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Decreased β-amyloid peptide$_{42}$ in cerebrospinal fluid of patients with progressive supranuclear palsy and corticobasal degeneration

Moeko Noguchi, Mitsuhiro Yoshita, Yasuko Matsumoto, Kenjiro Ono, Kazuo Iwasa, Masahito Yamada*

Department of Neurology and Neurobiology of Aging, Kanazawa University Graduate School of Medical Science, 13-1, Takara-machi, Kanazawa 920-8640, Japan

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Abstract

Several previous studies have identified biochemical markers for Alzheimer's disease (AD): cerebrospinal fluid (CSF)-β-amyloid peptide$_{42}$ (CSF-Aβ$_{42}$), CSF-total tau protein (CSF-tau) and CSF-phosphorylated tau protein (CSF-ptau). Progressive supranuclear palsy (PSP) and corticobasal degeneration (CBD) as well as AD are diseases with tauopathies. CSF-Aβ$_{42}$, CSF-tau, and CSF-ptau have not been rigorously investigated in PSP and CBD. In the present study, we assessed CSF-Aβ$_{42}$, CSF-tau, and CSF-ptau as biochemical markers for PSP and CBD, compared with AD. The subjects consisted of 18 cases of PSP, 9 cases with CBD, 69 cases with AD, and 43 control subjects. Genotyping or phenotyping of apolipoprotein E (apoE) was also performed. CSF-Aβ$_{42}$ levels were significantly decreased in patients with PSP and CBD as well as in AD patients. The ratio of CSF-ptau to CSF-Aβ$_{42}$ provided high diagnostic accuracy to distinguish both PSP from AD, and CBD from AD. ApoE genotype/phenotype was not associated with CSF-Aβ$_{42}$ levels in all groups. We concluded that CSF-Aβ$_{42}$ levels are reduced in PSP and CBD as well as in AD.

Keywords: β-Amyloid peptide$_{42}$; Total tau protein; Phosphorylated tau protein; Cerebrospinal fluid; Progressive supranuclear palsy; Corticobasal degeneration; Alzheimer's disease

1. Introduction

Several previous studies have identified biochemical markers for Alzheimer's disease (AD): cerebrospinal fluid (CSF)-β-amyloid peptide$_{42}$ (CSF-Aβ$_{42}$), CSF-total tau protein (CSF-tau) and CSF-phosphorylated tau protein (CSF-ptau) [1,2]. Decreased CSF-Aβ$_{42}$ levels may reflect mismetabolism of β-amyloid or possibly accumulation of senile plaques [3], while increased CSF-tau levels may reflect progressive death of neurons [4]. Increased CSF-ptau levels may reflect accumulation of neurofibrillary tangles in the brain [5]. A marked CSF-Aβ$_{42}$ reduction is, however, found in Creutzfeldt–Jacob disease (CJD) [6] and amyotrophic lateral sclerosis (ALS) [7], even in cases without Aβ deposition. Progressive supranuclear palsy (PSP) and Corticobasal degeneration (CBD) as well as AD are tauopathies. CSF-Aβ$_{42}$, CSF-tau, and CSF-ptau have not been rigorously investigated in PSP and CBD. We speculated that the levels of CSF-tau in PSP and CBD might change higher, reflecting accumulation of tau proteins in the brain. In this study, the levels of CSF-Aβ$_{42}$, CSF-tau, and CSF-ptau were determined in the patients with PSP and CBD, compared with AD.

2. Subjects and methods

Included in the study were 18 patients with PSP (8 men and 10 women, mean age: 69.2 ± 3.0 years), 9 patients with CBD (6 men and 3 women, mean age: 66.1 ± 7.2 years), 69

* Corresponding author. Tel.: +81 76 265 2290; fax: +81 76 234 4253.
E-mail address: m-yamada@med.kanazawa-u.ac.jp (M. Yamada).

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Table 1
Clinical characteristics of subjects

Diagnosis	Number of patients (Male/Female)	Age (years)	Duration of illness (years)	MMSE (points)
PSP	18 (8/10)	69.2±3.0	2.50±1.03	24.2±3.76
CBD	9 (6/3)	66.1±7.2	2.33±0.67	28.0±2.33
AD	69 (37/32)	70.5±2.0	2.37±0.62	21.6±1.57*
CTL	43 (22/21)	51.7±6.0	–	–

PSP: progressive supranuclear palsy, CBD: corticobasal degeneration, AD: Alzheimer's disease, CTL: control subjects, MMSE: Mini-Mental State Examination.

* Significant difference in AD from PSP and CBD ($p<0.05$).

patients with AD (37 men and 32 women, mean age: 70.5±2.03 years), and 43 neurologic disease controls (CTL; 22 men and 21 women, mean age: 51.7±6.0 years). All patients underwent thorough clinical examination, including providing medical and family history; neurological, internal, and psychiatric examinations; routine laboratory testing; neuropsychiatric examinations; and magnetic resonance imaging of the brain. The neurologic disease controls were the cases without involvement of the central nervous system, including myopathy, peripheral neuropathy, functional headache and myasthenia gravis. Their clinical characteristics are summarized in Table 1. The diagnoses were made according to the NINDS-SPSP criteria [8] for PSP (probable PSP, $n=11$; possible PSP, $n=7$), the published diagnostic criteria [9] for CBD, and the NINDS-ADRDA criteria [10] for AD. Among the PSP, CBD and AD patients, the severity of dementia was evaluated using the Mini-Mental State Examination

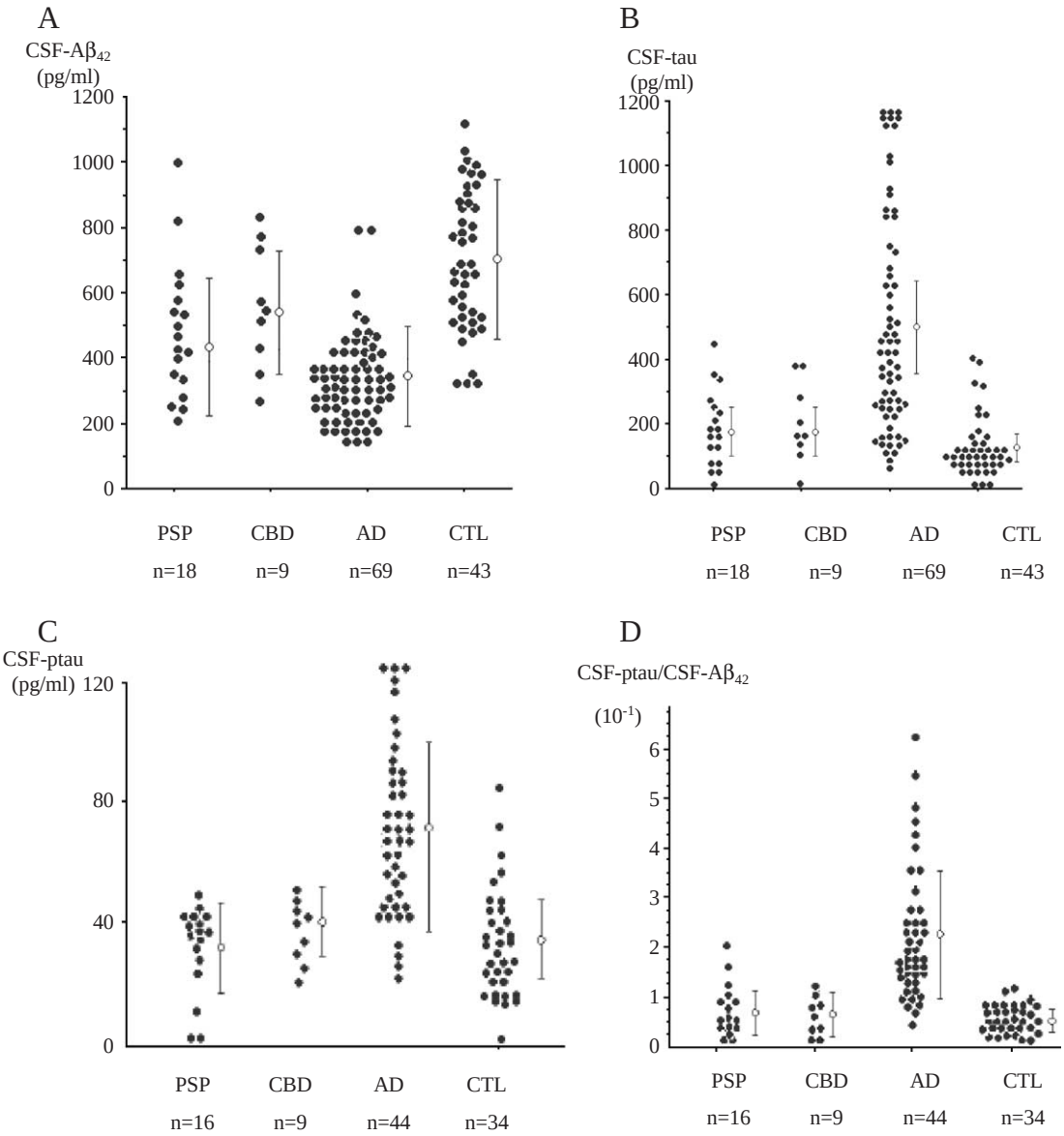

Fig. 1. Concentrations of β-amyloid peptide$_{1-42}$ (Aβ$_{42}$) (A), total tau protein (tau) (B), and phosphorylated tau protein (ptau) (C) in the cerebrospinal fluid (CSF), and the ratio of CSF-ptau to CSF-Aβ$_{42}$ (D) in patients with progressive supranuclear palsy (PSP), corticobasal degeneration (CBD), Alzheimer's disease (AD) and control subjects (CTL).