

Comparison of Post-Mortem 7.0-Tesla Magnetic Resonance Imaging of the Hippocampus in Lewy Body Dementia Brains with and without Cerebral Amyloid Angiopathy

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Abstract

Introduction and Purpose: Cerebral amyloid angiopathy (CAA) is frequently associated to Dementia with Lewy bodies (DLB). The impact of CAA on the degree of hippocampal atrophy (HA) and on the incidence of hippocampal cortical micro-infarcts (HCoMIs) and cortical micro-bleeds (HCoMBs) is unknown.

Materials and Methods: The examined post-mortem brains consisted 9 DLB-CAA cases and 20 DLB ones without CAA. The hippocampus was evaluated on the most representative coronal section with T2 and T2* 7.0-tesla MRI sequences. The average degree of HA was evaluated in both groups. The incidence of HCoMIs and HCoMBs was also compared as well as the frequency of CoMIs and CoMBs in the neocortex

Results: No differences were observed in the degree of HA and in the incidence of HCoMIs and HCoMBs between the DLB-CAA and the DLB brains. The incidence of these cerebrovascular lesions in both groups is similar to that in the neocortex.

Discussion and Conclusion: CAA has no influence on the degree of HA and on the incidence of HCoMIs and HCoMBs in the hippocampus of DLB brains.

Keywords: Post-Mortem 7.0-Tesla Magnetic Resonance Imaging; Dementia with Lewy Bodies; Cerebral Amyloid Angiopathy; Hippocampal Atrophy; Cortical Micro-Infarcts; Cortical Micro-Bleeds

Introduction

Dementia with Lewy bodies (DLB) is the second most frequent neurodegenerative dementia syndrome following Alzheimer's disease (AD) [1]. However, DLB has to be distinguished from Parkinson's disease dementia (PDD) although some overlap can occur between both entities [2]. Current consensus is to restrict a diagnosis of DLB only to patients with parkinsonism who develop dementia within 12 months of the onset of motor symptoms [3]. The mean neuritic Braak stage in DLB is more severe than in PDD [4].

In our previous neuropathological study cerebral amyloid angiopathy (CAA) was associated to 30% of DLB brains while the incidence of AD pathology was 70% [5]. Also amyloid- β imaging using Pitisbough Compound B supports the neuropathological studies which found that amyloid- β pathology is more common in DLB than in PDD [6].

The present post-mortem 7.0-tesla magnetic resonance imaging (MRI) compares the severity of the hippocampal atrophy (HA) between DLB brains with (DLB-CAA) and those without associated severe CAA (DLB). Also, the frequency of the hippocampal micro-infarcts (HMIs) and hippocampal micro-bleeds (HMBs) is compared between DLB-CAA and DLB brains. In addition, their incidence is compared to the frequency of cortical micro-infarcts (CoMIs) and cortical micro-bleeds (CoMBs) in the hemispheric neocortex.

Materials and Methods

The examined post-mortem brains consisted of 9 DLB-CAA ones and 21 DLB ones. A previously obtained informed consent of the patients or from the nearest family allowed an autopsy for diagnostic and scientific purposes. The brain tissue samples were acquired from the Lille Neuro-Bank of the Lille University that is part of the “Centres des Ressources Biologiques” and acts as an institutional review board.

The neuropathological examination was made according to a previously described standard procedure [7]. Severe degree of limbic and neocortical involvement was used to define DLB [8].

The presence of various degrees of CAA was made according the criteria of a consensus protocol and graded from 0 to 3 on examining four cortical samples with β -amyloid staining [9]. Grades 2 up to 3 were retained as diagnosis in the DLB-CAA group.

The degree of HA was determined according to the AD classification of Scheltens in 4 grades [10,11]. Also, the incidence of HMIs and HMBs was evaluated as previously described for cortical hemispheric CoMIs and CoMBs [12].

A 7.0-tesla MRI Bruker BioSpin SA was used with an issuer-receiver cylinder coil of 72 mm inner diameter (Ettlingen, Germany), according to a previously described method [13]. Before the brain sampling, three up to six coronal sections of a cerebral hemisphere were submitted to SPIN ECHO T2 and T2* MRI sequences. The hippocampus was evaluated on the most representative section.

Unvaried comparisons of unpaired groups were performed with the Fisher’s exact test for categorical data. The non-parametric Mann-

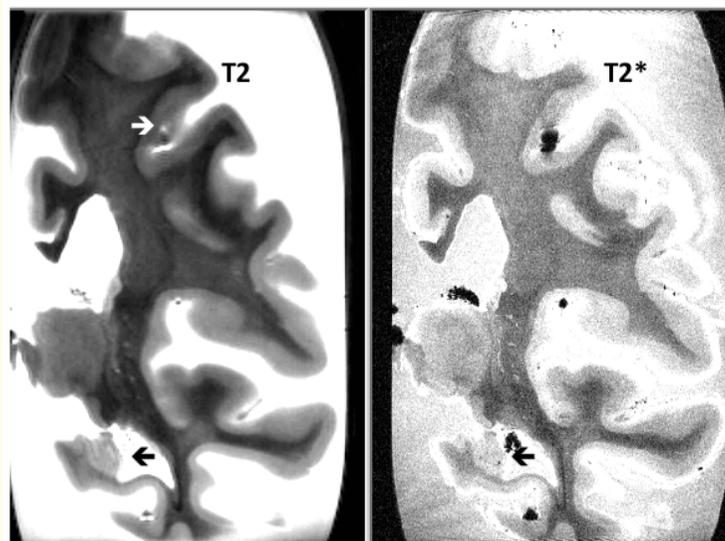


Figure 1: T2 and T2* sequences of a coronal section of a cerebral hemisphere in a dementia patient with Lewy bodies and with cerebral amyloid angiopathy. There is only a moderate atrophy of the hippocampus with a small infarct on the T2 sequence and a small bleed on the T2* sequence (black arrows). Also, a small neocortical infarct is present on the T2 sequence (white arrow).

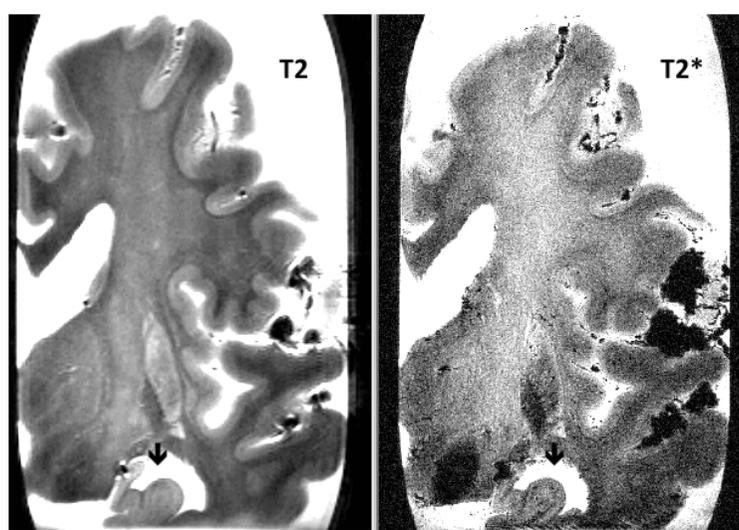


Figure 2: T2 and T2* sequences of a coronal section of a cerebral hemisphere in a patient with dementia with Lewy bodies and without cerebral amyloid angiopathy. Only moderate hippocampal atrophy is observed with on the T2* sequence two small bleeds (black arrows).

Whitney U test was used to compare continuous variables. The significance level, two-tailed, was set at ≤ 0.01 for significant and ≤ 0.001 for highly significant. Values set at ≤ 0.05 and more than > 0.01 were considered as marginal significant.

Results

The average age and gender distribution were more or less similar between the DLB-CAA and the DLB patients. Associated AD pathology (Braak stages between II and IV) was present in all cases of DLB-CAA, compared to 16% in the DLB group ($p < 0.001$). The incidence of lobar haematomas, territorial and lacunar infarcts was not significantly different between both groups (Table 1).

Items	DLB-CAA	DLB	Significance level
Number of brains	9	21	
Age (years)	78 (72 - 83)	81 (73 - 97)	N.S.
Male gender	80%	67%	N.S.
Alzheimer Pathology	100%	16%	$P < 0.001$
Lobar Haematoma	16%	0%	N.S.
Territorial Infarct	8%	0%	N.S.
Lacunar Infarct	8%	8%	N.S.

Table 1: Demographic and associated post-mortem neuropathology in dementia with lewy bodies with (DLB-CAA) and without cerebral amyloid angiopathy (DLB).

No statistical differences were observed concerning the degree of HA and the frequency of HMIs and HMBs between the DLB-CAA and the DLB groups. Also, comparison of their occurrence to those of CoMIs and CoMBs in the neocortex showed no significant differences (Table 2).

Items	Hippocampus		Neocortex	
	DLB -CAA	DLB	DLB -CAA	DLB
Hippocampal atrophy	1.7 (0.9)	2.0 (0.8)		
Cortical micro-infarcts	0.1 (0.3)	0.3 (0.5)	0.5 (0.8)	0.6 (0.5)
Cortical micro-bleeds	1.1 (0.8)	0.6 (0.6)	0.9 (0.8)	0.8 (0.5)

Table 2: Comparison of the degree of hippocampal lesions in dementia with Lewy bodies associated to cerebral amyloid angiopathy (DLB-CAA) and dementia without cerebral amyloid angiopathy (DLB), and the incidence of cerebrovascular lesions in the hemispheric neocortex. No statistical significant differences are observed between both groups.

Discussion

The present post-mortem study does not show differences in the degree of HA and the incidence of HCoMIs and HCoMBs between the LBD-CAA and the LBD groups. Also, the incidence of the latter’s is similar to that in the neocortex in the cerebral hemisphere. Although CAA pathology as pathological substrate is prominent in DLB [14] the incidence of CMIs and CoMBs in the present study is not very frequent in the hippocampus as well as in the neocortex. Coexistence of AD increases the frequency of leptomeningeal CAA [15]. The CoMIs are of smaller size in DLB than in AD patients [16]. The frequency of CoMBs is similar among patients with both DLB and AD [17,18]. Apolipoprotein E epsilon is strongly associated to the presence of both Lewy bodies and cerebral amyloid angiopathy pathologies [19,20].

Conclusion

It can be concluded that associated CAA does not influence the degree of HA and the frequency of associated HCoMIs and HCoMBs in DLB brains.

Disclosure

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