# Differential Atrophy of Hippocampal Subfields: A Comparative Study of Dementia with Lewy Bodies and Alzheimer Disease

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**Objectives:** *Dementia with Lewy bodies (DLB) is characterized by relative preservation of the medial temporal lobe compared with Alzheimer disease (AD). The differential involvement of the hippocampal subfields in both diseases has not been clearly established, however. We aim to investigate hippocampal subfield differences in vivo in a clinical cohort of DLB and AD subjects.* **Methods:** *104 participants (35 DLBs, 36 ADs, and 35 healthy comparison [HC] subjects) underwent clinical assessment and 3T T1-weighted imaging. A Bayesian model implemented in Freesurfer was used to automatically segment the hippocampus and its subfields. We also examined associations between hippocampal subfields and tests of memory function.* **Results:** *Both the AD and DLB groups demonstrated significant atrophy of the total hippocampus relative to HC but the DLB group was characterized by preservation of the cornu ammonis 1 (CA1), fimbria, and fissure. In contrast, all the hippocampal subfields except the fissure were significantly atrophied in AD compared with both DLB and HC groups. Among DLB subjects, CA1 was correlated with the Recent Memory score of the CAMCOG and Delayed Recall subscores of the HVLT.* **Conclusions:** *DLB is characterized by milder hippocampal atrophy that was accompanied by preservation of the CA1. The CA1 was also associated with memory function in DLB. Our findings highlight the promising role of hippocampal subfield volumetry, particularly that of the CA1, as a biomarker for the distinction between AD and DLB.* (Am J Geriatr Psychiatry 2015; ■:■−■)

**Key Words:** Lewy bodies, Alzheimer disease, neuroimaging, MRI, hippocampus

Dementia with Lewy bodies (DLB) is the second leading cause of degenerative dementia in older people after Alzheimer disease (AD), accounting for up to 15% of cases at autopsy.[1] DLB shares common clinical, neuropsychological, and pathological features with other dementia subtypes such as AD and

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Parkinson disease with dementia, making differentiation between these disorders challenging. Despite the development of consensus diagnostic criteria, the sensitivity for differential diagnosis of DLB in clinical practice remains low, with many DLB subjects misdiagnosed. In light of this uncertainty, and with important implications for subsequent patient management, there is need for reliable imaging markers to help distinguish DLB from other subtypes of dementia, most especially AD.

Structural neuroimaging studies have found reduced global atrophy in DLB compared with AD.[2] The relative preservation of the hippocampus in DLB compared with AD is recognized as one of the most consistent structural magnetic resonance imaging (MRI) findings,[2,3] and has been incorporated as a supportive feature in the revised criteria for the diagnosis of DLB.[1]

Most previous studies, however, have compared total hippocampal volumes using a region of interest approach. Considering the functional specialization of the histologically distinct subfields of the hippocampus, local analyses of the hippocampus are increasingly recognized as a viable method to characterize the involvement of cytoarchitectonic regions in the pathology of neurodegenerative diseases, most commonly in AD, mild cognitive impairment,[4] and Parkinson disease.[5]

Using a manual tracing technique on 4T MR images, Mueller and colleagues[6] have demonstrated atrophy of the cornu ammonis (CA)1 and the subiculum in AD. Interestingly, a similar pattern of hippocampal changes in healthy comparisons (HCs) has also been associated with development of amnestic mild cognitive impairment.[4] There is also histopathological evidence that the CA1 region is preferentially vulnerable to the neuropathology of AD.[7]

There have been few direct comparisons of the hippocampal subfields in DLB and AD. Two previous studies have reported a milder degree of atrophy in the subiculum and CA1 regions of the hippocampus in DLB compared with AD,[8,9] although another study did not find any significant difference in hippocampal volumes.[10] As such, the clinical utility of hippocampal subfield volumetry to aid in the differential diagnosis of DLB from AD remains unclear.

The discrepancy of findings in the literature could be attributed to the variability of methods that are currently used to examine the hippocampal subfields. To date, manual tracing is widely acknowledged as the gold standard of hippocampal subfield delineation. It is labor intensive, however, and its reproducibility might be limited by inter-/intra-rater variability. There is also the possibility of asymmetric bias in manual segmentations because of laterality of visual perception.[11] To overcome these limitations, we used a validated and automated technique[12] to compare the volumetric differences of the hippocampal subfields in DLB and AD and investigate their associations with memory performance.

## METHODS

### Subjects, Assessment, and Diagnosis

Seventy-one individuals over the age of 60 years (36 subjects with probable AD[13] and 35 with probable DLB[1]) were recruited from a community-dwelling population of patients referred to local Old Age Psychiatry, Geriatric Medicine, or Neurology Services. Thirty-five similarly aged HC subjects were recruited from relatives and friends of subjects with dementia or volunteered via advertisements in local community newsletters. The research was approved by the local ethics committee. All subjects or, where appropriate, their nearest relative, provided written informed consent.

Subjects underwent clinical and neuropsychological evaluation. Neuropsychological assessments of global cognitive measures included the Cambridge Cognitive Examination (CAMCOG),[14] which incorporates the Mini-Mental State Examination (MMSE)[15] in addition to a number of subscales assessing domains including orientation, language, memory, attention, praxis, calculation, abstract thinking, and perception. Verbal and visuospatial memory was assessed with the Hopkins Verbal Learning Test (HVLT)[16] and the Brief Visuospatial Memory Test (BVMT),[17] respectively. Motor parkinsonism was evaluated with the Unified Parkinson's Disease Rating Scale Part III (UPDRS)[18] (2003). For subjects with dementia, neuropsychiatric features were examined with the Neuropsychiatric Inventory (NPI),[19] and cognitive fluctuations were assessed with the cognitive fluctuation scale,[20] a test to obtain