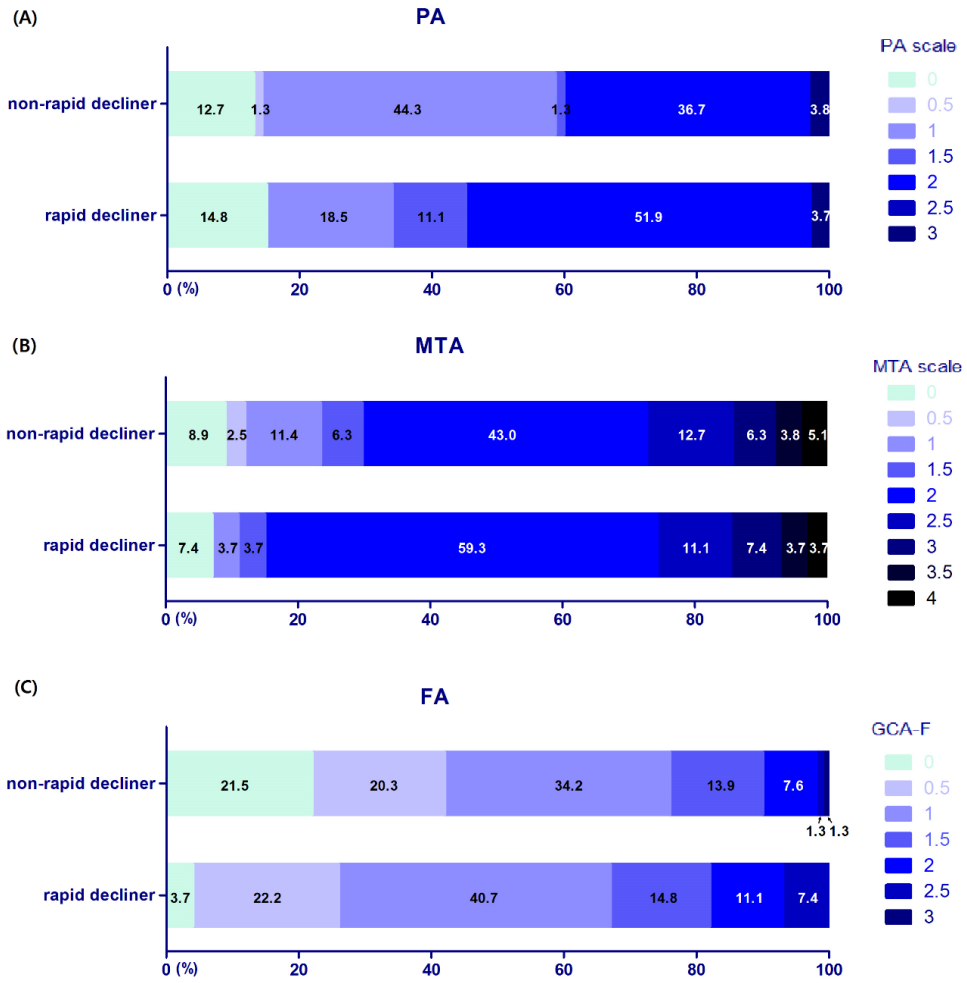

Figure 2 Visual rating score distribution of posterior atrophy (A), medial temporal atrophy (B) and frontal atrophy (C) in rapid cognitive decline and non-rapid cognitive decline group of AD patients.

PA, posterior atrophy; MTA, medial temporal atrophy; FA frontal atrophy.

Number in the bars indicate the percentage of patients.

국문초록

알츠하이머병으로 진단 받은 환자들은 인지기능의 저하가 진행하는 속도가 환자마다 모두 다르다. 이는 환자 개개인의 여러가지 특성에 의하여 좌우된다. 최근의 연구에 의하면 빠르게 진행하는 알츠하이머병 환자의 경우 그렇지 않은 환자와 비교하여 뇌의 후두-두정엽의 부피가 감소하여 있다는 것이 알려졌다. 하지만 뇌의 부피를 정량적으로 측정하는 것은 추가적인 분석과정을 거쳐야 한다는 점에서 실제 임상 진료 상황에서 적용하기에는 어렵다. 저자들은 뇌자기공명영상 소견을 가지고 빠르게 뇌의 위축 정도를 평가 할 수 있는 육안평가 측도를 이용하여 후뇌피질의 위축이 알츠하이머병의 빠른 진행과 연관되어 있는 가를 평가하고자 하였다. 처음 알츠하이머병으로 진단을 받은 환자들을 대상으로 1년간 약물치료를 하며 추적 관찰하였다. 처음 진단 당시와 1년 후의 한국형간이정신상태검사 점수를 측정하였고, 진단 당시의 뇌자기공명영상을 가지고 후뇌 위축의 정도를 평가하였다. 1년 후 빠른 진행을 보인 환자들은 전체 106명 중 27명 (25.5%) 이었다. 로지스틱 회귀 분석 결과 후뇌 위축 육안 평가 점수는 빠르게 진행하는 알츠하이머병과 유의한 상관관계를 보였다. (회귀 계수 4.37, 95% CI 1.40 to 13.69, p=0.011) 측두엽 위축 육안 평가 점수 또한 빠르게 진행하는 알츠하이머 병과 유

의한 상관관계를 보였으나 (회귀 계수 4.73, 95% CI 1.15 to 19.47, p=0.031) 전두엽 위축 육안평가 점수는 빠르게 진행하는 알츠하이머병과 유의한 상관관계를 보이지 않았다. (회귀 계수 0.945, 95% CI 0.19 to 4.61, p=0.944) 따라서 후뇌 위축 육안 평가 척도는 측두엽 위축 육안평가 척도와 더불어 초기 알츠하이머병 환자에서 병의 진행 속도를 예측하는 데 유용한 평가 측도가 될 수 있을 것이다. 이러한 육안 평가 척도를 이용하여 후뇌 위축 정도를 평가하는 것은 진단시에 병의 진행 속도를 예측하고 병의 진행 속도에 따라 적절한 치료와 적정 수준의 간호에 대한 계획을 수립하는 데 도움을 줄 수 있을 것으로 기대된다.

주요단어: 알츠하이머병, 빠른 인지기능저하, 후뇌 피질 위축, 육안 평가 척도

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