Detecting delirium superimposed on dementia: diagnostic accuracy of a simple combined arousal and attention testing procedure

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Detecting delirium superimposed on dementia: diagnostic accuracy of a simple combined arousal and attention testing procedure

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ABSTRACT

Background

Detecting delirium superimposed on dementia (DSD) can be challenging because assessment partly relies on cognitive tests that may be abnormal in both conditions. We hypothesised that a combined arousal and attention testing procedure would accurately detect DSD.

Methods

Patients aged ≥70 years were recruited from five hospitals across Europe. Delirium was diagnosed by physicians using DSM-5 criteria using information from nurses, carers, and medical records. Dementia was ascertained by the Informant Questionnaire on Cognitive Decline in the Elderly. Arousal was measured using the Observational Scale of Level of Arousal (OSLA), which assesses eye opening, eye contact, posture, movement, and communication. Attention was measured by participants signalling each time an "A" was heard when "S-A-V-E-A-H-A-A-R-T" was read out.

Results

The sample included 114 persons (mean age 82y (SD 7); 54% women). Dementia alone was present in 25% (n=28), delirium alone in 18% (n=21), DSD in 27% (n=31), and neither in 30% (n=34). Arousal and attention was assessed in n=109 (96%). Using OSLA, 83% participants were correctly identified as having delirium (sensitivity 85%, specificity 82%, AUROC 0.92). The attention task correctly classified 76% of participants with delirium (sensitivity 90%, specificity 64%, AUROC 0.80). Combining scores correctly classified 91% of participants with delirium (sensitivity 84%, specificity 92%, AUROC 0.94). Diagnostic accuracy remained high in the subgroup with dementia (93% correctly classified, sensitivity 94%, specificity 92%, AUROC 0.98).

Conclusions

This combined arousal-attention assessment to detect DSD was brief yet had high diagnostic accuracy. Such an approach could have clinical utility for diagnosing DSD.

INTRODUCTION

Delirium is an acute neuropsychiatric disorder characterised by fluctuating inattention, other cognitive deficits, altered arousal, and psychosis. It affects more than one in five hospital inpatients (Bellelli *et al.*, 2016). When delirium occurs in someone with dementia, it is referred to as delirium superimposed on dementia (DSD). Dementia is a major risk factor for delirium, and thus many patients with delirium also have comorbid dementia, with figures ranging from 22% to 89% depending on the setting and population (Fick *et al.*, 2002).

When compared to delirium alone, DSD is associated with worse outcomes including increased walking dependence, institutionalisation and mortality (Morandi *et al.*, 2014) along with worsening of existing cognitive decline (Gross *et al.*, 2012). , Delirium may be the first or only sign that someone with dementia is unwell. Therefore, the timely investigation and management of the serious underlying causes of the delirium relies upon the rapid recognition and documentation of DSD. Assuming that the impairment is due to pre-existing dementia may result in diagnoses of potentially reversible conditions being missed. There is considerable uncertainty regarding the assessment of DSD (Richardson *et al.*, 2016) and, partly as a consequence of this, it is often not recognised, particularly in acute medical admissions (Collins *et al.*, 2010). In the absence of specific tools (Morandi *et al.*, 2012), DSD is currently evaluated with instruments used for diagnosing delirium alone. This is problematic given that many of these tools rely on cognitive tests, which may be abnormal in both dementia and delirium (Meagher *et al.*, 2010; Tieges *et al.*, 2014).

Abnormal level of arousal and a patient's inability to focus, sustain and shift attention towards environmental stimuli are relatively specific to delirium (Brown *et al.*, 2011b; Chester *et al.*, 2012; Tieges *et al.*, 2013). Importantly, in patients with abnormal arousal (above the level of coma), the inability to engage in cognitive testing or interview is considered severe inattention for the purposes of delirium diagnosis (European Delirium Association and American Delirium Society, 2014). Thus, arousal and attention are effectively part of the same spectrum, and both need to be assessed as part of delirium assessment (American Psychiatric Association, 2013). However, there is a lack of research on how best to combine arousal and attention tests in delirium assessment, particularly in DSD, as highlighted in a recent review (Morandi *et al.*, 2016).

Arousal is not usually impaired in dementia, even in the advanced stages (Brown *et al.*, 2011a). The Observational Scale of Level of Arousal (OSLA) has been shown to specifically identify delirium (Tieges *et al.*, 2013) but has not previously been evaluated in the context of DSD. This measure is appealing as it is brief, observational, and does not require formal testing of cognition.

Multiple tests of attention have been studied in the context of delirium diagnosis (Brown *et al.*, 2011a; Meagher *et al.*, 2010; Tieges *et al.*, 2014; Tieges *et al.*, 2015). However, there is a relative lack of research specifically addressing the role of attentional tests in recognizing delirium in patients with dementia. This is an important issue as attentional deficits may already be present in dementia, particularly when it is severe, and also because many of the tools test multiple cognitive domains affected in dementia alongside attention (Tieges *et al.*, 2014). This suggests the need for a test of vigilant attention that could identify delirium, yet be simple enough to remain possible for those with dementia (Leonard *et al.*, 2016).

This study aimed to evaluate existing tools to detect inattention (a vigilance task) and altered arousal (OSLA) in patients with delirium superimposed on dementia by comparing their individual and combined performances in four groups of older inpatients: no delirium, no dementia; delirium, no dementia; no delirium, dementia; delirium and dementia. We hypothesised that a combined arousal and attention testing procedure would more accurately detect DSD than the arousal or attention tests alone.

METHODS

Subjects and design

A convenient sample of patients over the age of 70 years admitted to five acute or rehabilitation hospitals in Italy, Ireland, Portugal and Switzerland were invited to take part in the study. The study protocol was approved by the ethics committee of each clinical centre. The following exclusion criteria were applied: presence of aphasia; history of major stroke; coma at the time of admission as defined by a Richmond Agitation and Sedation Scale ≤-4; poor vision or hearing. Informed consent was obtained from all participants, or their next of kin when the participants were not capable of giving informed consent because of delirium or other cognitive impairment.

Dementia and delirium diagnosis

Demographic data was collected and participants were then assessed for delirium and dementia by experienced delirium clinician-researchers (A Morandi, DM, WH, JC, GB). The diagnosis of delirium was made according to DSM-5 criteria by using a standardised procedure (Table 1) combining specific tests, information from nurses, carers and next of kin and review of the medical records. This information was supplemented by the assessor´s judgement regarding subjective features and a final diagnosis made.

In non-delirious patients, a standardised MMSE (sMMSE) (Molloy and Standish, 1997) was completed in the local language. If the sMMSE score was <28, or if the participant had

delirium, pre-existing dementia diagnosis was ascertained using the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) in the local language with a cut-off of ≥3.5 used to indicate likely dementia (Jorm *et al.*, 1991). Following these assessments, participants were divided into the following 4 groups: no delirium, no dementia (control group); delirium, no dementia; no delirium, dementia; delirium, dementia (Figure 1).

Attention test

Attention was measured using a vigilance task, with participants signalling each time an "A" was heard when the sequence of 10 consecutive letters "S-A-V-E-A-H-A-A-R-T" was read out, each letter 3 seconds apart. As per previous studies using this test, errors were counted when a patient failed to signal on the letter "A" or when a patient signalled on any letter other than "A" (Ely *et al.*, 2001). There was no published cut-point for the attention test, so the best-performing cut-point was used.

Level of arousal

Arousal was measured using the Observational Scale of Level of Arousal (OSLA) (Tieges *et al.*, 2013). The OSLA provides a total score ranging from 0 (awake and normal response) to 19 (unresponsive) composed of 5 items: eye opening, eye contact, posture, movement, and communication (Figure 2). Previously derived OSLA cut-point of 3/4 was used (Tieges *et al.*, 2013).

Statistical analysis

Differences in characteristics of people with delirium, dementia, neither or both were assessed using χ^2 tests for proportions and nonparametric equality-of-medians tests for skewed continuous variables. Attention and level arousal scores were summed to derive a total score of 29 (S-A-V-E-A-H-A-A-R-T out of 10, OSLA out of 19), with cut-points for the combined scores derived from the point at which the highest proportion of participants were correctly classified. Diagnostic test accuracy was assessed using receiver operating characteristic (ROC) curves to yield sensitivity, specificity, positive and negative likelihood ratios and area under the ROC curve (AUROC), along with 95% confidence intervals. All statistical procedures were carried out in Stata 13.1 (StataCorp, Texas).

RESULTS

Patient characteristics

The sample included 114 people (Basel n=15; Coimbra n=26; Cremona n=21, Limerick n=28, Monza n=24); 6 patients were excluded for refusal of informed consent. Table 2 describes the characteristics of these participants. Mean age was 82 years (SD 7) and 54% (n=62) were female. Dementia alone was present in 25% (n=28), delirium alone in 18% (n=21), DSD in 27% (n=31), neither in 30% (n=34). 53% (31 of 59) of those with dementia had delirium on admission.

Arousal-attention were assessed in n=109 (96%). OSLA was scored in 114 participants (100%) and the vigilance task in 109 (96%). Of the five participants without scores for the vigilance task, three did not consent to testing and two were missing; these two had OSLA scores = 0.

Level of arousal

The OSLA scores ranged from 0 to 14/19 (median=2, interquartile range 0, 6). Using OSLA with the previously derived cut-off of 3/4 (Tieges *et al.*, 2013), 83% of participants with delirium were correctly identified (sensitivity 85%, specificity 82%, AUROC 0.92). Of those with dementia, delirium was correctly identified in 85% (sensitivity 74%, specificity 96%, AUROC 0.93).

Attention test

Errors ranged from 0 to 8/10 (median=5, interquartile range 1, 7). With a cut-off 3/4, the attention task correctly classified 76% (sensitivity 90%, specificity 64%, AUROC 0.80) of participants with delirium. Of those with dementia, delirium was correctly identified in 79% (sensitivity 84%, specificity 73%, AUROC 0.79) at a cut-off of 6/7.

Combined test

Combining scores (cut-off 9/10) correctly classified 91% (sensitivity 84%, specificity 97%, AUROC 0.94) (Figure 3(a)). Even in those with underlying dementia (n=59), the diagnostic accuracy for combining OSLA and attention tasks was very high, with 93% correctly classified (sensitivity 94%, specificity 92%, AUROC 0.98) (Figure 3(b)).

DISCUSSION

The main finding in this study is that combining simple bedside assessments of arousal and attention sensitively and specifically identified delirium in patients with and without dementia. Moreover, a single score representing the sum of the two tests performed better than the two tests individually.

Despite previous studies exploring methods of measuring level of arousal (Chester *et al.*, 2012; Han *et al.*, 2015; Tieges *et al.*, 2013), there was little consensus amongst delirium experts in a recent survey focusing on current clinical and research practice in DSD (Richardson *et al.*, 2016). Our study provides further validation of the OSLA, a tool specifically designed for use in delirium (Tieges *et al.*, 2013), and supports the view that measuring level of arousal using the OSLA has good specificity and sensitivity for delirium when used on admission to hospital, even in those with dementia.

Our findings support previous work which showed that vigilance, measured using a similar letter recognition test used in this study, distinguished patients with delirium from those with dementia alone, though there was some overlap in the scores (Leonard *et al.*, 2016). A limitation of measuring attention using any tool is that it is not possible to assess all participants as a minimum level of arousal is required in order to complete the task. In this study, delirium experts were able to complete an assessment of vigilant attention in 96% of participants. An assessment of level of arousal using the OSLA is by its observational nature always possible in all participants; the function of the OSLA here is to provide additional gradation of arousal beyond simply stating that the patient was 'untestable'. We highlight the utility of combining the two tests in order to include a purely observational measure which supports previous work by Voyer et al concluding that 'one size does not fit all' and the use of a single cognitive test is not the best option in people with cognitive impairment (Voyer *et al.*, 2016).

Other studies have examined alternative measures of vigilance and sustained attention and have reported comparable results (Brown *et al.*, 2011a; Chester *et al.*, 2012; Han *et al.*, 2015; Tieges *et al.*, 2015). Our work extends previous work by examining consecutive patients on acute admission to hospitals across four European countries demonstrating the reproducibility of the tools and their generalisability. Delirium assessments were performed by experts in the field according to the DSM-5 criteria using a standardised procedure. We did not exclude patients unable to communicate because of reduced arousal. Study limitations include the cross-sectional nature of assessment on admission, and so only prevalent delirium was examined. Although there was very little missing data, the sample size as a whole was relatively small, despite being larger than previous studies. This is

particularly true when considering each site in turn. Incorporation bias is also difficult to avoid where there is a single assessor. This study did not evaluate the performance of this combined arousal-attention assessment in the context of different dementia severities and subtypes. Eliciting the best methods to measure both arousal and attention in these contexts should provide the focus of future work. The feasibility of such tools in untrained assessors requires evaluation along with validating its use in other settings e.g. intensive care or care homes. Interrater-reliability was not tested as the multicentre design of the study made this logistically challenging. However, the vast experience of those collecting the data along with the standardized approach for data collection ensured that the data was collected consistently between centres.

Our findings have direct clinical applicability. Currently, DSD is usually diagnosed through obtaining a collateral history, but often there is a lack of informant who can report an acute change from baseline. This may delay diagnosis or result in delirium being missed, resulting in worse outcomes (Kakuma *et al.*, 2003). Therefore, combining simple and brief assessments of attention and arousal in order to sensitively and specifically identify DSD is appealing in this setting where time is limited and an informant is not always immediately available. Further work may explore other non-cognitive assessments of delirium including those that assess simple motor tasks. A recent study (Bellelli *et al.*, 2011) has proposed a non-cognitive measure such as the assessment of motor fluctuations as a possible tool to distinguish DSD from advanced dementia. Individuals with DSD may have greater perturbation in motor agitation and retardation than those with dementia alone but better descriptions of motor disturbance are required.

This combined arousal-attention assessment to detect DSD was brief yet demonstrated high diagnostic accuracy even in dementia. Such an approach could have major clinical utility for diagnosing DSD.

CONFLICT OF INTEREST

None

DESCRIPTION OF AUTHORS' ROLES

Study conception and design was done by all the authors except S. Richardson, who joined the team after this stage. Acquisition of data was done by G. Bellelli, D. Meagher, A. Morandi, W Hasemann and J. Cerejeira. Data analysis was done by A. Morandi, D. Davis and S. Richardson. Interpretation of results was done by all the authors. Manuscript was drafted by S. Richardson. Critical revision and final approval of the manuscript was done by all the authors.

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FIGURES/TABLES

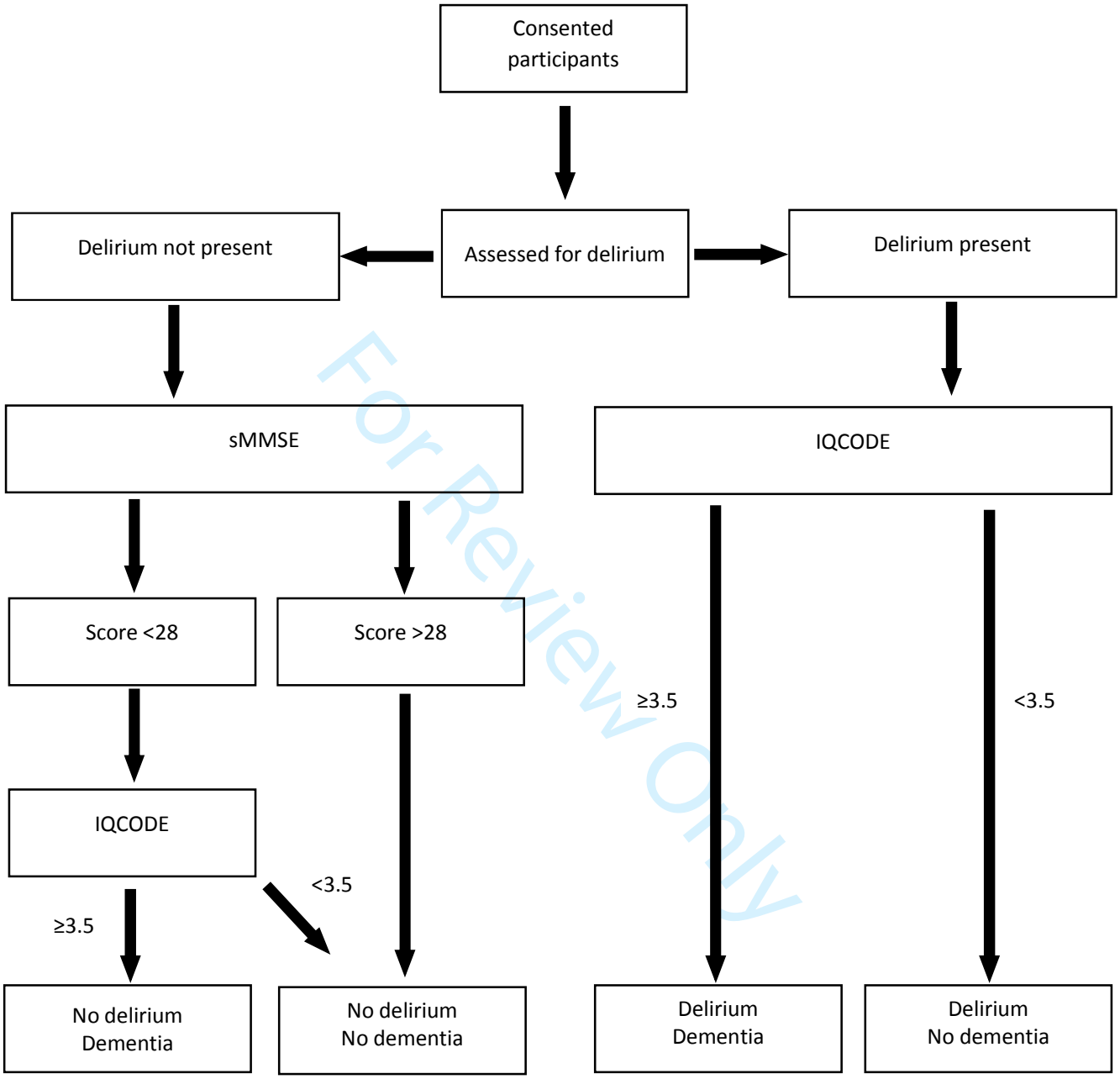

Figure 1: Flowchart demonstrating methods used to categorise participants

Eye opening

0 Open on arrival and remain so, under patient's control, outlasts stimulus
1 Open on arrival but close if stimulus removed
1 Open to voice but then outlast stimulus
2 Open to voice but close if stimulus removed
3 Open to gentle physical stimulation (squeezing hand, gently shaking shoulder)
4 Open to pain only
5 No eye opening

Eye contact

0 Spontaneously makes and holds eye contact appropriately
1 Drowsy and makes eye contact to command but can't hold it for very long
1 Alert but eyes wandering, some appropriate eye contact
2 Alert but eyes wandering, little or no appropriate eye contact
2 Drowsy but makes brief eye contact
3 Eyes will / are open but no eye contact

Posture (NB take into account weakness due to stroke or neurological disease etc)

0 Sitting out in chair or up in bed, holding appropriate posture
1 Slumped in chair or bed but attempts to sit upright and sustain posture on request
2 Slumped in chair or bed and unable to sustain posture
3 Lying in bed and unable or no response to request to sustain posture

Movement

0 Moves spontaneously and purposefully with no restless or agitated movements
1 Occasional or mild restless or fidgety movements, no aggressive or vigorous movements
1 Reduced frequency of movement, mildly slowed up
2 Frequent restless or fidgety movements, no aggressive or vigorous movements
2 Moderately reduced frequency and speed of movement, interfering with assessment or self care
3 Aggressive or vigorous, recent pulling out of lines
4 Overtly combative, violent
4 Severely reduced frequency and speed of movement, few spontaneous movements

Communication

0 Orientated, alert and converses normally
1 Disorganised or disorientated speech but able to hold a conversation
2 Alert and inattentive, unable to focus on you long enough to hold a meaningful conversation, infrequent partial sentences
2 Drowsy, infrequent partial sentences in answer to questions
3 Alert and inattentive, unable to focus, one word answers
3 Drowsy, one word answers to questions
4 No verbal response

Score (0-19) _____

Figure 2: Observational Scale of Level of Arousal

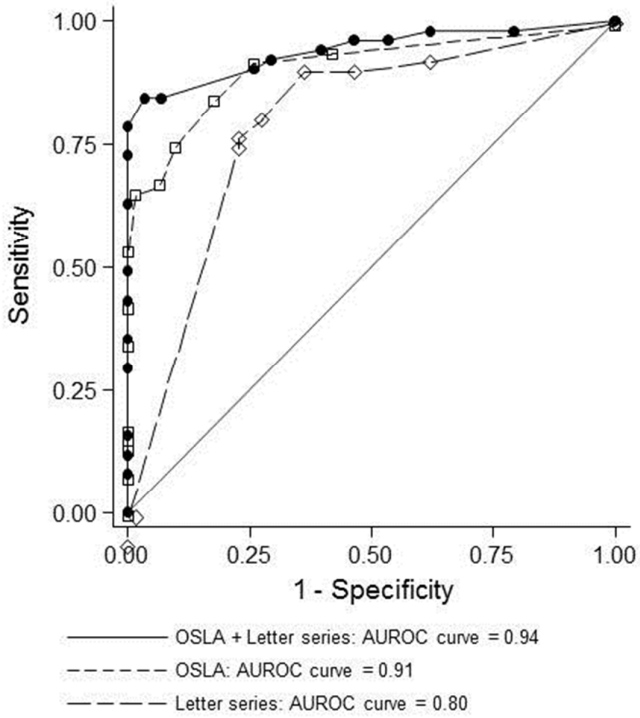

Figure 3(a): ROC curves for whole cohort n=109

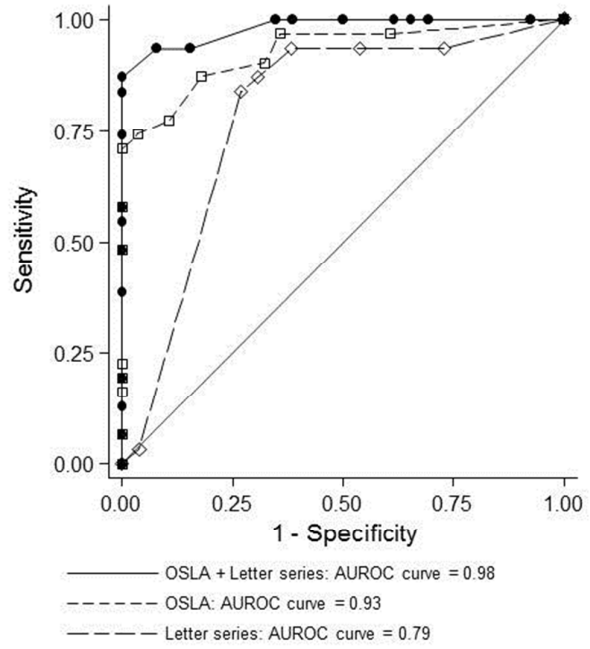

Figure 3(b): ROC curves for participants with dementia n=57

DSM-5 criteria	**Test to be performed or information needed**	
A. Disturbance in attention (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment).	*Test*	*Cut-off*
	Observation by the examiner	Distractible; tending to lose thread of conversation; lacking comprehension
	Orientation to time, place, person	Any error
	Months of the year backwards	Any error
	Spatial span test	Score of <5
B. The disturbance develops over a short period of time (usually hours to a few days), represents a change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day.	Informant history from nursing staff, carers and clinical notes	
C. An additional disturbance in cognition (e.g., memory deficit, disorientation, language, visuospatial ability, or perception).	Impairment in any of the following domains: MEMORY: inability to recall all of three items at three minutes ORIENTATION: disorientation to any of time, place or person LANGUAGE: impaired verbal communication in word naming or comprehension VISUOSPATIAL: impaired performance of overlapping pentagons test or spatial orientation questioning PERCEPTION: evidence of illusions or hallucinations by collateral or direct observation/questioning	
D. The disturbances in criteria A and C are not explained by another pre-existing, established, or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal, such as coma.	Information from history/chart/clinical examination	
E. There is evidence from the history, physical examination, or laboratory findings that the disturbance is a direct physiologic consequence of another medical condition, substance intoxication or withdrawal (i.e., because of a drug of abuse or to a medication), or exposure to a toxin or is because of multiple aetiologies.	Information from history/chart/clinical examination	

Table 1: Operationalisation of the DSM-5 criteria for delirium

	None n=34	Dementia n=28	Delirium n=21	DSD n=31	p
Age (Mean (SD))	81 (±6)	82 (±7)	84 (±6)	84 (±7)	0.03
Female (Number (%))	19 (56%)	14 (50%)	11 (52%)	18 (58%)	0.9
CCI (Median (IQR))	2 (1, 3)	3 (2, 4)	3 (2, 4)	3 (2, 5)	0.3
s-MMSE (Median (IQR))	28 (26, 29)	17 (12, 21)	-	-	<0.01
IQCODE (Median (IQR))	3 (3, 3.3)	4.1 (3.6, 5)	3 (3, 3.2)	4.5 (4, 5)	<0.01

Table 2: Patient characteristics

FIGURE/TABLE LEGENDS

Figure 2: Flowchart demonstrating methods used to categorise participants

Participants were divided into four groups based on whether delirium was present or not according to DSM-5 criteria and then whether cognitive impairment was present or not, based upon the Standardised Mini-Mental State Examination (s-MMSE) (Molloy and Standish, 1997) or the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) (Jorm *et al.*, 1991)

Figure 2: Observational Scale of Level of Arousal

The OSLA (Tieges *et al*., 2013) was used to measure level of arousal. It provides a total score ranging from 0 (awake and normal response) to 19 (unresponsive) composed of 5 items: eye opening, eye contact, posture, movement, and communication.

Figure 3(a): ROC curves for whole cohort n=109

Figure 3(b): ROC curves for participants with dementia n=57

The combined attention-arousal testing procedure performed better than either tool individually when used to detect delirium. This was true in all participants studied (Figure 3(a)) and continued to perform well when examining just those participants with dementia (Figure 3(b)). [OSLA: Observational Scale of Level of Arousal (Tieges *et al.*, 2013)]

Table 1: Operationalisation of the DSM-5 criteria for delirium

The diagnosis of delirium was made according to DSM-5 criteria by using the standardised procedure described in the table. The final diagnosis of delirium was made based upon the information obtained from the specific tests, from nurses, carers and next of kin, review of the medical records and the assessor´s judgement regarding subjective features.

Table 2: Patient characteristics

Abbreviations used in table 2:

CCI: Charlson co-morbidity index (Charlson *et al.*, 1987)

DSD: Delirium Superimposed on Dementia

IQR: interquartile range

SD: standard deviation

s-MMSE: Standardised Mini-Mental State Examination (Molloy and Standish, 1997)

IQCODE: Informant Questionnaire on Cognitive Decline in the Elderly (Jorm *et al.*, 1991)