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Subject: screening, brain blood flow imaging

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Diagnosing Dementia in Rural NSW.

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Abstract

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189 words

Keywords: screening, brain blood flow imaging.

What is already known on this subject:

- Rural circumstances result in diagnostic disadvantage for determination of dementia and specifically dementia type;
- Neuroimaging in the form of SPECT, when combined with neuropsychological testing is capable of assisting in providing a differential diagnosis in dementia.

What this study adds:

- SPECT is available in many rural areas of Australia and can be successfully utilised to aid in dementia diagnosis potentially lessening the rural disadvantage, particularly in the absence of neuropsychological testing.
- The MMSE, despite being discriminate for cognitive decline in large statistical studies for cognitive decline, does not necessarily demonstrate such patterns in individuals.

Introduction

In 1999, NSW Health undertook a major survey of those aged 65 years or more that determined 3% of the aged community had or were likely to have dementia.¹ Based upon the local government area population statistics this translates potentially into 50 persons for each GP residing in the rural area of this study.² In 1998 the ABS listed presenile conditions as the eighth leading cause of death. The dementia sufferer has a higher risk of morbidity due to the nature of the cognitive impairments that result in an inability to report symptoms.³ By 2041 it is expected that 22% of the Australian population will be aged 65 years or more.⁴

An accurate sole diagnostic test of dementia type remains problematic and diagnosis remains largely by exclusion of other causes. There are more than 20 different causes of dementia.^{5,6} Pharmacological interventions to mediate progression are increasing however, effective prescribing requires a semblance of accurate diagnosis. There remains no clear boundary between cognitive decline and dementia diagnosis. It is known that only some of these patients will progress to dementia. Identification of prodromal stages for instigation of therapy has the potential to assist these patients. The Lidcombe Hospital Memory Clinic, NSW, found 11% of 100 reviewed records of those deemed with cognitive disorders had potentially reversible causes.⁷ Misdiagnosis has been recorded as high as 25%.⁸ It is also worth noting that fronto-temporal dementia (FTD) has an onset up to 10 years earlier than SDAT and has been documented in people as young as 21 years.⁹ Earlier diagnosis results in earlier treatment and better social and medical management. However, a study in rural Texas found that limited access to specialists and educational resources were major impediments to dementia diagnosis for primary care

providers and another determined that less than half of dementia cases are diagnosed by physicians.¹⁰

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Developed clinical pathways, including the DSM IV criteria, do not, as yet, include neuroimaging as discriminating components. Anatomical lesions as causation are excluded using CT when indicated. Blood flow imaging indicates blood flow distribution to the brain regions for cell metabolism. Imaging has steadily improved in resolution and many imaging agents have been developed, the optimal equipment being a positron emission tomography (PET) camera and associated radiopharmaceuticals. Although these facilities are increasing in numbers in Australia where they now exist in some capital cities, they by no means approach the levels of availability in the USA where the Food and Drug Administration (FDA) has recognised PET imaging as a worthwhile diagnostic test for differential diagnosis of Alzheimer's disease.¹² Single Photon Emission Tomography (SPECT) is available in regional Australia and although lacking the resolution of PET, (SPECT is approximately 7mm whereas PET is approximately 4mm)¹³ it does provide good quality blood flow images that mirror the patterns displayed on PET studies. As a sole diagnostic test, SPECT correctly identified 83% of persons with dementia (200 dementia cases, 143 with autopsy results and 119 age matched controls) and when combined with neuropsychological testing increased this value to 86%.¹⁴ Neuropsychological testing to determine SDAT is reported as having 86% accuracy as a baseline tool relative to neuropathology, which improves to 91.4% when follow-up studies are conducted over 5 years (Becker et al, 1994). A systematic review published in 2004 indicated that although clinical criteria may have better sensitivity than SPECT for SDAT, this form of imaging had a higher specificity against other dementia types than clinical criteria (91% versus 70%) when compared to pathology results.¹⁵ An Australian study in 2005 evaluated SPECT in light of newer protocols with 18 patients finding that the technique does have potential to assist in diagnosis.¹⁶ It has been demonstrated that rCBF SPECT can identify pre-clinical SDAT with a sensitivity and specificity of 77.8%.¹⁷ Combining SPECT and Neuropsychological testing at initial presentation might result in achieving more accurate results earlier. A negative test result in a SPECT or MRI gives a high specificity of 93 to 98%.¹⁸

Full neuropsychological testing can take between two and four hours to complete. Tests assess functions of attention and concentration, orientation, general insight, learning and memory, abstraction, multi-tasking and behavioural flexibility to name a few. These test results may be influenced by cultural diversity: available research into their appropriateness for Indigenous populations is limited. The Mini Mental State Exam (MMSE) developed by Folstein, Folstein and McHugh (1975) continues to be used as an indicator of dementia despite the development of other screening tools and is usually included as part of a neuropsychological assessment.¹⁹ The MMSE contains 19 items that provide a maximum score of 30 for normal cognition and can be delivered in five minutes. In large statistical studies it has been shown to be an effective method of determining cognitive decline although corrections for education and socio-economic status may be necessary and persons with FTD can achieve a high normal MMSE score.^{20, 21} The sensitivity and specificity have been recorded as high as 87% for a score of 24 or less and 96% respectively.^{22, 3} To accommodate higher education levels it has been recommended that the discriminate score should be 27.³ Depression has also been shown to hinder patients achieving 'true' scores for their cognitive status.²³ The MMSE has been tested specifically for its use in general practice finding little difference: 65% sensitivity and 93% specificity and for rural versus urban differences finding the greatest variance in sensitivity – 83% versus 73% respectively.^{20, 21} Specificity was 74% versus 78% and accuracy 75% versus 77%.^{24, 25} Ethnic diversity may also influence MMSE scores and may not reliably indicate cognitive decline, therefore, in Indigenous people whose population are a significant component of rural areas, the MMSE may not be an appropriate tool.²²

Method

The method used for this study was a retrospective medical audit. All information in the medical records is textual in nature and interpretation dependant on the reader. Hence, the framework for this study was that of a hermeneutical circle, where credibility is conferred by reiteration whilst acknowledging that understanding is due to the inheritance of language and non-conscious processes of discipline socialisation.²⁶ The first author of this paper does not claim expertise in all the disciplines for which medical reports were available. To minimise this limitation, a general and specialist physician, with extensive experience in blood flow imaging, provided necessary insights.

The regional population was approximately 172,000 within a geographical region of 59,835 sq. km. and the specialists servicing this region also support the population of the neighbouring 116,720 sq. km.²⁷ SPECT brain perfusion imaging referrals numbered 88 over a two year period. For each SPECT report clinical histories were constructed from records held at the Base Hospital and Extended Care Facility. They included: reasons for Aged Care Assessment Team (ACAT) referral, previous medical history, medication lists, blood pathology results, CT, neurology and neuropsychology reports including MMSE; occupational therapy reports, hospital discharge summaries and letters between medical specialists. Diagnostic test results were reviewed and compared.

Results

Equal numbers of males and females records were retrieved. No reversible causes of dementia were identified. Of the SPECT referrals only two were for conditions other than suspected dementia. One study had an indeterminate result due to patient movement causing imaging artefacts. A repeat study was not found.

SDAT was diagnosed for 40% of those referred, vascular causes were determined for a further 27% and 6% demonstrated mixed disease patterns. Where a final diagnosis was given, MMSE were available for 27 matched for the time of diagnosis. These are given in Table 1. No particular pattern in scores is suggestive for any diagnostic category.

Matching neuropsychological reports and CTs were available for 17 patients that had undergone SPECT. These are reported in Table 2. For those studies (coded D1 – 6 in Table 2) where consensus for a diagnosis was not reached a follow-up study was recommended, the results for which were not evident. Depression can demonstrate as decreased blood perfusion on PET which may be confounding these SPECT results.^{28,29} The low numbers of neuropsychology reports reflects the availability of the service in this regional area. No known MRIs were performed. Those studies coded A1 – 7 in Table 2 demonstrate the agreement in diagnosis based upon the wording of the reports. Those coded B1 – 4 demonstrate some level of agreement but not entirely matched diagnostic report text. A paired *t*-test was calculated (the wording reduced to numerical codes) indicating that there was no significant difference between the neuropsychological reports and the SPECT reports (0.05). No matching brain biopsy or pathology at autopsy were found.

Matching CT results were available for 37 of the SPECT studies. The low number of CTs may have been due to the need to travel away for the study prior the time the data was retrieved. The CT result concurred with a diagnosis of ischaemia in only five of the ten cases identified by SPECT. Four of these cases were determined by SPECT to also have SDAT. The CT reports indicated a further five patients as having ischaemia whose SPECT demonstrated normal cerebral blood perfusion.

It is of interest that 31% of the referrals for SPECT for dementia screening were requested by general practitioners. The remaining 69% of referrals came from the regions three physicians, two neurologists and two (one full-time and one part-time) gerontologists.

Discussion

Differentiating dementia, depression and delirium have always been a major concern for aged care health workers. Not all cases of cognitive impairment progress to dementia and this can further confound diagnosis. Post-mortem pathology has identified that as many as 34% of those with a dementia diagnosis have no pathological signs beyond the normal aging process.³⁰ Given the increasing treatment options to improve the quality of life for those with dementia it behoves the medical profession to better diagnose the condition so that these can be tailored for maximum effectiveness.

Rural circumstances result in many disadvantages including less variability in medical resources. The existing resources must be used for their maximum benefit. Large overseas studies have demonstrated the advantages of using neuropsychological testing in concert with neuroimaging for diagnosing and differentiating dementia types. This has been recognised by the US FDA by the provision of funding for PET studies for SDAT. Although this study is a small and retrospective it has indicated that SPECT imaging can assist in rural areas. The consensus reached for patients A1-7 provides a measure of confidence that tailored treatment regimes are appropriate. In patients B1-4, where the report

narratives overlap but not agree in entirety, then the alternate diagnosis may prove helpful or follow-up studies may prove beneficial. When reviewing patients D1-6 the difficulty of confounding issues become evident. Depression is proposed as a possibility for dementing behaviours in half these studies. Best practice evidenced by the literature indicates no one test is entirely reliable but a consensus of test results is helpful. If SPECT is available in the absence of neuropsychological testing services then some level of diagnostic accuracy is possible when there remains no 'gold standards', to enable potential tailored treatment plans to be commenced. However, this study can only be interpreted in the context of the available literature for accuracy, sensitivity and specificity of SPECT and neuropsychological testing given that no pathology results are available regarding these patients.

This medical record audit also provided MMSE scores from the medical reports that when matched against the resultant diagnosis raise the question whether, despite its promise determined by large statistical studies, it is useful in differentiating dementia. Other tools have been developed for use by general practitioners such as the GPCOG.³¹ The large number of referring GPs reflects the nature of rural practice and the burden of diagnosis that resides with them. Specialists have an opportunity to provide further education via their diagnostic reports and the development of updated diagnostic pathways to assist GPs may be of benefit.

Conclusion and Recommendations

The literature review material and this small retrospective medical record audit has indicated that SPECT can be of assistance in rural areas for the diagnosis of dementia and differentiating dementia type. In light of the current literature an information paper concerning clinical considerations for the referral for SPECT would be timely.

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2340 words without including those in the Tables.

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Table 1.
MMSE scores corresponding to dementia diagnosis.

Final diagnostic result	MMSE score
Vascular dementia	21, 16, 27, 19, 23
SDAT	27, 15, 16, 18, 20, 25, 17, 25, 23, 30, 22, 29, 19
? Pick's disease	20, 22
Depression	27, 25, 24, 28, 20
NAD	24, 30

Table 2.

Matched results for neuropsychological, CT and SPECT reports.

No significant difference was found between test results (P - 0.05); (NAD – no abnormality detected).

Code	SPECT result	Neuropsychology report	CT report
A1	NAD	Non dementing process	NAD
A2	Early SDAT	Early SDAT	NAD for age
A3	SDAT	SDAT	NAD
A4	SDAT and depression	Early SDAT	NAD
A5	NAD	Anterograde memory disorder, probably not SDAT	? TIA in left carotid artery, otherwise NAD for age
A6	Ischaemia left cerebral artery involving left fronto-temporal lobe	Subcortical pathology, not SDAT	Opacity Right temporal region, cerebral aneurysm
A7	Vascular disease	Subcortical pathology, not SDAT	NAD for age
B1	Frontal lobe SDAT or Pick's disease	Frontal lobe SDAT and ? depression	NAD
B2	Atypical for SDAT but consistent with dementia (hypoperfusion right fronto-parietal, left tempo-parietal lobes).	Early frontal lobe dementia or depression	Old infarct right side of pons, else NAD for age
B3	Possible depression, otherwise frontal lobe disease should be considered	Very early frontal lobe variant of SDAT, no depression.	NAD
B4	? Pick's disease	Suggestive of SDAT	NAD
D1	SDAT	Impairment consistent with a number of disorders, ? depression	NAD for age
D2	NAD	? depression	NAD
D3	NAD	depression	NAD for age
D4	NAD	? early SDAT	NAD
D5	Subtle hypoperfusion right parietal occipital lobe, else NAD	Probable SDAT	NAD
D6	Indeterminate due to severe movement in study	Early middle dementing process probably SDAT	NAD for age