The GADS is an acceptable instrument that can distinguish between older women with and without mental health problems.

Key points
- Anxiety and depression in older women may be viewed as a unitary construct.
- There are qualitative differences in the expression and co-morbidity of anxiety and depression in later life.
- The GADS is an acceptable instrument that can distinguish between older women with and without mental health problems.

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Conflicts of interest
None.

References

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Rapidly progressive Alzheimer’s disease and elevated 14-3-3 proteins in cerebrospinal fluid

SIR—A 74-year-old Scottish male was admitted to a university hospital after being found on the floor of his home, following a 5-week history of vomiting, difficulty preparing meals, weight loss, loss of interest in hobbies, decreased mobility, impaired driving skills and myoclonus. His family and friends were adamant that his cognition and function were normal until 5 weeks earlier. His past medical history included hypertension, hypercholesterolaemia and Meniere’s disease. He had no known family history of any disease. He emigrated to Australia over 40 years ago, but revisited the United Kingdom...
on several occasions. He lived alone, and until 7 years previously had consumed 150 g of alcohol per day. The duration of heavy alcohol consumption and the reasons for cessation were unknown.

On review, he was disorientated to time and place and had poor concentration. He scored 18/30 in the Mini-Mental State Examination of Folstein, with deficits primarily in orientation, recall and visuo-spatial tasks. Physical examination found myoclonus but no other neurological signs. He had no stigmata of chronic liver disease. He was mildly dehydrated (urea 6.5 mmol/l [3.0–8.5], creatinine 134 μmol/l [60–120], 3.8 and 80, respectively, after rehydration). Routine investigations were otherwise normal and he was free of infection.

During his admission, multiple tonic clonic seizures were treated with carbamazepine. Serial electroencephalographs (EEGs) showed changes consistent with an encephalopathy but without epileptiform patterns. Though not fulfilling the objective diagnostic criteria for sporadic Creutzfeldt-Jakob disease proposed by Steinhoff [1], one of six EEGs showed periodic sharp wave complexes. All six EEGs showed increased delta wave activity. Two cerebral magnetic resonance imaging (MRI) scans 1 month apart showed moderate generalised atrophy, and scattered hyperintense signals on FLAIR and T2 images. Cerebrospinal fluid collected 9 days after the last seizure was positive for 14-3-3 proteins. Other investigations for rapidly progressive dementia, including those for neoplastic disease (thoracic and abdominal CT, and tumour markers) and vasculitis (erythrocyte sedimentation rate [ESR], DNA-binding, antibodies to extractable nuclear antigens [ENA] and anti-neutrophil cytoplasmic antibodies [ANCA]) were negative. A positive antinuclear antibody (ANA) at a titre of 1:160 was considered to be non-specific [2] and unrelated to his neurological disease. Despite treatment for a nosocomial urinary tract infection and seizures, his cognition and function continued to decline rapidly, and he was discharged to residential care. Sporadic Creutzfeldt-Jakob disease was thought to be the most likely explanation for his rapidly progressive mental deterioration and myoclonus.

He was readmitted to hospital 8 days later with vomiting associated with urinary tract infection and pneumonia. His myoclonus had worsened and was now easily provoked by startled. He was given antibiotics and standard supportive care, but continued to deteriorate rapidly, dying 28 days after re-presentation to hospital, and 4.5 months after the onset of his neurological illness. Post-mortem examination showed histological features of Alzheimer’s disease (Braak neocortical stage 5–6) [3], with neuritic plaques and neurofibrillar tangles in the frontal, parietal and temporal lobes (Figure 1). An old microinfarct was seen in the right putamen. There were no features of spongiform encephalopathy, and prion protein immunohistochemistry was not undertaken.

**Discussion**

The 14-3-3 proteins are a family of regulatory molecules expressed in all eukaryotic cells, but which are found in large quantities in cerebral tissue, predominantly within the cytoplasm of neurones [4]. By binding to, and modulating the function of a wide array of cellular proteins, the 14-3-3 proteins participate in many biological processes, including mitogenic signal transduction, cell cycle control and apoptotic cell death. Though the detection of 14-3-3 proteins in cerebrospinal fluid also occurs in many other diseases that cause acute or sub-acute neuronal damage, including Alzheimer’s disease, stroke, cerebral vasculitis, infectious and paraneoplastic encephalitis, anoxic and metabolic encephalopathy and Creutzfeldt-Jakob disease [4, 7, 8].

Very few tests predict the progression and severity of neurodegenerative diseases. Though levels may vary with the stage of the illness and the sub-type, limited evidence in Creutzfeldt-Jakob disease suggests that the presence of 14-3-3 proteins in cerebrospinal fluid indicates more rapid disease progression [9]. Such evidence in Alzheimer’s disease has been scant. Patients with rapidly progressive Alzheimer’s disease and positive cerebrospinal 14-3-3 proteins have been reported, though rarely. Reinwald [10] described a patient with rapidly progressive dementia, cerebellar symptoms, visual disturbances and akinetic mutism, who died in a nursing home 40 days after the first symptoms had been noticed. Huang [4] described another patient who died within 12 months of disease onset. Few other authors report an association between the presence of 14-3-3 proteins, or their concentration in the cerebrospinal fluid, with rapid illness progression. Whilst available treatments for early Alzheimer’s disease are few and offer only limited symptomatic benefits,
Further research is needed on the association between the presence of 14-3-3 proteins in the cerebrospinal fluid and the progression of Alzheimer's disease. However, other neurological diseases associated with extensive neurological damage and 14-3-3 proteins in the cerebrospinal fluid should always be considered, and excluded with a detailed history and physical examination, together with appropriate investigations and imaging.

Key points
- In some cases of Alzheimer's disease, the progression of dementia can be extremely rapid.
- The presence of 14-3-3 proteins in the cerebrospinal fluid occurs in many diseases that cause acute or sub-acute neurological damage.
- Further research is needed on the association between rapidly progressive dementias and positive 14-3-3 proteins.

Conflicts of interest
None

References

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Research letters

Comprehensive approach of donepezil and psychosocial interventions on cognitive function and quality of life for Alzheimer’s disease: the Osaki-Tajiri Project

SIR—There is a major need to develop an appropriate therapy for Alzheimer’s disease (AD). Impairment of cholinergic transmission [1, 2] is important for the defects, and cholinesterase inhibitors (e.g. donepezil) [3, 4] cause symptomatic improvement. In Japan, only donepezil is available, and the drug has been reported to maintain cognitive function up to 6 months [5].

Given the lack of a curative treatment for AD, psychosocial interventions have emerged over the years that are directed at optimising the function of patients and supporting their families. One of the most common approaches is reminiscence [6–9]. The primary goal is to facilitate recall of past experiences to promote intra/interpersonal functioning and improve quality of life (QOL). Relatively reserved remote memory [10] can provide a neurological basis to support the effectiveness. Reality orientation (RO) [6, 9, 11] is also used which stimulates time and place orientation. Reminiscence and RO are the most popular interventions [12, 13]. Lai et al. [14] performed a randomised controlled trial (RCT) to investigate whether a reminiscence program leads to higher levels of psychosocial well-being in dementia and found a significant improvement in QOL, although the intervention did not lead to significant cognitive improvement.

Although the effect of donepezil in slowing cognitive decline in AD has been established, and psychosocial...