High serum high-density lipoprotein-cholesterol is associated with memory function and gyri
cification of insular and frontal opercular cortex in an elderly memory-clinic population

Ryuta Kinnoa,⁎, Yukiko Morib, Satomi Kubbota, Shohei Nomotoa, Akinori Futamurab, Azusa Shiromarub, Takeshi Kurodab, Satoshi Yanob, Seiichiro Ishigakic, Hidetomo Murakamib, Yasuhiro Babaa, Kenjiro Onob,⁎

aDepartment of Neurology, Showa University Fujigaoka Hospital, 1-30 Fujigaoka Aoba-ku, Yokohama-Shi, Kanagawa 227-8501, Japan
bDivision of Neurology, Department of Medicine, Showa University School of Medicine, 1-5-8 Hatanodai Shinagawa-ku, Tokyo 142-8666, Japan
cDivision of Neurology, Department of Internal Medicine, Showa University Northern Yokohama Hospital, 35-1 Chigasaki-chuo Tatsuzi-ku, Yokohama-Shi, Kanagawa 224-8503, Japan

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ABSTRACT

The issue of whether serum lipid marker values are cognitively and neurologically significant for elderly individuals attending a memory clinic has been controversial. We investigated the associations of serum lipid markers with the memory function and cortical structure in 52 patients aged ≥75 years who had attended our memory clinic based on their subjective memory complaints. None had a history of medication for hyperlipidemia. The Wechsler Memory Scale-Revised (WMS-R) was administered to all patients for the assessment of their memory function. Serum low-density lipoprotein cholesterol, high-density lipoprotein cholesterol (HDLC), and triglyceride (TG) were measured for each patient. Surface-based morphometry (SBM) was performed for the calculation of each patient’s cortical thickness and gyri
cification index based on structural MRI data. Our analyses revealed that the serum HDLC level was positively and significantly correlated with the WMS-R subtests of visual paired associates I/II and logical memory I (p < 0.05). The serum TG level was negatively correlated with the logical memory I subtest. The SBM results showed positive correlations between the serum HDLC level and the gyri
cification indices of the bilateral insular and frontal opercular cortices, and those two gyri
cification indices were positively correlated with the logical memory I and visual paired associates I/II. These results suggest that in these elderly patients, a high serum HDLC level was associated with not only preserved memory function but also gyri
cification of the insular and frontal opercular cortex. We conclude that elderly individuals’ serum lipid markers should be carefully assessed in memory clinic settings, because serum HDLC may be a biomarker for memory function and cortical structure.

1. Introduction

Dementia is characterized by memory loss, cognitive decline, and disability in daily activities. Vascular risk factors such as hypertension, hyperlipidemia, diabetes mellitus, overweight, and smoking are known to enhance the risk of dementia (Blom et al., 2013). Among these factors, the association between hyperlipidemia and dementia remains particularly unclear. Epidemiologic studies examining the association between cholesterol and dementia have reported conflicting results, including an association between adverse hyperlipidemia and an increased dementia risk (Kivipelto et al., 2005; Whitmer et al., 2005), the absence of such an association (Li et al., 2005; Muller et al., 2007b), and inverse associations (Mielke et al., 2005; Reitz et al., 2010). One of the important differences among these studies is the timing of the measurement of serum lipid markers. Significant associations between hyperlipidemia and dementia are described in studies where the subjects’ serum lipid levels were measured in midlife (Whitmer et al., 2005). Studies with serum lipid levels measured in later life showed no association (Li et al., 2005) or an inverse association with dementia risk (Mielke et al., 2005). It has been speculated that the association between hyperlipidemia and dementia is affected by several factors, such as apolipoprotein E (APOE) ε4 and the type of dementia (Dufouil et al.,

⁎ Corresponding authors.
E-mail addresses: kinno@med.showa-u.ac.jp (R. Kinno), onoken@med.showa-u.ac.jp (K. Ono).

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2. Patients and methods

2.1. Participants

We retrospectively analyzed the cases of 52 individuals ≥75 years old (82.7 ± 4.86, range 75–93 years); 21 males and 31 females with 12.3 ± 2.66 years of education who had attended the Division of Neurology in the Department of Medicine at the Showa University School of Medicine because of subjective memory complaints. The following four conditions were the inclusion criteria for the study: (1) right-handedness; (2) no history of neurological and neuropsychiatric diseases, including cerebrovascular disease; (3) no medication for hyperlipidemia; and (4) no medical problems related to MRI acquisition. For our evaluations of the significance of the values of serum lipid markers in a memory clinic setting, all of the individuals who met the criteria were examined, regardless of their disease profiles.

The main cause of dementia was AD in 24 patients, MCI in 15, vascular dementia (VaD) in two, diffuse Lewy body disease (DLB) in two, frontotemporal dementia (FTD) in three, and idiopathic normal pressure hydrocephalus (iNPH) in one patient. We also evaluated the cases of five healthy individuals who had attended our memory clinic due to subjective memory complaints and were diagnosed as neurologically normal. Each diagnosis was based on the following diagnostic criteria: the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (American Psychiatric Association, 2013); the U.S. National Institute on Aging-Alzheimer’s Association workgroup for MCI and AD (Albert et al., 2011; McKhann et al., 2011); the Third Report of the DLB Consortium for DLB (McKeith et al., 2005); the criteria for vascular dementia from the International Society for Vascular Behavioral and Cognitive Disorders (Sachdev et al., 2014); the International Behavioral Variant Frontotemporal Dementia Criteria for FTD (Lamarre et al., 2013; Rascovsky et al., 2011); and frequently used criteria for iNPH (Relkin et al., 2005).

Serum low-density lipoprotein cholesterol (LDLC), high-density lipoprotein cholesterol (HDLC), and triglyceride (TG) were measured for each participant. Each patient’s alcohol intake was assessed by self-report, in which there were no patients who drank > 20 g/day for men and > 10 g/day for women (43 patients reported no history of drinking, eight reported social drinking, and one male reported < 20 g/day). We used the Wechsler Memory Scale-Revised (WMS-R) for the assessment of memory function (Wechsler and Stone, 1987). Approval for this study was obtained from the Institutional Review Board of the Showa University School of Medicine. We provided the participants, their closest family member, or legal guardian the opportunity to opt out of the study.

2.2. MRI data acquisition

The structural MRI scans were conducted on a 1.5T MR scanner (Magnetom: Essenza, Siemens, Germany). The high-resolution T1-weighted images of the whole brain (144 sagittal slices, 1.0 × 1.0 × 1.25 mm) were acquired from all of the participants with a gradient echo sequence: repetition time = 1600 msec, echo time = 4.7 msec, flip angle = 15°, field of view = 256 × 256.

2.3. SBM analysis

We performed the SBM analysis using the CAT12 Toolbox (http://dbm.neuro.uni-jena.de/cat/) in SPM12 (Wellcome Trust Centre for Neuroimaging, http://www.fil.ion.ucl.ac.uk/spm/) (Friston et al., 1995) implemented on MATLAB R2017b software (MathWorks, Natick, MA, USA). The CAT12 Toolbox contains a processing pipeline for SBM, which includes an established novel algorithm for extracting the cortical surface (Dahnke et al., 2013), which then allows the computation of multiple morphometric parameters (including cortical thickness as well as gyrification index).

For the estimation of white matter distances, we subjected the T1-weighted images to tissue segmentation. Local maxima were then projected to other gray matter voxels by using a neighbor relationship described by the white matter distance (Dahnke et al., 2013). These values equal cortical thickness. This projection-based method also includes partial volume correction, sulcal blurring, and sulcal asymmetries without sulcus reconstruction. Topological correction is performed through an approach based on spherical harmonics. For inter-patient analyses, an algorithm for spherical mapping of the cortical surface is included (Yotter et al., 2011). An adapted volume-based diffeomorphic anatomical registration through the exponentiated lie algebra (DARTEL) algorithm was then applied to the surface for spherical registration (Ashburner, 2007).

In addition to cortical thickness analysis, we extracted the local gyrification index based on the absolute mean curvature (Luders et al., 2006). Central cortical surfaces were created for both hemispheres.
separately. Finally, all scans were re-sampled and smoothed with a Gaussian kernel of 15 mm full-width at half-maximum (FWHM) for the cortical thickness and 20 mm FWHM for the gyri fication index.

2.4. Statistical analysis

We used R (ver. 3.5.0) software for the statistical analyses of the patients’ controls’ clinical and neuropsychological features. Regarding the SBM analysis, we applied the general linear models to the individual maps and then performed a multiple regression analysis on the individual cortical thickness and gyri fication index maps. The serum TG, HDLC, and LDLC levels were then included as covariates in the design matrix of the SBM analysis. Age was included as a nuisance factor in order to correct for the age differences. For the multiple regression analysis, we used threshold-free cluster enhancement (TFCE) (Smith and Nichols, 2009) with 10,000 permutations to identify the significant clusters were determined with reference to the multi-modal analyses of magnetic resonance images from the Human Connectome Project (HCP) (Glasser et al., 2016).

3. Results

3.1. The patients’ demographics

Table 1 summarizes the demographics of the 52 elderly patients. Eighteen patients (six males, 12 females) showed high serum TG levels (i.e., > 149 mg/dl). Five patients (four males, one female) showed low serum HDLC levels (i.e., < 40 mg/dl). Thirteen patients (three males, 10 females) showed high serum LDLC levels (i.e., > 139 mg/dl). The serum LDLC levels of the female participants were significantly higher than those of the males (p = 0.0014), whereas the serum TG and HDLC levels showed no such differences between the genders. The Spearman partial rank correlation analysis in which gender differences were controlled showed no correlation between any serum lipid markers and age (all, p > 0.05). The duration of education was not correlated with the serum lipid markers (all, p > 0.05). Regarding the WMS-R, the subtest scores were not affected by gender (Table 1). Age and duration of education were not correlated with the subtest scores (Spearman, all, p > 0.05).

3.2. Correlation analysis between WMS-R and the serum lipid markers

We next examined whether serum lipid markers are associated with memory function. We performed a Spearman partial rank correlation analysis in which the correlation between serum lipid markers and WMS-R subtests was evaluated while controlling for age and gender differences (Table 2). We found that the serum HDLC level was positively correlated with the WMS-R scores on the subtests of visual paired associates I, visual paired associates II, and logical memory I, whereas the serum TG level was negatively correlated with the logical memory I score (all, corrected p < 0.05). In contrast, we found no correlations between the serum LDLC level and the WMS-R subtest scores (all, corrected p > 0.05). These results suggest that both a high level of serum HDLC and a low level of TG were associated with preserved memory function of the elderly memory clinic population.

3.3. SBM analysis for serum lipid markers

We next examined the association of cortical structure with serum HDLC and TG levels, both of which were significantly correlated with memory function (Table 2). The SBM analysis showed that the serum HDLC level was positively associated with the gyri fication index in the bilateral insular cortex and frontal opercular cortex (Fig. 1, Table 3). The gyri fication indices of the polar frontal cortex, posterior opercular cortex, and premotor cortex also showed weak associations with the serum HDLC level. There were no significant associations of the serum HDLC level with cortical thickness.

Regarding the serum TG level, we found no significant association with cortical thickness or gyri fication. These results suggest that the serum HDLC level was not only cognitively but also neurologically as- sociated with preserved memory function of the elderly memory clinic population.

3.4. Correlation analysis between the gyri fication index and WMS-R scores

We also investigated whether a change in the gyri fication index reflects cognitive changes. We performed a Spearman partial rank correlation analysis in which we evaluated the correlation of the WMS-R subtest scores for logical memory I, visual paired associates I, visual paired associates II, and logical memory I, whereas the serum TG level was negatively correlated with the logical memory I score (all, corrected p < 0.05). In contrast, we found no correlations between the serum LDLC level and the WMS-R subtest scores (all, corrected p > 0.05). These results suggest that both a high level of serum HDLC and a low level of TG were associated with preserved memory function of the elderly memory clinic population.

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Table 1

Demographics of the 52 elderly participants.

|                | Female (n = 31) | male (n = 21) | Statistical value |
|----------------|----------------|---------------|-------------------|
| Age            | 82.6 ± 0.88    | 82.9 ± 1.07   | Z = 0.21, p = 0.83 |
| Education      | 12. 8 ± 2.78   | 11.5 ± 2.32   | Z = 1.78, p = 0.076 |
| Serum lipid markers |                |               |                   |
| TG (50–149 mg /dl) | 137.8 ± 74.89  | 153.0 ± 129.95| Z = 0.18, p = 0.86 |
| HDLC (male: 40–80; female: 40–90 mg /dl) | 63.5 ± 12.48  | 57.4 ± 16.75  | Z = 1.43, p = 0.15 |
| LDLC (70–139 mg /dl) | 126.2 ± 27.20  | 99.7 ± 29.04  | Z = 3.20, p = 0.0014 |
| WMS-R |                |               |                   |
| Visual Reproduction I | 18.6 ± 8.98  | 17.5 ± 10.18  | Z = 0.48, p = 0.63 |
| Visual Reproduction II | 5.6 ± 8.30   | 5.6 ± 10.08   | Z = 0.67, p = 0.50 |
| Logical Memory I | 8.5 ± 5.93    | 7.6 ± 6.51    | Z = 0.52, p = 0.61 |
| Logical Memory II | 3.0 ± 4.40    | 2.9 ± 5.3     | Z = 0.69, p = 0.49 |
| Verbal Paired Associates I | 7.9 ± 6.08  | 5.8 ± 5.0     | Z = 1.29, p = 0.20 |
| Verbal Paired Associates II | 3.2 ± 2.88   | 2.6 ± 2.22    | Z = 0.75, p = 0.45 |
| Visual Paired Associates I | 4.7 ± 4.76   | 3.5 ± 4.2     | Z = 0.85, p = 0.40 |
| Visual Paired Associates II | 1.9 ± 2.12  | 1.9 ± 2.00    | Z = 0.11, p = 0.91 |
| Design memory  | 4.4 ± 1.89     | 4.2 ± 1.76    | Z = 0.029, p = 0.98 |
| Dgit span      | 10.2 ± 2.70    | 10.8 ± 4.06   | Z = 0.85, p = 0.39 |
| Mental control | 3.1 ± 1.53     | 3.1 ± 1.79    | Z = 0.087, p = 0.93 |
| Visual span    | 12.3 ± 2.45    | 13.2 ± 4.11   | Z = 1.45, p = 0.15 |

Z-values are by Wilcoxon rank sum test.

* p < 0.05.
and visual paired associates II with the gyri
cation indices of the right frontal opercular and right insular
cortex (Fig. 1, Table 3). These results suggest that increased gyri
cation indices were

4. Discussion

Our analyses revealed a significant association between two serum lipid markers and the memory function of our patients; i.e., 52 patients aged ≥75 years who had attended our memory clinic based on their subjective memory complaints. We observed that the patients’ serum HDLC and TG levels correlated with their scores on three subtests of the WSM-R: visual paired associates I, visual paired associates II, and logical memory I (Table 2). Among the lipid markers, the serum HDLC level is associated with poor cognitive performance. On the other hand, cholesterol is an essential structural component in the cell membranes (Ikonen, 2008), and it is thus theoretically possible that the low LCLC level may be associated with poor cognitive function (Wagsta

cerebrovascular and Alzheimer’s pathological changes frequently coin-
cide in cases of dementia and may synergistically affect an individual’s cognitive decline (Xuereb et al., 2000), it is possible that a high LDLC level is associated with poor cognitive performance. On the other hand, cholesterol is an essential structural component in the cell membranes (Ikonen, 2008), and it is thus theoretically possible that the low LCLC level may be associated with poor cognitive function (Wagsta

Table 2
Correlation coefficient between serum lipid markers and the WMS-R subtests.

|                     | HDLC                | LDLC                | TG                   |
|---------------------|---------------------|---------------------|----------------------|
| Mean ± SD           | 61.1 ± 14.52 (mg/dl)| 115.5 ± 30.63 (mg/dl)| 144.0 ± 99.89 (mg/dl)|
| Visual Reproduction I | 18.2 ± 9.40          | 0.0056              | 0.09                 | 0.16                 |
| Visual Reproduction II | 5.6 ± 6.96           | 0.25                | 0.004                | −0.18                |
| Logical Memory I    | 8.1 ± 6.12           | 0.48                | 0.18                 | −0.38                |
| Logical Memory II   | 2.9 ± 4.74           | 0.20                | 0.27                 | −0.17                |
| Verbal Paired Associates I | 7.0 ± 5.71         | 0.22                | 0.10                 | −0.18                |
| Verbal Paired Associates II | 3.0 ± 2.63        | 0.18                | 0.09                 | −0.20                |
| Visual Paired Associates I | 4.2 ± 4.54            | 0.32                | 0.06                 | −0.24                |
| Visual Paired Associates II | 1.9 ± 2.01          | 0.36                | 0.20                 | −0.24                |
| Design Memory       | 4.3 ± 1.82           | 0.03                | 0.04                 | −0.13                |
| Digit Span          | 10.4 ± 3.29          | −0.07               | 0.02                 | 0.003                |
| Mental Control      | 3.1 ± 1.62           | 0.02                | 0.08                 | 0.01                 |
| Visual Span         | 12.7 ± 3.22          | −0.03               | 0.18                 | 0.23                 |

Spearman’s p-values are shown. Age and gender differences were controlled.

⁎ p < 0.05 (Bonferroni correction).

Fig. 1. Brain regions with a significant association between the cortical gyration index and the serum HDLC level. Significant regions are identified by SBM, which was projected onto the left and right lateral surfaces of the standard inflated brain. Medial sections are also shown. The threshold was set at p < 0.05 (TFCE, FWE-corrected). See Table 3 for the details of the regions. Note that no significant correlation was observed for the serum TG level. AVI: anterior ventral insular area, FOP4: frontal opercular area 4, L: left, MI: middle insular area.
to the characteristics of our patients, who were all \( \geq 75 \) years old and had no history of hyperlipidemia medication. The serum HDLC level may be especially important for such an elderly memory-clinic population.

Our results demonstrated that the serum HDLC level is associated not only with memory function (Table 2) but also with cortical structure in an elderly memory-clinic population (Fig. 1, Table 3). The evidence of HDLC’s involvement in the brain as a whole remains rather limited (Yates et al., 2012). A positive relationship between the serum HDLC level and gray matter volume in the bilateral temporal regions was reported (Ward et al., 2010; Wolf et al., 2004). These studies focused on the gray matter volume, and to our knowledge, no study has

| P-value | Size | Overlap of atlas region   | P-value | Size | Overlap of atlas region   |
|---------|------|----------------------------|---------|------|----------------------------|
| 0.02110 | 754  | 18% Middle insular area    | 0.01580 | 1678 | 9% Area PFcm              |
| 0.05120 | 58%  | 15% Posterior insular area 2 | 0.01580 | 8%   | Frontal opercular area 4  |
| 0.04920 | 13%  | 12% Area 45                 | 0.01580 | 7%   | Anterior ventral insular area |
| 0.04920 | 11%  | 11% Frontal opercular area 5 | 0.01580 | 7%   | Retroinsular cortex      |
| 0.04920 | 10%  | 10% Posterior insular area 1 | 0.01580 | 6%   | Area OF-2-3/VS          |
| 0.04920 | 9%   | 9% Para-insular area        | 0.01580 | 6%   | Area 47                  |
| 0.04920 | 8%   | 8% Frontal opercular area 4 | 0.01580 | 5%   | Area 44                  |
| 0.04920 | 6%   | 6% Anterior ventral insular area | 0.01580 | 5%   | Frontal opercular area 2  |
| 0.04920 | 5%   | 5% Area 44                  | 0.01580 | 5%   | Insular granular complex |
| 0.04920 | 4%   | 4% Frontal opercular area 3 | 0.01580 | 5%   | Area OF4/PV              |
| 0.04920 | 12%  | 13% Peri-Sylvian language area | 4%     | Area OF1/SIV                |
| 0.04920 | 6%   | 6% Area PF complex          | 4%     | Frontal opercular area 3   |
| 0.04920 | 5%   | 5% Anterior ventral insular area | 4%     | Frontal opercular area 1   |
| 0.04920 | 4%   | 4% Area PF complex          | 3%     | Area PF complex            |
| 0.04920 | 3%   | 3% Frontal opercular area 5 | 3%     | Frontal opercular area 5   |
| 0.04920 | 2%   | 2% Rostral area 6           | 2%     | Area 47                   |
| 0.04920 | 2%   | 2% Area 47                  | 2%     | Area 52                   |
| 0.04920 | 2%   | 2% Posterior insular area 2 | 2%     | Area 52                   |
| 0.04920 | 2%   | 2% Medial belt complex      | 2%     | Area 9 posterior           |
| 0.04920 | 2%   | 2% Middle insular area      | 2%     | Area 9 posterior           |
| 0.04920 | 2%   | 2% Area PF opercular        | 2%     | Area 46                   |
| 0.04920 | 1%   | 1% Peri-Sylvian language area | 2%     | Area 46                   |
| 0.04920 | 0%   | 0% Medial belt complex      | 1%     | Area 8B lateral            |

The threshold was set at \( p < 0.05 \) (TFCE, FWE-corrected). Each label of the brain regions was based on HCP multi-modal parcellation (Glasser et al., 2016).

![Fig. 2. Scatterplots of the association of the gyrification index of the insular and front operculum with the patients’ scores on the logical memory I subtest. Spearman partial rank correlation tests showed a significant and positive correlation for each pair (each, \( p < 0.05 \)). Each label of the brain regions was based on HCP multi-modal parcellation (Glasser et al., 2016). The gyrification index of the left middle insular area and the right frontal opercular area 4 were significantly correlated with the scores on the logical memory I subtest, which are shown in red and yellow, respectively. FOP4: frontal opercular area 4, L: left, MI: middle insular area, R: right. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)](image)
investigated the association between gyri
cification and the serum lipid
level. Gyri
cification is known to be a
ff
ected by both age and gender (Liu
et al., 2010). However, our
findings are not likely to be explained by the
differences in age and gender, as we controlled our analyses for these
differences. We therefore propose that the gyri
cification change of the
insula and frontal opercular cortex is related to the serum HDLC level.

HDLC contains APOE and facilitates the transport of other types of
cholesterol from various tissues, including the brain, to the liver. APOE
has a major physiological role in the regulation of lipid and lipoprotein
homeostasis, and the APOE-ε4 isoform is a well-known risk factor for
AD (Raber et al., 2004). Several findings indicate that the association
between APOE-ε4 and low HDLC level increases the susceptibility to AD
(Hoshino et al., 2002; Raygani et al., 2006). Amyloid β-protein (Aβ), a
pathological hallmark of AD, binds to HDLC, maintaining its solubility
in cerebrospinal fluid and plasma. This HDLC-Aβ interaction prevents
the deposition of Aβ into the brain and can serve as a marker for
neurodegenerative disease (Koudinov et al., 2001). APOE-ε4 has been
shown to adversely affect this HDLC-Aβ interaction and has been im-
plicated as a risk factor for cerebral amyloid angiopathy, another pro-
minent pathologic hallmark of AD (Mulder and Terwel, 1998). The
target of the present study was an elderly memory-clinic population,
and therefore, no data of the APOE genotype were available in our
present patients, as the use of APOE genotyping is not recommended in
routine clinical diagnosis (Farrer et al., 1995). However, considering
that the insular cortex is often involved in AD (Bonthius et al., 2005)
and the lower gyri
cification index in AD (Im et al., 2008; King et al.,
Gyrification of the insular and frontal opercular cortices was positively correlated with the patients' scores on WMS-R subtests (Figs. 2 and 3). The insular and frontal opercular cortex shows similar recruitment for cognitive function (Duncan and Owen, 2000). Indeed, both regions have been shown to be involved in memory function. The insular cortex was described as involved in recognition memory (Bermudez-Rattoni et al., 2005; Zhao and Wang, 2018). Patients with left insular lesions showed significantly poorer verbal memory as measured by the WMS-R logical memory I subtest, indicating that left insular damage is associated with poorer performance on verbal memory tasks (Mances et al., 1999). The frontal operculum is also known to be involved in several types of memory such as semantic memory and episodic memory (Andreasen et al., 1995; Lepage et al., 2000). These two regions are thought to be connected to each other, as reported regarding cortico-cortical evoked potentials (Enatsu et al., 2016). Indeed, a number of studies have reported the association of these two connected regions with strategic processing during episodic retrieval and working memory (Donaldson et al., 2010; Kahn et al., 2004). A VBM analysis also showed a significant gray matter intensity decrease that covaried with the episodic memory recall performance of patients with familial behavioral variant FTD (Irish et al., 2013), indicating the importance of this connectivity for memory function. Taking the above findings together, we consider that gyrification change of the insular and frontal opercular cortex is related to memory function.

A computer simulation study suggested that thicker cortical sheets lead to less cortical convolutions (Toro and Burmed, 2005). The negative relationship between gyrification and cortical thickness is most likely related to both space constraints and brain functionality. Besides allowing an increase of neuronal numbers within a limited space, another way to increase brain functionality would be to improve the efficiency of cortical communication. Decreasing cortical thickness could shorten the distance of the white matter fibers running between adjacent brain regions, and it could increase the efficiency of cortical communication. Smaller cortico-cortical distances not only aid rapid communication; they also increase the overall efficiency of cortical signaling by reducing the energy expenditure, which may result in better cognitive performance. Indeed, it was reported that greater cortical gyrification is related to better cognitive function, but not to greater cortical thickness (Gautam et al., 2015). Although we observed no significant correlations between critical thickness and memory functions, we suspect that the increased gyrification of the insular and frontal opercular cortex may be reflected by effective cortico-cortical communication, which may contribute to better cognitive performance.

In our elderly memory-clinic population, the WMS-R logical memory and visual paired associate subtest scores were positively correlated with the serum HDLC level (Figs. 2 and 3). Logical memory is known to be used for the assessment of verbal declarative memory (Kessels et al., 2011; Papalambros et al., 2017) whereas visual paired associates have been used to assess visual declarative memory tasks (Clarke, 1992). This study has some limitations. First, patients with heterogeneous profiles were allowed to participate in the study. In other words, as we aimed to assess the usefulness of the measurement of serum lipid markers for elderly individuals who attended a memory clinic, all participants who met the inclusion criteria (see Methods) were included, regardless of their profiles. However, the disease pattern of our patient series was consistent with that of another study in a memory-clinic setting (Wada-Isoe et al., 2009). Second, as our sample size was relatively small (n = 52), the significance of serum LDLC or TG levels remains unclear. Future studies should clarify the cognitive and neurological significance of these serum lipid markers for specific neurological profiles.

5. Conclusion

Our results demonstrate that a high serum level of HDLC was associated with not only preserved memory function but also gyrification of the insular and frontal opercular cortex in an elderly memory-clinic population. This suggests the importance of the assessment of serum lipid markers in clinical practice for the elderly, because their serum HDLC may be a biomarker of both memory function and cortical structure. Further studies are required to establish the significance and the precise effects of an increased serum HDLC level on memory function.

Declaration of interest

The authors declare no conflict of interest, financial or otherwise, related to this study.

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