



ORIGINAL RESEARCH

Hit or Miss? Diagnostic contributions of neuropsychological assessment in patients with suspected dementia

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Abstract

Objectives: Accurate early diagnosis of dementia has important implications for prognosis, treatment, and management. In hospital settings, neuropsychological assessment is frequently included in the diagnostic work-up for dementia, particularly in clinically ambiguous cases. However, the diagnostic contributions of neuropsychological testing in this population are not well established. This paper reports the findings from a preliminary study examining the diagnostic utility of such assessment in patients with suspected dementia.

Methods: A retrospective review of hospital medical records was performed for 84 patients who underwent neuropsychological assessment for diagnostic purposes within a five-year time frame. A proxy measure of diagnostic accuracy was obtained using the level of agreement between the neuropsychologist's opinion and the most recent working diagnosis of the medical treatment provider, allowing a minimum follow-up period of twelve months.

Results: Using defined clinical coding criteria to account for differences between clinical conditions (e.g., mild neurocognitive disorder) and underlying pathology (e.g., Alzheimer's disease), the baseline diagnosis of the neuropsychologist concurred with the most recent diagnosis of the treatment provider in 88% of cases with an exact match in 77% of cases. Follow-up neuropsychological assessments over time did not lead to a significant improvement in diagnostic accuracy.

Conclusion: A high level of diagnostic agreement emerged between neuropsychology and treating medical consultant opinions, independent of available neuroimaging evidence. The findings highlight the contribution of neuropsychological testing in the diagnosis of dementia in hospital settings. Replication of these results is required using prospective designs, larger samples, multiple sites, and autopsy confirmed diagnoses.

Keywords: Alzheimer's disease, Dementia, Diagnostic accuracy, Neuropsychological assessment.

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Background

Dementia Diagnosis

Traditionally, dementia was conceptualised as a global impairment in intellectual function [2]. In more recent years, however, distinct dementia profiles have been identified which reflect the differential distribution of degenerative changes within the brain and, by extension, the underlying pathology. Accuracy of dementia diagnosis has been aided by the development of specific clinical criteria and guidelines. The most commonly used criteria for diagnosing Alzheimer's disease (AD) were developed by the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) [3], with a recommended revision in 2011 [4]. It has been reported that the NINCDS-ADRDA criteria provide a sensitivity of 81% and a specificity of 70% for a diagnosis of probable AD [5]. Diagnostic criteria have also been developed for frontotemporal dementia (FTD) [6], Lewy body dementia [7], dementia due to Parkinson's disease [8], and vascular dementia [9]. New consensus criteria for variants of FTD [10] and the progressive aphasia [11] have also been identified. Though, these criteria will need to be refined as additional information regarding disease-specific pathophysiological changes becomes available.

A number of neuroimaging techniques and biomarker studies have been developed to aid the diagnosis of dementia, particularly AD. These techniques include magnetic resonance imaging (MRI), computed tomography (CT), fludeoxyglucose positron emission tomography (FDG-PET), Pittsburgh compound B (PiB) PET [12], single-photon emission computed tomography (SPECT) [13], and biomarkers such as concentration of amyloid- β and phosphorylated tau (p-Tau) protein in the cerebrospinal fluid (CSF) or serum [14] [see 15 for a review]. Nevertheless, while there has been significant progress in the development of diagnostic investigations for dementia, early neurodegenerative changes are not necessarily evident on imaging studies [16, 17] and, at this stage, the capacity for biomarkers to discriminate different types of dementia is less than remarkable. Additionally, *in vivo* measures such as CSF and serum amyloid, CSF p-Tau, and PET studies are not performed routinely in hospital settings. To this end, neurologists, psychiatrists, and geriatricians typically rely on a combination of clinical interviews, physical examinations, laboratory tests, neuroimaging (CT, MRI, SPECT) studies, and neuropsychological assessments as part of the diagnostic work-up [18, 19].

In terms of diagnostic accuracy of neuropsychological assessment, one German study [20] compared the sensitivity and specificity of cognitive testing and MRI relative to a clinical diagnosis of vascular dementia, no dementia, or other neurodegenerative condition. Neuropsychological assessment demonstrated high levels of sensitivity and specificity in identifying people with no

dementia (98%), while MRI had similar sensitivity and specificity in identifying any neurodegenerative condition.

Snowden and colleagues [21] evaluated diagnostic accuracy in a sample of 228 patients referred to a specialist early-onset dementia clinic. Diagnosis was determined based on structured clinical history, neurological examination, and abbreviated neuropsychological assessment, supported by neuroimaging. Diagnostic confirmation was obtained through post-mortem examination of brain tissue. Within the sample, 42% had a clinical diagnosis of one of the three syndromes of frontotemporal lobar degeneration (FTLD) while 46% of patients were clinically diagnosed with AD. The remaining 12 cases were diagnosed with Lewy body disease, Creutzfeldt-Jakob disease, vascular and unclassified dementia. Using a diagnostic algorithm, FTLD was identified with 100% sensitivity and 97% specificity, and AD with 97% sensitivity and 100% specificity. However, the study focused on differentiating AD and FTLD in patients with early-onset dementia. Thus, the sample was not necessarily representative of the clients who typically present in a hospital outpatient clinic.

In other research, Geroldi and colleagues [22] investigated the diagnostic value of structural neuroimaging (CT or MRI) and neuropsychological testing in routine dementia assessments across nine Italian expert centres (e.g., memory clinic, scientific institute). General practitioners and community health providers correctly recognised AD in a modest 12% of cases and non-AD in 5% of cases. The addition of an imaging study or neuropsychological assessment improved accuracy to 50% for AD and 22% for non-AD. After subsequent review in an expert centre with an imaging study and/or neuropsychological assessment, accuracy rates increased to 99% for AD cases and 83% for non-AD cases. The authors highlighted the incremental value of structural imaging and neuropsychological testing in the routine clinical assessment of dementia. Nevertheless, diagnostic statistics for neuropsychological assessment and neuroimaging were not reported separately in this study. Moreover, there is a paucity of research investigating the specific contribution of comprehensive neuropsychological assessment in dementia diagnosis in clinical settings.

Neuropsychological Assessment

Neuropsychological assessment involves the synthesis of information from clinical interviews, review of the medical history, behavioural observations, and administration of standardised, validated psychometric instruments. Neuropsychological tests target a range of cognitive domains, including attention, memory, language, processing speed, motor skills, visuospatial/constructional abilities, general intellectual abilities, and executive functioning. Test scores for an individual are contextualised relative to a normative reference group, taking into account personal characteristics such as age, level of education, and estimated premorbid abilities [23]. By examining the pattern of

performance across tests, in conjunction with the relevant history and behavioural observations, neuropsychologists can help to specify the diagnosis, level of severity, and prognosis. Inclusion of a neuropsychological assessment as part of a comprehensive investigation purportedly improves diagnostic accuracy in dementia patients over and above routine clinical evaluation [22].

There are many studies demonstrating the effectiveness of specific neuropsychological tests in distinguishing between groups of cognitively normal and cognitively impaired adults [24, 25], MCI from AD [e.g., 25, 26], and groups of patients with specific neurological conditions [e.g., 27, 28, 29]. One study [30], for example, found that the seven subtests of the Neuropsychological Assessment Battery achieved a high level of accuracy in detecting AD. Another study by Wolfsgruber et al. [31] investigated the diagnostic accuracy of the Consortium to Establish a Registry for Alzheimer's Disease Neuropsychological Battery (CERAD-NP). The CERAD-NP Total Score was found to be an efficacious diagnostic tool for detecting AD, both in cross-sectional terms and in the prediction of incident AD.

While specific neurocognitive profiles have been identified for the dementia syndromes, in a recent review, Karantzoulis and Galvin [32] have acknowledged that there is substantial symptom overlap between disorders. Conversely, in the presence of a common underlying aetiology, there can be considerable variability in individual symptom and neurocognitive profiles. There can also be significant overlap between two or more comorbid pathologies, such as AD with vascular changes [33, 34] or AD with Lewy bodies [35, 36], which further complicates the diagnostic process. As a result, resolving diagnostic questions in dementia populations can be difficult.

The literature is replete with studies examining the utility of specific cognitive tests in differentiating normal ageing from dementia, or characterising the cognitive profiles of various diagnostic groups. The efficacy of these instruments in detecting group differences has led to an assumption that the same tests are effective at diagnosing *individuals* with those conditions. A level of caution should be exercised, however, in assuming that statistically significant differences between known groups on a given cognitive test reflect the same degree of diagnostic power at an individual level [37]. Moreover, neurodegenerative conditions have been increasingly defined by profiles of impaired performance on neuropsychological assessments, and this has led to a form of diagnostic circularity [38].

In summary, neuropsychological assessments are routinely employed in hospital settings to help establish or clarify a diagnosis of suspected dementia. To date, however, the diagnostic contribution of neuropsychological assessment in a representative sample of hospital patients has not been clearly delineated. Ideally, studies investigating diagnostic accuracy in this population should involve prospective research designs, randomised control trial methodology, large patient samples, and diagnostic confir-

mation by autopsy. These methods are, however, less than practical when working in applied settings.

An alternative method of data evaluation commonly employed in healthcare disciplines such as epidemiology, medical education, clinical research, and quality assessment involves the retrospective review of medical records. Although the limitations associated with this method are well described [39], chart reviews provide ease of access to information, are relatively low in cost to perform, and offer a practical means to inform future prospective studies [40, 41]. Using this approach, the current study aimed to examine the utility of neuropsychological assessment in patients with suspected dementia through measuring agreement between the diagnostic opinions of the neuropsychologist and medical treatment provider.

Methods

Case Selection and Procedure

A review of medical records was performed for a sample of outpatients of The Prince Charles Hospital, Brisbane, Australia, who were referred for neuropsychological assessments between 2009 and 2013, inclusive. All patients were referred for assessment by a geriatrician ($n = 64$), geriatrics registrar ($n = 13$), neurologist ($n = 4$), general medical physician ($n = 2$), or psychiatrist ($n = 1$) internal to the hospital. The group of referrers comprised 8 geriatricians, 10 geriatrics registrars, 3 neurologists, 2 general physicians, and 1 psychiatrist. Inclusion was limited to patients who were followed-up by the referring service for a minimum of 12 months post-neuropsychological assessment to allow sufficient time for diagnostic revision if warranted. Patients who were followed up in services external to the hospital were excluded from the sample due to constraints on health information access.

Of 163 cases identified initially, 60 patients received less than 12 months of follow-up while an additional 19 patients were followed-up in private facilities. These cases were excluded. The final sample comprised 84 patients; 44 males aged 56 to 86 years ($M = 69.64$, $SD = 7.49$) and 40 females aged 43 to 84 years ($M = 67.38$, $SD = 10.21$). All patients were fluent in English. The duration of patient follow-up in the referring medical service ranged from one to nine years ($M = 2.98$, $SD = 1.69$) and patients attended an average of 5.01 follow-up medical appointments ($SD = 3.27$, $range = 1 - 17$).

For 73 patients (87%), at least one neuroimaging study (CT, MRI, SPECT) was performed some time during their care, and 64 patients (76%) underwent neuroimaging prior to the baseline neuropsychological assessment (CT $n = 17$, MRI $n = 6$, SPECT $n = 19$, multiple studies $n = 22$). Due to historic electronic access restrictions, radiology reports were only accessible by the neuropsychologist prior to the baseline assessment in 46 cases (55% of the sample).

In accordance with standard clinical practice, the diagnostic opinions of the neuropsychologists drew on the available health status information at the time of assess-

ment (i.e., presenting signs and symptoms, personal and family history, medical examination results, behavioural observations, performance on neuropsychological test results and, where available, neuroimaging reports). For the purposes of diagnostic clarification or progress review, 20 patients were subsequently referred for a follow-up neuropsychological assessment (24%; *range* = 1 – 4 reviews).

A review of the neuropsychological reports revealed very limited variability in the test batteries administered, and all assessments specifically measured orientation, auditory and visual attention, verbal working memory, receptive and expressive language, verbal and visual memory, visuospatial/constructional abilities, praxis, cognitive and psychomotor processing speed, and executive functioning (i.e., mental flexibility, verbal generation, abstract reasoning, and inhibition of an over-learned response). Over the designated five-year period for chart review, eight neuropsychologists were involved in performing the assessments due to staffing changes.

Data Coding

For each case, a diagnostic opinion was obtained from the “Summary and Conclusions” section of the neuropsychology report. At the time of data coding, the researcher was blind to the most recent working diagnosis of the medical

treatment provider documented in the medical record. In a randomly selected subsample of 20 cases, two clinicians coded the reports independently, and agreement on the diagnosis emerged in all cases. In three additional cases from the larger sample ($n = 84$), diagnostic consensus was reached through further case discussion. The medical record for each patient was then reviewed separately from the neuropsychology report (i.e., in the absence of the neuropsychologist’s diagnosis).

Cases were coded as a “match” or “mismatch” between the neuropsychology diagnosis and the current diagnosis of the treatment provider. For the purposes of comparison, two coding processes were undertaken. The first coding process aimed to take into account the diagnostic complexity that arises from: (1) the difference between a clinical diagnosis and underlying pathology (e.g., MCI arising from Alzheimer’s disease versus vascular ischaemia); (2) the high prevalence of comorbid pathologies in this population (e.g., mixed Alzheimer’s and vascular); (3) uncertainty about a specific diagnosis early in the disease process; and (4) the significant overlap in symptom profiles (refer to Table 1 for the coding criteria). For the second coding process, cases were only considered a match where the diagnosis of the neuropsychologist was identical to that of the treatment provider.

Table 1. Secondary Coding Criteria for Diagnostic Agreement between Neuropsychology and the Current Diagnosis of the Treatment Provider.

Baseline Neuropsychology Diagnosis ($n = 84$)	Current Medical Working Diagnosis										
	^a MCI	^b AD	^c Vasc	^d Mixed AD/Vasc	^e FTD	^f LBD	^g PCA	^h PSP	ⁱ Logopenic	> Two Diagnoses	Not Specified
Alzheimer’s disease/early AD ($n = 20$)	✓	✓	×	✓	×	×	×	×	×	×	×
Mild cognitive impairment ($n = 19$)	✓	✓	✓	✓	×	×	×	×	×	×	×
Vascular-related impairment/dementia ($n = 8$)	✓	×	✓	✓	×	×	×	×	×	×	×
Mixed AD and vascular ($n = 6$)	×	✓	✓	✓	×	×	×	×	×	×	×
Lewy body dementia ($n = 5$)	×	×	×	×	×	✓	×	×	×	×	×
Frontal variant FTD ($n = 3$)	×	×	×	×	✓	×	×	×	×	×	×
ⁱ Two differentials (e.g., AD vs. FTD $n = 2$; AD vs. vascular $n = 1$)	×	✓	✓	×	✓	×	×	×	×	×	×
Multiple aetiologies ($n = 4$)	×	×	×	×	×	×	×	×	×	✓	×
Progressive non-fluent aphasia ($n = 3$)	×	×	×	×	✓	×	×	×	×	×	×
Posterior cortical atrophy ($n = 3$)	×	×	×	×	×	×	✓	×	×	×	×
No dementia (with previous diagnosis; $n = 3$)	✓	×	×	×	×	×	×	×	×	×	×
Primary psychological disorder (e.g., depression, anxiety; $n = 3$)	✓	×	×	×	×	×	×	×	×	×	×
Logopenic progressive aphasia ($n = 2$)	×	×	×	×	×	×	×	×	✓	×	×
Semantic dementia ($n = 1$)	×	×	×	×	✓	×	×	×	×	×	×
Progressive Supranuclear Palsy ($n = 1$)	×	×	×	×	×	×	×	✓	×	×	×

Note. Checkmark = “match”; cross = “mismatch”. ^aMCI = Mild Cognitive Impairment; ^bAD = Alzheimer’s disease; ^cVasc = vascular pathology; ^dMixed AD/Vasc = mixed Alzheimer’s and vascular pathology; ^eFTD = frontotemporal dementia (including behavioural variant, semantic dementia, and progressive non-fluent aphasia); ^fLBD = Lewy body dementia; ^gPCA = posterior cortical atrophy; ^hPSP = progressive supranuclear palsy; ⁱLogopenic progressive aphasia; where one differential is a match.

Results

From the baseline neuropsychological assessment report ($n = 84$), the most frequent diagnosis was AD ($n = 20$), followed by MCI ($n = 19$), vascular dementia ($n = 8$), mixed Alzheimer's and vascular ($n = 6$), Lewy body dementia ($n = 5$), frontal variant frontotemporal dementia (fvFTD; $n = 3$), progressive non-fluent aphasia ($n = 3$), posterior cortical atrophy ($n = 3$), logopenic progressive aphasia ($n = 2$), semantic dementia ($n = 1$), and progressive supranuclear palsy ($n = 1$). The remaining neuropsychological reports proposed two differential diagnoses (e.g., Alzheimer's disease versus frontotemporal dementia; $n = 3$), multiple aetiologies ($n = 4$), a primary diagnosis of a psychological disorder ($n = 3$), or a finding of "no dementia" in cases with a previous working diagnosis of dementia ($n = 3$).

Applying the coding criteria detailed in Table 1, the diagnosis of the neuropsychologist at the time of the baseline assessment concurred with the most recent diagnosis of the treatment provider in 74 cases (88%). No significant difference in diagnostic agreement emerged for patients with ($n = 46$) and without ($n = 38$) an imaging report prior to the neuropsychological assessment, $z = 0.6$, $p > .05$. With regard to follow-up, 20 patients completed serial neuropsychological assessments for the purposes of diagnostic clarification. A diagnostic revision was only recommended in three of these cases (15%; or 4% of the full sample). Furthermore, diagnostic agreement did not improve when the most recent assessment time points for all patients were examined, taking into account the 20 patients who received repeat assessment (i.e., agreement in 75 cases [89%]; $z = 0.9$, $p > .05$). Refer to Figure 1.

In terms of exact matches, the diagnosis of the neuropsychologist at baseline concurred with the most recent medical diagnosis in 65 of the 84 cases reviewed (77%). Again, there was no statistical difference in diagnostic agreement for patients with ($n = 46$) and without ($n = 38$) an available imaging report prior to the baseline neuropsychological assessment, $z = 1.6$, $p > .05$. Of the 19 mismatched cases, nine were attributable to one versus two differentials, but where one differential matched (e.g., AD or FTD versus AD); three were discrepant between clinical diagnosis and pathology (MCI versus AD); and the remaining eight were different pathologies (e.g., AD versus FTD, Lewy body versus Multiple Systems Atrophy). When data pertaining to the most recent assessments for all patients were examined, no significant improvement in diagnostic agreement emerged (81%; $z = 0.6$, $p > .05$).

Discussion

This study investigated the diagnostic contribution of neuropsychological assessment in patients with suspected dementia. From a review of 84 cases, there was a high level of agreement between the diagnostic opinion of the neuropsychologist at baseline and the most recent diagnosis

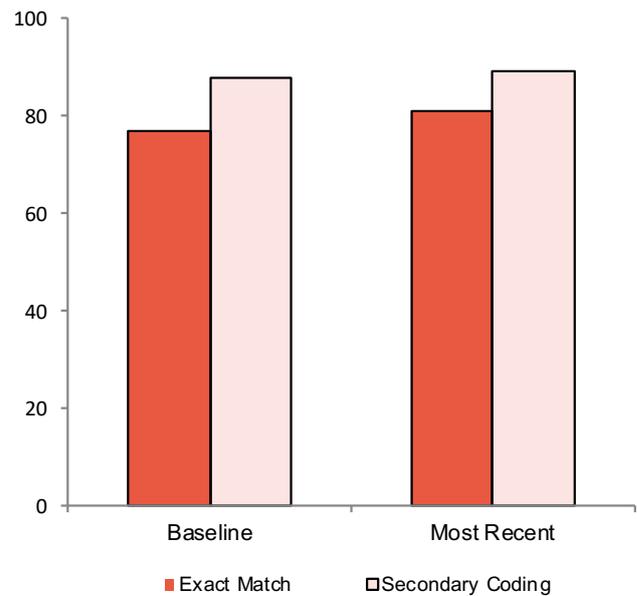


Figure 1. Agreement (in percentages) between the neuropsychological and medical diagnoses ($n = 84$) at baseline and most recent follow-up (refer to Table 1 for multifactorial coding parameters).

of the medical treatment provider, independent of whether or not the neuropsychologist had access to an existing neuroimaging study prior to the assessment. For diagnostic clarification, 20 patients were later re-referred for a neuropsychological review, although no improvement in diagnostic agreement was found in this sample for patients who received serial assessments. A range of factors could account for this finding including the limited sample size, and increased case complexity and ambiguity. Only the most diagnostically challenging cases were referred for a re-assessment. The treatment provider may therefore have been more inclined to adopt the diagnosis of the neuropsychologist due to complexity and ambiguity in these cases. Nevertheless, the findings suggest that neuropsychological assessment contributes to distinguishing between neurocognitive disorders in older adults with a relatively high level of accuracy.

In addition to informing diagnosis, neuropsychological findings can influence treatment decisions, either by diagnostic implication or by recommending management strategies. A further benefit of neuropsychological testing is the opportunity to identify areas of residual strength to inform therapeutic interventions and maximise patients' everyday functioning [42]. A number of the neuropsychology reports reviewed in this study provided specific recommendations for additional medical investigations (e.g., sleep studies, genetic screening, psychiatry reviews), community support services (e.g., dementia support groups, respite services), lifestyle and safety considerations (e.g., impact on functional abilities, implications for driving), psychological interventions (e.g., treatment for depression and anxiety disorders), and/or inclusion in a clinical research trial. Neuropsychological assessment also remains the preferred method to evaluate dementia treat-

ment response, and predict functional potential/recovery [43]. Furthermore, neuropsychological findings can have legal implications for guardianship and other matters of decision-making capacity [44]. This holistic approach to the care of older adults ensures that patients are informed about, and given access to, the most appropriate assessment, treatment, and management options available at any given time point.

Cautions and Limitations

While the current findings provide useful information regarding the utility of neuropsychological assessment of dementia, the study was based on a retrospective review of medical records, and several cautions are warranted in light of recognised limitations in the methodology. Specific issues, for example, relate to sampling methods, inter-rater reliability, blind coding, inclusion and exclusion criteria, and data extraction methods. The current study relied on a single-centre, convenience sample of patients and the clinicians who coded the data were not blind to the purpose of the study. Blinding of raters can represent a significant barrier to the validity of diagnostic accuracy studies in dementia. However, unlike research settings where a number of personnel may be available to undertake separate aspects of data collection and analysis, blinding procedures can be challenging to implement in a small clinical team working in an applied outpatient setting. Although a number of measures were taken to standardise the data coding and extraction procedures during the pilot phase, further research is needed using prospective designs and blind coding processes.

A second limitation pertains to the limited sample size relative to the subset of neurodegenerative conditions captured, resulting in minimum cell sizes for several diagnostic entities (e.g., Lewy body dementia, posterior cortical atrophy, semantic dementia). These factors could obscure interpretation of the results and limit the detection of improved or reduced diagnostic agreement based on factors such as base rates and case complexity. Other neurological disorders that are characterised by cognitive decline such as corticobasal degeneration, multiple systems atrophy, and prion diseases (e.g., Creutzfeldt Jakob Disease; CJD) have lower prevalence rates in the general population [45, 46] but continue to pose a diagnostic challenge. Further research is therefore needed to examine the diagnostic contribution of neuropsychological assessment in these patient groups for which our own data were limited.

A third caution concerns the secondary data coding criteria. The primary standard for diagnostic agreement in this study was an exact match between the diagnostic opinion of the neuropsychologist and that of the treatment provider. A second coding process was undertaken, however, to allow for the diagnostic complexities that arise in this population. Such complexities include the high prevalence of comorbid pathologies (i.e., Alzheimer's and vascular), diagnostic uncertainty early in the disease

process, the significant overlap in symptom profiles, and the distinction between a clinical diagnosis and underlying pathology (e.g., MCI and Alzheimer's disease). While this approach to data analysis may be reasonable from a clinical perspective, an artificially inflated level of agreement with regard to the secondary coding process cannot be excluded, and those specific results should be interpreted with caution.

Finally, while diagnostic accuracy in this study was operationalised as agreement between neuropsychology and treating medical consultant opinion, the "gold standard" for diagnostic confirmation of dementia involves prospective research design with post-mortem examination of brain tissue. Thus, efforts should be made to obtain data linked to neuropathological confirmation of diagnoses. In vivo measures such as CSF and serum amyloid, CSF p-Tau, and PET imaging also provide valuable diagnostic information. These investigative methods were well beyond the scope of the present work, which was conducted in an allied health clinical setting where advanced imaging and biomarker studies were not available. Given this, these findings can only be considered preliminary but have practical value in informing future prospective studies in diagnostic accuracy.

Conclusions

The current findings provide evidence of the significant contribution that neuropsychological assessment makes in the diagnosis of dementia in an applied setting, helping to distinguish different underlying pathologies when changes may not be evident on neuroimaging studies [16, 17]. A high level of agreement emerged between the diagnostic opinion of the neuropsychologist and the most recent diagnosis of the medical treatment provider, independent of neuroimaging evidence. Although retrospective methods of evaluating diagnostic accuracy, as used here, have inherent limitations, clinical investigations in this realm should continue in an effort to evaluate and improve clinical practice.

Methods of optimising diagnostic accuracy, including neurocognitive testing, will play an increasingly critical role into the future by assisting clinicians, policy-makers, and patients to make informed decisions about healthcare. Additionally, with the advent of ligands to detect beta amyloid on PET imaging, individuals will be informed that they are at heightened risk of experiencing degenerative changes in the future. Detection of such changes in the brain raises the question of functional impact in everyday life, a construct that is well informed by neuropsychological assessment. Furthermore, as cortical degeneration has been identified post-mortem in individuals with no discernible evidence of cognitive impairment during life, there will be an increased need to perform neuropsychological assessment following diagnostic imaging [43].

Further refinement of standardised neuropsychological assessment tools will aim to contribute to improved diagnostic accuracy, and have important implications for

the treatment and management of patients with cognitive disturbances. Neuropsychological testing provides information that cannot be obtained through other modalities regarding specific abilities, motivation, and potential for future outcomes. Even with advances in imaging technology, it is therefore likely that neuropsychological assessment will continue to play a pivotal role in the diagnosis and management of dementia.

Abbreviations

AD: Alzheimer's disease; CERAD-NP: Consortium to Establish a Registry for Alzheimer's Disease Neuropsychological Battery; CSF: Cerebrospinal fluid; CT: Computed tomography; FDG-PET: Fluorodeoxyglucose positron emission tomography; FTD: Frontotemporal dementia; FTLD: Frontotemporal lobar degeneration; MRI: Magnetic resonance imaging; NINCDS-ADRDA: National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association; PiB: Pittsburgh compound B; p-Tau: Phosphorylated tau; SPECT: Single-photon emission computed tomography

References

- Panegyres PK, Berry R, Burchell J. Early dementia screening. *Diagnostics* 2016; 6.
- Snowden JS, Thompson JC, Stopford CL, Richardson AMT, Gerhard A, Neary D, et al. The clinical diagnosis of early-onset dementias: Diagnostic accuracy and clinicopathological relationships. *Brain* 2011; 134(Pt 9):2478-92. <https://doi.org/10.1093/brain/awr189>
- McKhann GM, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology* 1984; 34(7):939-44. <https://doi.org/10.1212/WNL.34.7.939>
- McKhann GM, Knopman DD, Chertkow H, Hyman BT, Jack CR, Kawas CH, et al. The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging and the Alzheimer's Association workgroup. *Alzheimer's and Dementia* 2011; 7(3):263-9. <https://doi.org/10.1016/j.jalz.2011.03.005>
- Knopman DS, DeKosky ST, Cummings JL, Chui H, Corey-Bloom J, Relkin N, et al. Practice parameter: diagnosis of dementia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2001; 56(9):1143-53. <https://doi.org/10.1212/WNL.56.9.1143>
- Neary D, Snowden J, Gustafson L, Passant U, Studd D, Black S, et al. Frontotemporal lobar degeneration: A consensus of clinical diagnostic criteria. *Neurology* 1998; 51(6):1546-54. <https://doi.org/10.1212/WNL.51.6.1546>
- McKeith I, Galasko D, Kosaka K, Perry EK, Dickson DW, Hansen LA, et al. Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): Report of the Consortium on DLB International Workshop. *Neurology* 1996; 47(5):1113-24. <https://doi.org/10.1212/WNL.47.5.1113>
- Emre M, Aarsland D, Brown R, Burn DJ, Duyckaerts C, Mizuno Y, et al. Clinical diagnostic criteria for dementia associated with Parkinson's disease. *Movement Disorders* 2007; 22(12):1689-707. <https://doi.org/10.1002/mds.2150>
- Roman GC, Tatemichi TK, Erkinjuntti T, Cummings JL, Masdeau JC, Garcia JH, et al. Vascular dementia. Diagnostic criteria for research studies: Report of the NINDS-AIREN International Workshop. *Neurology*. 1993; 43(2):250-60. <https://doi.org/10.1212/WNL.43.2.250>
- Rascovsky K, Hodges JR, Knopman D, Mendez MF, Kramer JH, Neuhaus J, et al. Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. *Brain* 2011; 134:456-77. <https://doi.org/10.1093/brain/awr179>
- Gorno-Tempini ML, Hillis AE, Weintraub S, Kertesz A, Mendez M, Cappa SF, et al. Classification of primary progressive aphasia and its variants. *Neurology* 2011; 76:1006-14. <https://doi.org/10.1212/WNL.0b013e31821103e6>
- Klunk WE, Engler H, Nordberg A, Wang Y, Blomqvist G, Holt DP, et al. Imaging brain amyloid in Alzheimer's disease with Pittsburgh Compound-B. *Annals of Neurology* 2004; 55(3):306-19. <https://doi.org/10.1002/ana.20009>
- Jagust W, Thisted R, Devous MD, Sr., Van Heertum R, Mayberg H, Jobst K, et al. SPECT perfusion imaging in the diagnosis of Alzheimer's disease: a clinical-pathologic study. *Neurology* 2001; 56(7):950-6. <https://doi.org/10.1212/WNL.56.7.950>
- Schoonenboom NS, van der Flier WM, Blankenstein MA, Bouwman FH, Van Kamp GJ, Barkhof F, et al. CSF and MRI markers independently contribute to the diagnosis of Alzheimer's disease. *Neurobiology of Aging* 2008; 29(5):669-75. <https://doi.org/10.1016/j.neurobiolaging.2006.11.018>
- Noel-Storr AH, Flicker L, Ritchie CW, Nguyen GH, Gupta T, Wood P, et al. Systematic review of the body of evidence for the use of biomarkers in the diagnosis of dementia. *Alzheimer's & Dementia* 2013; 9(3):e96-e105. <https://doi.org/10.1016/j.jalz.2012.01.014>
- Bigler ED. Neuropsychological testing defines the neurobehavioral significance of neuroimaging-identified abnormalities. *Archives of Clinical Neuropsychology* 2001; 16(3):227-36. <https://doi.org/10.1093/arclin/16.3.227>
- Hüsing B, Jäncke L, Tag B. Impact assessment of neuroimaging: Final report. Netherlands: IOS Press; 2006.
- Braun M, Tupper D, Kaufman P, McCrea M, Postal K, Westerveld M, et al. Neuropsychological assessment: A valuable tool in the diagnosis and management of neurological, neurodevelopmental, medical, and psychiatric disorders. *Cognitive and Behavioral Neurology* 2011; 24(3):107-14. <https://doi.org/10.1097/WNN.0b013e3182351289>
- American Psychological Association. Guidelines for the evaluation of dementia and age-related cognitive change. *American Psychologist* 2012; 67(1):1-9. <https://doi.org/10.1037/a0024643>
- Hentschel F, Kreis M, Damian M, Krumm B, Frolich L. The clinical utility of structural neuroimaging with MRI for diagnosis and differential diagnosis of dementia: A memory clinic study. *International Journal of Geriatric Psychiatry* 2005; 20(7):645-50. <https://doi.org/10.1002/gps.1333>
- Snowden JS, Thompson JC, Stopford CL, Richardson AMT, Gerhard A, Neary D, et al. The clinical diagnosis of early-onset dementias: Diagnostic accuracy and clinicopathological relationships. *Brain* 2011; 134:2478-92. <https://doi.org/10.1093/brain/awr189>
- Geroldi C, Canu E, Bruni AC, Dal Forno G, Ferri R, Gabelli C, et al. The added value of neuropsychologic tests and structural imaging for the etiologic diagnosis of dementia in Italian expert centers. *Alzheimer's Disease and Associated Disorders* 2008; 22(4):309-20. <https://doi.org/10.1097/WAD.0b013e3181871a47>
- Lezak MD, Howieson DB, Bigler ED, Tranel D. *Neuropsychological assessment*. 5th ed. New York: Oxford University Press; 2012.
- Yagi T, Ito D, Sugiyama D, Iwasawa S, Tabuchi H, Konishi M, et al. Diagnostic accuracy of neuropsychological tests for classification of dementia. *Neurology Asia* 2016; 21(1):47-54.

25. Salmon DP, Thomas RG, Pay MM, Booth A, Hofstetter CR, Thal LJ, et al. Alzheimer's disease can be accurately diagnosed in very mildly impaired individuals. *Neurology* 2002; 59(7):1022-8. <https://doi.org/10.1212/WNL.59.7.1022>
26. Martinelli JE, Cecato JF, Bartholomeu D, Montiel JM. Comparison of the Diagnostic Accuracy of Neuropsychological Tests in Differentiating Alzheimer's Disease from Mild Cognitive Impairment: Can the Montreal Cognitive Assessment Be Better than the Cambridge Cognitive Examination? *Dementia and Geriatric Cognitive Disorders EXTRA* 2014; 4(2):113-21. <https://doi.org/10.1159/000360279>
27. Hanyu H, Sato T, Kume K, Takada Y, Onuma T, Iwamoto T. Differentiation of dementia with Lewy bodies from Alzheimer disease using the Frontal Assessment Battery test. *International Journal of Geriatric Psychiatry* 2009; 24(9):1034-5. <https://doi.org/10.1002/gps.2219>
28. Jimenez-Huete A, Riva E, Toledano R, Campo P, Esteban J, Del Barrio A, Franch, O. Differential diagnosis of degenerative dementias using basic neuropsychological tests: Multivariable logistic regression analysis of 301 patients. *American Journal of Alzheimer's Disease and Other Dementias* 2014; 29(8):723-31. <https://doi.org/10.1177/1533317514534954>
29. Libon DJ, Xie SX, Moore P, Farmer J, Antani S, McCawley G, et al. Patterns of neuropsychological impairment in frontotemporal dementia. *Neurology* 2007; 68(5):369-75. <https://doi.org/10.1212/01.wnl.0000252820.81313.9b>
30. Gavett BE, Lou KR, Daneshvar DH, Green RC, Jefferson AL, Stern RA. Diagnostic accuracy statistics for seven Neuropsychological Assessment Battery (NAB) variables in the diagnosis of Alzheimer's disease. *Applied Neuropsychology: Adult* 2012; 19(2):108-15. <https://doi.org/10.1080/09084282.2011.643947>
31. Wolfsgruber S, Jessen F, Wiese B, Stein J, Bickel H, Mösch E, et al. The CERAD neuropsychological assessment battery total score detects and predicts Alzheimer disease dementia with high diagnostic accuracy. *American Journal of Geriatric Psychiatry* 2014; 22:1017-28. <https://doi.org/10.1016/j.jagp.2012.08.021>
32. Karantzoulis S, Galvin JE. Distinguishing Alzheimer's disease from other major forms of dementia. *Expert Review of Neurotherapeutics* 2011; 11(11):1613-20. <https://doi.org/10.1586/ern.11.155>
33. Attems J, Jellinger KA. The overlap between vascular disease and Alzheimer's disease - lessons from pathology. *BMC Medicine* 2014; 12(1):206. <https://doi.org/10.1186/s12916-014-0206-2>
34. Iadecola C. The overlap between neurodegenerative and vascular factors in the pathogenesis of dementia. *Acta Neuropathologica* 2010; 120. <https://doi.org/10.1007/s00401-010-0718-6>
35. Mrazek RE, Griffin WST. Dementia with Lewy bodies: Definition, diagnosis, and pathogenic relationship to Alzheimer's disease. *Neuropsychiatric Disease and Treatment* 2007; 3(5):619-25.
36. McKeith I. Dementia with Lewy bodies. *Dialogues in Clinical Neuroscience* 2004; 6(3):333-41. [https://doi.org/10.1016/S1474-4422\(03\)00619-7](https://doi.org/10.1016/S1474-4422(03)00619-7)
37. Ivnik RJ, Smith GE, Petersen RC, Boeve BF, Kokmen E, Tangalos EG. Diagnostic accuracy of four approaches to interpreting neuropsychological test data. *Neuropsychology* 2000; 14(2):163-77. <https://doi.org/10.1037/0894-4105.14.2.163>
38. McCaffrey RJ, Palav AA, O'Bryant S, Labarge AS. Practitioner's guide to symptom base rates in clinical neuropsychology. New York: Springer Publishing; 2003. <https://doi.org/10.1007/978-1-4615-0079-7>
39. Vassar M, Holzmann M. The retrospective chart review: Important methodological considerations. *Journal of Educational Evaluation for Health Professions* 2013; 10:12. <https://doi.org/10.3352/jeehp.2013.10.12>
40. Gearing RE, Mian IA, Barber J, Ickowicz A. A Methodology for Conducting Retrospective Chart Review Research in Child and Adolescent Psychiatry. *Journal of the Canadian Academy of Child and Adolescent Psychiatry* 2006; 15(3):126-34.
41. Wickson-Griffiths A, Kaasalainen S, Ploeg J, McAiney C. Revisiting retrospective chart review: An evaluation of nursing home palliative and end-of-life care research. *Palliative Medicine and Care* 2014; 1(2):1-8.
42. Fields JA, Ferman TJ, Boeve BF, Smith GE. Neuropsychological assessment of patients with dementing illness. *Nature Reviews Neurology* 2011; 7(12):677-87. <https://doi.org/10.1038/nrneuro.2011.173>
43. Harvey PD. Clinical applications of neuropsychological assessment. *Dialogues in Clinical Neuroscience* 2012; 14:91-9.
44. Crosson B. Application of neuropsychological assessment results. In: Vanderploeg RD, editor. *Clinician's guide to neuropsychological assessment*. Mahwah, N. J.: Lawrence Erlbaum Associates; 2000. p. 195-244.
45. Pedersen NS, Smith E. Prion diseases: Epidemiology in man. *APMIS* 2002; 110(1):14-22. <https://doi.org/10.1034/j.1600-0463.2002.100103.x>
46. Tison F, Yekhelef F, Chrysostome V, Sourgen C. Prevalence of multiple system atrophy. *The Lancet*; 355(9202):495-6. [https://doi.org/10.1016/S0140-6736\(00\)82050-4](https://doi.org/10.1016/S0140-6736(00)82050-4)