LETTERS

**C9ORF72 in Dementia with Lewy bodies**

**INTRODUCTION**
Recent studies have shown that a large hexanucleotide expansion in *C9ORF72* is the most common cause of inherited Frontotemporal Lobar Degeneration (FTLD) and Motor Neuron Disease (MND).1 In pathological terms, expansion carriers show a distinctive molecular signature within the dentate gyrus granule cells and CA4 pyramidal cells of the hippocampus and granule cells of the cerebellum characterised by TDP-43-negative, but p62-positive, neuronal cytoplasmic inclusions (NCI).2 Such inclusions contain p62-positive, neuronal cytoplasmic inclusions and granule cells of the cerebellum.2 Characterised by TDP-43-negative, but p62-immunoreactive NCI within the dentate gyrus and CA2/3/4 regions of the hippocampus, and within the granule cells of the cerebellum.2

**RESULTS**
No p62-immunoreactive NCI were seen within the hippocampus or cerebellum in any of the 53 cases.

**DISCUSSION**
Previously, when screening a series of 102 patients fulfilling criteria for probable DLB we detected an expansion in *C9ORF72* in two patients.9 Similar to expansion carriers with FTLD8 and/or MND,5 both patients displayed psychotic features, though in neither was a previous family history of dementia recorded, nor was there pathological confirmation of DLB or other underlying neurodegenerative disease. Therefore, it remains possible that these two individuals were misdiagnosed. Indeed, a frontotemporal dementia phenotype that mimics DLB has been reported.10 We therefore investigated 53 pathologically confirmed cases of DLB for an expansion in *C9ORF72*, using the presence of p62-immunoreactive NCI in hippocampus and cerebellum as a surrogate marker, but did not detect any cases where relevant tissue changes were present. Although only three of the cases had undergone formal genetic analysis for an expansion in *C9ORF72* and had been shown to be negative, evidence indicates that the presence of p62-positive NCI in these brain regions, like the presence of DPR, can nevertheless act robustly as a marker of the expansion in the absence of genetic analysis.2 3 From the present study, we therefore conclude that expansions in *C9ORF72* in pathologically confirmed cases of DLB are unlikely, and in those patients bearing expansions in clinically assessed cohorts, an atypical presentation of an underlying process of FTLD is likely to be present. Nonetheless, Cooper-Knock and colleagues have reported one of 377 pathologically confirmed patients with Parkinson’s disease to bear an expansion in *C9ORF72*, and one of 17 other patients with an expansion in *C9ORF72* to show pathological changes in synuclein, suggesting that overlaps between an expansion in *C9ORF72* and synucleinopathies can, if infrequently, indeed occur.11

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Contributors DMAM conceived the study, performed microscopic analyses and prepared the manuscript.
AR and YD prepared tissue sections and performed immunohistochemical staining. JS5 assisted with clinical characterisation of the cohort.

Competing interests None.

Ethics approval Ethics approval was provided by Newcastle and North Tyneside 1 Local Research Ethics Committee under Generic Tissue Bank Ethical Agreement.

Provenance and peer review Not commissioned; externally peer reviewed.


Received 10 January 2014
Revised 4 March 2014
Accepted 5 March 2014
Published Online First 19 March 2014

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