Clinical criteria for three types of dementia had low sensitivity and high specificity


Questions
How valid are the following diagnostic criteria: (1) the NINCDS-ADRDA criteria for Alzheimer’s disease (AD); (2) the NINDS-AIREN criteria for vascular dementia (VaD); and (3) the consensus criteria for dementia with Lewy bodies (DLB)? Do prevalence rates and cophatibility compromise these criteria?

Design
Blinded comparison of the resulting diagnoses using the NINCDS-ADRDA criteria, the NINDS-AIREN criteria, and the CDLB with the diagnostic standard, postmortem examination.

Setting
Community based in the UK.

Patients
The first 80 patients (58% women) from the Camberwell Dementia Case Register to come to postmortem (mean age at death 82 y).

Description of tests and diagnostic standard
Clinical diagnosis was made independently by 2 psychiatrists, blind to postmortem findings. Diagnostic criteria of the NINCDS-ADRDA for AD, the NINDS-AIREN for VaD, and the CDLB for DLB were used.

Main outcome measures
Sensitivity, specificity, and positive and negative predictive values.

Main results
38 patients (48%) fulfilled NINCDS-ADRDA criteria for probable AD, 7 (9%) fulfilled NINDS-AIREN criteria for probable VaD, and 2 (3%) fulfilled CDLB for probable DLB. 27 patients (34%) had mixed pathology. The table shows sensitivity, specificity, and positive and negative predictive values of the tests.

Conclusions
Clinical diagnostic criteria for Alzheimer’s disease, vascular dementia, and dementia with Lewy bodies had low sensitivity and relatively high specificity. Approximately one third of patients had mixed pathology.

Sensitivity, specificity, and positive and negative predictive values of the clinical diagnosis compared with postmortem examination*

<table>
<thead>
<tr>
<th>Clinical diagnosis</th>
<th>Detected neuropathology</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (CI)</th>
<th>PPV (CI)</th>
<th>NPV (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NINCDS probable</td>
<td>Neuritic plaques alone</td>
<td>66% (50 to 80)</td>
<td>75% (58 to 88)</td>
<td>76% (59 to 89)</td>
<td>72% (59 to 85)</td>
</tr>
<tr>
<td>AIREN probable</td>
<td>Infarctions alone</td>
<td>50% (37 to 62)</td>
<td>70% (55 to 59)</td>
<td>92% (78 to 98)</td>
<td>17% (7 to 31)</td>
</tr>
<tr>
<td></td>
<td>Infarctions alone and</td>
<td>43% (10 to 82)</td>
<td>95% (87 to 98)</td>
<td>45% (10 to 82)</td>
<td>95% (86 to 98)</td>
</tr>
<tr>
<td></td>
<td>with other pathologies</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DLB probable</td>
<td>Lewy bodies alone and</td>
<td>30% (13 to 53)</td>
<td>100% (94 to 100)</td>
<td>100% (59 to 100)</td>
<td>78% (67 to 87)</td>
</tr>
<tr>
<td></td>
<td>with other pathologies</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Neuritic plaques alone</td>
<td>22% (3 to 60)</td>
<td>100% (95 to 100)</td>
<td>100% (10 to 999)</td>
<td>91% (82 to 96)</td>
</tr>
<tr>
<td></td>
<td>with other pathologies</td>
<td>16% (2 to 48)</td>
<td>100% (95 to 100)</td>
<td>100% (10 to 999)</td>
<td>87% (77 to 94)</td>
</tr>
</tbody>
</table>

*PPV = positive predictive value; NPV = negative predictive value.

Commentary
This study by Holmes et al addresses the correspondence between clinical and pathological criteria for AD, VaD, and DLB. This work is reminiscent of a study by Litvan et al in which rater’s used data from 15 cases pathologically proved to have Parkinson’s disease, 14 with DLB, and 76 with neither.1 For DLB, as in the present study, sensitivity was low and specificity was high. Mixed pathologies were considered in the context of parkinsonian syndromes, and inter-rater reliabilities were also considered. For AD, Nagy et al found high sensitivity (91–98%), low specificity (40–61%), and low negative predictive values for both the NINCDS-ADRDA and DSM-III-R criteria.2 The higher sensitivity found might have been from having less mixed pathology. For VaD, comparisons between NINDS-AIREN criteria and 3 other current criteria showed poor concordance, again perhaps reflecting the problem of mixed disease discussed by the present authors.3 Clinicians should appreciate the current work because it stresses the importance of (1) recognising disease prevalence, (2) appreciating the complexity introduced by mixed pathology, and (3) encouraging the clinician to consider the patient’s values in tactfully informing the patient or the patient’s family, about the possibility of false positives and negatives when proceeding from a differential diagnosis to a provisional diagnosis. Although physicians should be cognisant of these and other diagnostic guidelines, this study does not support shifting the standard of care from the currently recommended one (general medical, neurological, and psychiatric assessment and an informed consent process indicating the nature of the differential diagnoses, relevant evaluation, and treatment alternatives and their prospective risks and benefits) to an algorithmic dependence on a specific set of guidelines.4 5

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