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A Comparison of Neuropsychiatric and Cognitive Profiles in Delirium, Dementia, Comorbid Delirium-Dementia, and Cognitively Intact Controls

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ABSTRACT

Purpose: Delirium and dementia have overlapping features that complicate differential diagnosis. Delirium symptoms overshadow dementia symptoms when they co-occur, but delirium phenomenology in comorbid cases has not been compared to both conditions alone.

Methods: Consecutive adults with DSM-IV delirium, dementia, comorbid delirium-dementia, and cognitively intact controls were assessed using the Revised Delirium Rating Scale (DRS-R98) and Cognitive Test for Delirium (CTD).

Results : Delirium and comorbid delirium-dementia groups had comparable DRS-R98 and CTD total scores which were greater than in dementia or control groups. On the DRS-R98, multiple non-cognitive symptoms, inattention and disorientation were more severe in delirium groups compared with dementia-alone. Patients with dementia differed from both delirium groups on the CTD test of attention. Spatial span backwards was significantly lower in all patients with cognitive impairment (delirium, comorbid delirium-dementia, dementia alone) compared to controls, whereas spatial span forwards distinguished delirium groups from dementia.

Conclusions: Delirium phenomenology is similar with or without comorbid dementia. A wide range of neuropsychiatric symptoms distinguish delirium from dementia. Spatial span forward is disproportionately diminished in delirium , suggesting usefulness as a differentiating screening test.

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Competing Interest: None declared.

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Introduction

Delirium and dementia are the two major generalised cognitive disorders that historically have been distinguished by features such as temporal course and reversibility, with delirium considered more acute in onset and fluctuating in daily symptom severity while dementias associated with a deteriorating course. The cardinal cognitive disturbance in delirium is inattention while in most dementias there is disproportionate memory disturbance with relatively preserved attention. Distinction of these disorders is important because the urgency of investigation and treatment is greater for delirium which can reflect a medical emergency. However, some dementias have a more acute onset (e.g. dementia of Lewy body type, large CVA-related dementia) and distinction is further complicated by the high comorbidity such that dementia co-occurs in as many as two thirds of delirium cases in elderly populations (1). Moreover, persistent cognitive impairments have been described during longer term follow up of elderly patients experiencing delirium, raising questions about reversibility and prognosis after a delirium episode (2).

While acute onset, fluctuating course, and attribution to an identifiable temporally related etiology are useful distinguishing features for delirium diagnosis, there are surprisingly few studies that have compared delirium phenomenology between delirium and dementia. Most compared delirium symptoms between delirium and comorbid delirium-dementia groups, but without a 'pure' dementia group (3-7). Moreover, there has been limited study comparing cognitive profiles in these

disorders. Floor effects for neuropsychological tests also make it challenging to find instruments useful in delirium where the level of cognitive impairment is quite severe. Two specific and validated tools have allowed for more detailed study of delirium: the Cognitive Test for Delirium [CTD](8) that measures five cognitive domains using standard neuropsychological methods and the Delirium Rating Scale-Revised-98 [DRS-R98](9) that measures a broad range of delirium symptoms not measured by other delirium instruments including language, thought process, visuospatial ability, and both short and long-term memory.

We report a study in a palliative care setting comparing the severity of delirium symptoms in nondemented control patients to those with delirium, dementia, and comorbid delirium-dementia using the DRS-R98 and the CTD. In particular we aimed to address: (1) How does neuropsychiatric and cognitive profile in comorbid delirium-dementia compare to that of either disorder alone when analysed in conjunction with controls in the same setting and (2) Which features best differentiate controls from delirium or dementia, and delirium groups from dementia.

METHODS

Subjects and Design

We conducted a prospective cross-sectional study of delirium symptoms and cognitive performance in consecutive adult cases of delirium, dementia, comorbid delirium-dementia, and cognitively normal comparison subjects

receiving care in the same palliative care inpatient service. Cases with altered mental state were identified on daily rounds by the palliative care medical team and consecutively referred for delirium diagnosis according to DSM IV criteria by the research team. Assessments were conducted by trained raters in the use of the DRS-R98 and CTD (ML or DM) and to further enhance interrater reliability, difficult ratings were discussed and rated by consensus between both raters. Patients who had normal cognition as determined by an Abbreviated Mental Test (10) score greater than 6 points and no prior history of cognitive disturbance were randomly recruited for assessment. Dementia was defined as the presence of persistent cognitive impairment for at least 6 months prior to the assessment and per DSM criteria based on all available information at the time of assessment including clinical case notes and collateral history from family and / or carers (11). Comorbid delirium-dementia was defined as the presence of both disorders. Each case was then assessed by first completing the DRS-R98 followed by administration of the CTD. The DRS-R98 rated the preceding 24 hour period whereas the CTD measured cognition at the time of its administration. CTD responses were not used to rate DRS-R98 items. Both the DRS-R98 and the CTD are well validated instruments, highly structured and anchored for rating and scoring.

Informed Consent

The procedures and rationale for the study were explained to all patients but because many patients had cognitive impairment at entry into the study it was presumed that most were not capable of giving informed written consent. Because of the non-invasive nature of the study ethics committee approval was

given to augment patient assent with proxy consent from next of kin (where possible) or a responsible caregiver for all participants in accordance with the Helsinki Guidelines for Medical research involving human subjects (12).

Assessments

Demographic data, medical diagnoses, and medication at the time of the assessment were recorded. All available information from medical records and where possible collateral history was used. Nursing staff were interviewed to assist rating of symptoms over the previous 24 hours.

The Delirium Rating Scale-Revised-98 [DRS-R98](9) is designed for broad phenomenological assessment of delirium. It is a 16-item scale with 13 severity and 3 diagnostic items with high interrater reliability, sensitivity and specificity for detecting delirium in mixed neuropsychiatric and other hospital populations (9). Each item is rated 0 (absent/normal) to 3 (severe impairment) with descriptions anchoring each severity level. Severity scale scores range from 0-39 with higher scores indicating more severe delirium. Delirium typically involves scores above 15 points (Severity scale) or 18 points (Total scale) when dementia is in the differential diagnosis. For determination of item frequencies in this study, any item score ≥ 1 was considered as being “present”. DRS-R98 items can be divided into cognitive (#9-13) and non-cognitive (#1-8) subscales based on construct validity.

The Cognitive Test for Delirium [CTD](8) was specifically designed to assess hospitalized delirium patients, in particular those who are intubated or unable to

speak or write. It assesses five neuropsychological domains (orientation, attention, memory, comprehension, and vigilance) emphasizing nonverbal (visual and auditory) modalities. Tests are components of standardized and widely used neuropsychological tests. Attention on the CTD is assessed visually using the spatial span test (forwards and backwards) from the Wechsler Memory Scale (13). Each individual domain is scored from 0-6 by 2 point increments, except for comprehension (single point increments). Total scores range between 0-30 with higher scores indicating better cognitive function and scores of less than 19 consistent with delirium. It reliably differentiates delirium from other neuropsychiatric conditions including dementia, schizophrenia and depression (13).

Statistical Analyses

Statistical analysis was conducted using the SPSS-14.0 package. Demographic and rating scale data were expressed as means plus standard deviation. Continuous variables (e.g. age, total DRS-R98 and CTD scores) were compared by one way ANOVA with independent t-tests used for post hoc comparisons. Non-normal data (e.g. DRS-R98 and CTD item scores) were compared with Mann-Whitney U tests for between group comparisons with a Bonferroni correction level of $p < 0.005$ applied for the DRS-R98 item comparisons. Correlations between DRS-R98 and CTD item scores were made using Spearman's rank correlation coefficient.

RESULTS

Demographic and medication data for patients from the four groups are shown in Table 1. Both groups with evidence of dementia were significantly older ($p<0.001$) than the delirium and cognitively intact control groups. The principal causes of delirium ($n=80$) were systemic infection (29), metabolic disturbance (26), drug intoxication (17) while 11 subjects from the delirium groups had a documented CNS neoplastic lesion. The dementia had been diagnosed in 10 cases (3 with Alzheimer's dementia, 2 with vascular dementia, 5 with unspecified type) and was newly documented in a further 10 cases. Two patients from the dementia group had a documented CNS neoplastic lesion. The overall number of medications used was similar for the four groups but when analysis was restricted to psychotropic agents, the delirium groups both had more than the other groups. This principally reflected greater use of antipsychotic agents in delirium (67%) and delirium-dementia (58%) groups vs. dementia (22%) and controls (30%) ($p=0.002$).

Table 2 compares mean scores for delirium groups vs dementia and control groups for the DRS-R98 total and severity scales, DRS-R98 cognitive and non-cognitive subscales, and total CTD. Controls were significantly less impaired on all scores than any other group, scoring in normal ranges ($P<0.001$). Comorbid delirium-dementia was not significantly different from delirium except that the non-cognitive subscale was higher in delirium ($p=0.04$). Comorbid delirium-dementia differed from dementia on all DRS-R98 and CTD scores. Total CTD score showed only a trend ($p=0.07$) for delirium vs dementia. Only 2 in the dementia group (10%) had DRS-R98 total scores above 15 while 6 had total CTD scores less than 19. Figure

1 compares median total DRS-R98 scores for the 4 groups. Scores were higher for both delirium groups compared with dementia ($p<0.001$) and greater for dementia compared with controls ($p<0.001$). Scores did not differ between delirium groups.

Mean scores for DRS-R98 items are described in Table 3. Only language was similar across all groups. Both delirium and delirium-dementia groups had higher scores for the majority of symptoms when compared with dementia alone and were comparable to each other except for thought process abnormality that was worse in delirium than delirium-dementia. A wide range of DRS-R98 noncognitive items (sleep-wake cycle, perceptual abnormality, affective lability, thought process abnormality, motor agitation and motor retardation) were more severe in both delirium groups as compared to dementia, but only thought process abnormalities and motor agitation remained statistically significant after correction for multiple testing. The only cognitive items that distinguished these groups were attention and orientation but in both cases this did not reach statistical significance after correction for multiple testing. Delirium diagnostic items (symptom fluctuation, acute onset, and attributable physical disorder) significantly distinguished delirium groups from the other groups but did not distinguish dementia from controls. The dementia group differed from the control group only on the five cognitive symptoms.

Table 4 shows the comparison of individual CTD item scores between the four groups. Controls performed in the normal range and were significantly less

impaired than any other group on each item ($p < 0.001$) except orientation. No item distinguished comorbid delirium-dementia from delirium and only attention distinguished delirium-dementia from dementia ($p < 0.05$). However, both attention and vigilance distinguished delirium from dementia ($p < 0.05$). Dementia differed from controls on all 5 items of the CTD at $p < 0.001$.

Closer examination of the components of the CTD attention item - spatial span forward (SSF) and backward (SSB) measured in a visual modality - revealed that mean SSF in controls (5.7 ± 1.6), dementia (4.1 ± 2.1), delirium (2.6 ± 1.9) and delirium dementia (2.8 ± 2.3) was significantly worse for delirium vs. dementia ($p = 0.02$) and for comorbid delirium-dementia vs dementia ($p = 0.05$) but did not differ between delirium groups. Mean SSB did not distinguish the three cognitively impaired groups from each other (dementia = 2.1 ± 1.7 ; delirium = 1.3 ± 1.6 ; and delirium-dementia 1.3 ± 1.7) but readily distinguished all three groups from controls (mean 4.0 ± 1.5) at $p < 0.001$. Normal performance on SSF is 7 ± 2 and on SSB is typically $5+2$ points (14). Additionally, median scores differed significantly in a similar fashion, where distributions (see figure 2) of the middle two quartiles overlapped only partially for dementia and the comorbid group for SSF whereas there was no overlap for SSB across the three cognitively impaired groups.

Only one person (2.5%) in the cognitively intact control group and 3 (15%) in the dementia group scored less than four points on the spatial span forwards, while 26 (65%) of the delirium group and 25 (62%) of the comorbid delirium-dementia group scored three or less. Using a cutoff score of less than 4 on the SSF to indicate

delirium, within the three cognitively impaired groups Positive Predictive Value was 95% and Negative Predictive Value 35%. This suggests that subjects that score 3 or less on the SSF carry a high likelihood of having delirium (95%) but that higher scores are less useful for outruling the presence of delirium.

The relationship between perceptual disturbances / hallucinations, visuospatial function and inattention in the cognitively impaired groups was compared with correlational analysis of DRS-R98 item 2 (perceptual disturbances and hallucinations), item 10 (inattention) and item 13 (visuospatial function) as well as the SSF and SSB scores from the CTD. This indicated no significant relationship between perceptual disturbances and any of the measures of visuospatial function or attention in any of the cognitive groups (r_s all < 0.15). In contrast, scores for visuospatial function correlated significantly with SSF ($r_s=0.53$; $p<0.001$) and SSB ($r_s=0.46$; $p<0.001$) for the delirium groups but not for the dementia-only group.

DISCUSSION

In contrast to previous studies, we compared delirium phenomenology in comorbid delirium-dementia to that of both delirium and dementia groups, with a control group in the same medical setting (3-7,15). Further, our study used two well-validated instruments for delirium symptom severity – the DRS-R98 and CTD - which allow for more detailed investigation of cognitive and neuropsychiatric profile in this complex syndrome.

The need to distinguish delirium and dementia is emphasized by the greater urgency of diagnosis for delirium which can be the first indication of serious medical morbidity (16), and where late or non-detection is associated with markedly poorer outcomes including elevated mortality rates (17). Treatment response to antipsychotics is superior to use in dementia (18) where use for dementia agitation and psychosis is associated with increased mortality (19). These concerns highlight the need to carefully evaluate features, including phenomenological profile, in order to better distinguish these disorders (20) with revised diagnostic criteria in DSM-V and ICD-11 more accurately reflecting those differences. Further, comorbid delirium and dementia is understudied regarding its phenomenology and other implications, though evidence to date suggests that it is more similar to delirium. Some reports of persistent cognitive impairment in elderly delirious patients may reflect progression of previously undiagnosed dementia with poorer longer term prognosis than in uncomplicated delirium episodes. This notion is supported by a range of neuropsychological studies (21) and is consistent with longitudinal work showing an increased delirium risk in patients who have executive cognitive impairment upon admission, which reflects prehospitalization baseline cognitive status (22).

Our data using both the DRS-R98 and CTD confirmed that the domain of attentional deficits is the key distinguishing element of delirium as is represented in ICD (23) and DSM (11) diagnostic criteria where it is the cardinal and required symptom. We also found significantly higher scores in delirium groups on DRS-R98 items for acute onset, fluctuating course and attribution to a physical disorder.

These features are well-represented in diagnostic criteria for delirium in DSM-IV and ICD-10. Further, we found evidence that supports the recently proposed 3 core domains of delirium – inattention (accompanied by other cognitive deficits), circadian activity disruption (sleep-wake cycle disturbance and motor activity alterations), and impaired higher level thinking ability (24) – being specific to delirium because items were more impaired in both delirium groups as compared to dementia. These core domain phenomenological features may be useful clinically in distinguishing delirium from dementia and should be considered for inclusion in revised ICD and DSM diagnostic criteria descriptions because current editions provide little or no guidance as to distinguishing features between delirium and dementia other than temporal course.

This study also supports previous work that comorbid delirium-dementia is virtually indistinguishable from delirium alone but that it can be distinguished from dementia on a number of features, especially noncognitive ones. Altered motor activity, affective lability, and thought process abnormalities emerged as particularly useful in distinguishing both delirium groups from dementia while severity of thought process abnormalities was the only item which also distinguished delirium from comorbid delirium-dementia. These findings are largely consistent with those of Trzepacz and colleagues (25) where DRS-R98 items for sleep-wake cycle disturbance, thought process abnormality, motor agitation, perceptual disturbances, affective lability, attention, visuospatial ability, acute onset of symptoms, fluctuation of symptoms and physical disorder were significantly worse in delirium vs. dementia, though their samples were

smaller. Our findings contrast with the work of Cole et al (15) regarding thought process and motor agitation levels in dementia vs. delirium, but they used instruments that detect only the presence or absence of delirium symptoms and not severity as the DRS-R98 does. Further, their work found no impairment of consciousness in hyperalert delirium subgroups but did in the hypoalert, which is disconcerting because delirium is by definition a disorder of impaired consciousness. This also begs the question of what symptoms constitute impaired consciousness (sometimes called “clouding”) and how it is defined because this is an essential difference between delirium and dementia.

The CTD attention item, consistent with the DRS-R98 findings, best differentiates delirium groups from control and dementia groups. Further, the SSF component of this item differentiated dementia from delirium groups whereas the SSB did not. SSF is a more specific test of simple attention involving primarily sequential processing while SSB requires greater processing of information, working memory, planning ability and sequential processing (26-28) with higher demands for exceptional levels of attention and concentration (29). Our data (e.g. positive predictive value of 95% for a score of less than 4) suggest that SSF may be a useful bedside test that is relatively simple and specific to help distinguish delirium from dementia but that it is less suited to outruling delirium due to a relatively high false negative rate. Confirmatory work is needed.

Brown and coworkers (30) identified significantly poorer performance in patients with delirium versus Alzheimer’s dementia on a range of tests of visual perception

while delirious patients performed better on tests of memory. This work raises the question as to the extent to which deficits in these tests are related to impairments of visual processing (e.g. in the occipital cortex) or attentional systems that direct processing towards visual inputs. Some work (31) has indicated a correlation between perceptual abnormalities / hallucinations and impairment of visual perception and attention in patients with dementia but the relationship between perceptual disturbances, visuospatial function and visual attention in different cognitive disorders remains unclear. Previous work using the Clock Drawing Test has indicated that it is useful for identifying patients with cognitive impairment but lacks specificity for delirium vs dementia (32). Our work suggests that differences between delirium and dementia are more evident in tests of visual attention than tests of visuospatial function. Moreover, we did not identify a major relationship between perceptual abnormalities/hallucinations and either visual attention or visuospatial performance. Further work involving patients with different dementia types are needed.

Noncognitive delirium symptoms failed to distinguish dementia patients from medically ill controls suggesting that the presence of noncognitive symptoms should alert clinicians to the possibility of delirium. Because we did not measure noncognitive symptoms with a dementia-specific scale like the Neuropsychiatric Inventory (33) that captures characteristic details of dementia phenomenology, we cannot be certain to what extent this would hold true for demented patients who are not hospitalized because neuropsychiatric symptoms are also common in dementia (34). However there are particular characteristics of noncognitive

delirium symptoms that distinguish delirium from dementia patients such as type of sleep-wake cycle and perceptual disturbances, extreme and rapid nature of affective lability and degree of thought process abnormality that are captured differently on the DRS-R98 than on the NPI. Additionally, we did not evaluate the stage or type of dementia which could affect the presentation of noncognitive symptoms. While future work should evaluate dementia more carefully to tease apart these more subtle features for differential diagnosis, it remains that delirium symptoms overshadow dementia when comorbid and that delirium, not dementia, is the medical priority not to be missed.

Unfortunately, differentiating symptoms other than inattention and temporal course are not emphasized in DSM-IV and ICD-10 delirium definitions, whereas disorganised thinking and sleep-wake cycle disturbance were emphasized in the DSM-III-R. Our data support their reinclusion in DSM-V. Providing better guidance regarding the distinction of delirium from dementia – and dementia from delirium - is a key challenge for future definitions of delirium in DSM-V (20) and ICD-11 (35).

STUDY LIMITATIONS

Cross-sectional studies cannot fully capture the phenomenological profile of conditions such as delirium whose symptom severity fluctuates, though the DRS-R98 utilizes a 24-hour reporting period. In keeping with the routine assessments conducted on all admissions to the unit, the cognitively intact group were identified according to scores on the abbreviated mental test rather than a more

standard test such as the MMSE (36) which would more accurately outrule the presence of cognitive impairment typical of delirium and / or dementia. Dementia was diagnosed according to the presence of prior cognitive impairment of at least six months duration. As such, a more accurate diagnosis might be obtained by using more specific criteria or an instrument such as the IQCODE (37). We could not specify the primary cause of dementia (i.e. whether dementia was due to a degenerative process, vascular lesions, frontal dementia, alcohol, brain metastases, etc). There were fewer patients included in the dementia group perhaps reflecting the restrictions of our criteria, but also a function of the study setting where dementia is not as prevalent as in elderly medicine settings. Patients in the two groups with dementia were significantly older which might have impacted upon the performance in cognitive tests in particular but it is relevant that the principal finding in relation to cognition indicated a superior performance in the older patients with dementia-alone as well as significant differences with both the delirium-alone group and the comorbid delirium-dementia group which are not likely to relate to any age-associated effects. In addition, the different patterns of medication use, particularly in relation to antipsychotic agents, may have impacted our findings and warrant more detailed analysis in future work. We used only delirium instruments to compare groups and future work should also include use of the NPI (33) which measures dementia neuropsychiatric phenomenology. However, many of the NPI items are not descriptive of delirium and the ADAS-Cog (38) has not been reported in delirium heretofore and may have floor effects. The degree to which observations in a palliative care service (where patients have terminal illness and are often in receipt of polypharmacy)

can be generalised to patients in other settings is uncertain. However, our data were remarkably similar to those of Trzepacz and colleagues (24) from other medical settings. Future work in other populations where delirium and various types of dementia are common, incorporating tools designed to assess neuropsychiatric profile in dementia, can address these shortcomings and further improve our understanding of the interface between these important and highly prevalent conditions.

REFERENCES

- (1) Fick DM, Agostini JV, Inouye SK. Delirium superimposed on dementia: a systematic review. *J Am Geriatr Soc* 2000; 50:1723-32.
- (2) Trzepacz PT, Meagher DJ. Neuropsychiatric aspects of delirium. Chapter 11 in the American Psychiatric Publishing Textbook of Neuropsychiatry and Behavioral Neurosciences (5th Edition). Eds Yudofsky SC, Hales RE, American Psychiatric Publishing Inc, Washington DC, 2008, pp 445-517
- (3) Liptzin B, Levkoff SE, Gottlieb GL, Johnson JC. Delirium: background papers for DSM-IV. *J Neuropsychiatry Clin Neurosci* 1993; 5:154–160.
- (4) Trzepacz PT, Mulsant BH, Dew MA, et al (1998). Is delirium different when it occurs in dementia? A study using the Delirium Rating Scale. *J Neuropsychiatry Clin Neurosci* 1998; 10:199-204.
- (5) Laurila JV, Pitkala KH, Strandberg TE, Tilvis RS. Delirium among patients with and without dementia: does the diagnosis according to the DSM-IV differ from the previous classifications? *International Journal of Geriatric Psychiatry* 2004; 19:271-277.
- (6) Voyer P, Cole MG, McCusker J, Belzile E. Prevalence and symptoms of delirium superimposed on dementia. *Clinical Nursing Research* 2006; 15:46-66.

- (7) Edlund A, Lundstrom M, Sandberg O, Bucht G, Brannstrom B, Gustafson Y. Symptom profile of delirium in older people with and without dementia. *J Geriatr Psych Neurol* 2007; 20: 166-171.
- (8) Hart RP, Levenson JL, Sessler CN, Best AM, Schwartz SM, Rutherford LE. Validation of a cognitive test for delirium in medical ICU patients. *Psychosomatics* 1996; 37:533-46.
- (9) Trzepacz PT, Mittal D, Torres R, Canary K, Norton J, Jimerson N. Validation of the Delirium Rating Scale-Revised-98 (DRS-R-98). *J Neuropsychiatry Clin Neurosci* 2001; 13:229-242.
- (10) Hodkinson HM. Evaluation of a mental test score for assessment of mental impairment in the elderly. *Age and Ageing* 1972; 1:233-8.
- (11) American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4th Edition. Washington DC, 1994.
- (12) World Medical Association. Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects, 2004.
<http://www.wma.net/e/policy/pdf/17c.pdf>.

- (13) Hart RP, Best AM, Sessler CN, Levenson JL. Abbreviated Cognitive Test for delirium. *Journal of Psychosomatic Research* 1997; 43; 417-23.
- (14) Wilde NJ, Strauss E, Tulskey DS. Memory Span on the Wechsler Scales. *Journal of Clinical and Experimental Psychology* 2004;26:539-49.
- (15) Cole M, McCusker J, Dendukuri N, Han L. Symptoms of delirium among elderly medical inpatients with or without dementia. *J Neuropsychiatry Clin Neurosci* 2002; 14:167-175.
- (16) Wahlund LA, Bjorlin GA. Delirium in clinical practice: experiences from a specialized delirium ward. *Dement Geriatr Cogn Disord* 1999; 10:389–392.
- (17) Kakuma R, du Fort GG, Arsenault L, Perrault A, Platt RW, Monette J, Moride Y, Wolfson C. Delirium in older emergency department patients discharged home: effect on survival. *J Am Geriatr Soc* 2003; 51:443-50.
- (18) Meagher D, Leonard M. The active management of delirium: improving detection and treatment. *Advances in Psychiatric Treatments* 2008; 14: 292-301.
- (19) Jeste DV, Blazer D, Casey D, Meeks T, Salzman C, Schneider L, et al . ACNP White Paper: Update on use of antipsychotic drugs in elderly persons with dementia. *Neuropsychopharmacology* 2008; 33: 957-70.

- (20) Meagher DJ, Trzepacz PT (2007). Phenomenological distinctions needed in DSM-V: delirium, subsyndromal delirium and dementias. *J Neuropsychiatry Clin Neurosci* 2007 19:468-70.
- (21) MacLulich AMJ, Beaglehole A, Hall RJ, Meagher DJ. Delirium and long-term cognitive impairment. *Int Rev Psychiatry* 2009; 21: 30-42.
- (22) Rudolph JL, Jones RN, Grande LJ, Milberg WP, King EG, Lipsitz LA, Levkoff SE, Marcantonio ER. Impaired executive function is associated with delirium after coronary artery bypass graft surgery. *J Am Geriatr Soc* 2006; 54:937-941.
- (23) World Health Organization. International Statistical Classification of Diseases and Related Health Problems, 10th Revision. Geneva, World Health Organization, 1993
- (24) Franco J, Trzepacz P, Mejia M, Ochoa S. Factor analysis of the Colombian translation of the Delirium Rating Scale-Revised-98. *Psychosomatics* 2009; 50:255-62.
- (25) Trzepacz PT, Mittal D, Torres R, Kanary K, Norton J, Jimerson N. Delirium vs dementia symptoms: Delirium Rating Scale-Revised- 98 (DRS_R-98) and Cognitive Test for Delirium (CTD) item comparisons. *Psychosomatics* 2002; 43:156-7

- (26) Crowder RG. Short-term memory: Where do we stand? *Memory & Cognition* 1993; 21:142-145.
- (27) Lichtenberger EO, Kaufman AS, Lai ZC. Essentials of WMS-III assessment. New York, Wiley, 2002.
- (28) Wilde NJ, Strauss E, Tulskey DS. Memory span on the Wechsler Scales. *J Clin Exp Neuropsychology* 2004; 26:539-49.
- (29) Searls EF. How to Use WISC Scores. University of Florida: International Reading Association, 1975.
- (30) Brown LJE, McGrory S, McLaren L, Starr JM, Deary IJ, MacLulich AMJ. Cognitive visual perceptual deficits in patients with delirium. *J Neurol Neurosurg Psychiatry* 2009;80:594-99.
- (31) Collerton D, Perry E, McKeith I. Why people see things that are not there: a novel perception and attention deficit model for recurrent complex visual hallucinations. *Behav Brain Sci* 2005;28:737-57.
- (32) Adamis D, Morrison C, Treloar A, MacDonald AJ, Martin FC. The performance of the clock Drawing Test in elderly medical inpatients: does it have utility in the identification of delirium. *J Ger Psychiatry Neurol* 2005;18:129-133.

- (33) Cummings J. The Neuropsychiatric Inventory: Assessing psychopathology in dementia patients. *Neurology* 1997; 48: S10-S16.
- (34) Lyketsos CG, Sheppard JM, Steinberg M, Tschanz JA, Norton MC, Steffens DC, Breitner JC. Neuropsychiatric disturbance in Alzheimer's disease clusters into three groups: the Cache County study. *Int J Geriatr Psychiatry* 2001;16:1043-53.
- (35) Meagher D, MacLulich AMJ, Laurila J. Defining delirium for the International Classification of Diseases, 11th Revision. *J Psychosomatic Res* 2008; 65: 207-214.
- (36) Folstein MF, Folstein SE, McHugh PR: Mini-Mental State: a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189–198.
- (37) Jorm AF. The Informant Questionnaire on cognitive decline in the elderly (IQCODE): a review. *Int Psychogeriatr* 2004;16:275-93
- (38) Rosen WG, Mohs RC, Davis KL. A new rating scale for Alzheimer's disease. *Am J Psychiatry* 1984; 141: 1356-64.

Table1. Demographic and medication data for the patient groups (mean $\pm$ SD)

	Controls (n=40)	Delirium (n=40)	Comorbid delirium-dementia (n=40)	Dementia (n=20)
Age (years)^a	66.3 $\pm$ 10.9	68.7 $\pm$ 12.6	74.9 $\pm$ 8.5	78.6 $\pm$ 7.8
Sex (% male)	47	57	45	55
Number of medications	9.4 $\pm$ 3.3	11.0 $\pm$ 3.7	9.9 $\pm$ 4.1	9.5 $\pm$ 3.2
Number of psychotropic medications^b	2.3 $\pm$ 1.2	3.4 $\pm$ 1.4	3.2 $\pm$ 1.7	2.4 $\pm$ 1.2

^aANOVA $p < 0.001$; dementia groups vs delirium and controls.

^bANOVA $p = 0.002$; delirium groups vs dementia and controls

Table 2. Comparison of means $\pm$ SD on DRS-R98 scale scores and total CTD score in four groups

	Controls^a (n=40)	Delirium (n=40)	Comorbid delirium-dementia (n=40)	Dementia (n=20)
DRS-R98 Total	4.1 $\pm$ 1.8	22.0 $\pm$ 6.6 ^b	21.0 $\pm$ 5.1 ^b	11.2 $\pm$ 3.5 ^e
DRS-R98 Severity	3.2 $\pm$ 1.6	17.9 $\pm$ 6.1 ^b	16.7 $\pm$ 4.8 ^b	10.2 $\pm$ 3.5 ^e
DRS-R98 Noncognitive subscale	2.1 $\pm$ 1.4	9.7 $\pm$ 5.2 ^b	7.4 $\pm$ 3.3 ^b	3.2 $\pm$ 1.3 ^f
DRS-R98 Cognitive subscale	0.9 $\pm$ 1.2	8.6 $\pm$ 3.1 ^d	9.5 $\pm$ 3.2 ^c	7.0 $\pm$ 3.1 ^e
CTD Total	27.0 $\pm$ 1.9	13.1 $\pm$ 7.9	12.7 $\pm$ 7.7 ^d	17.2 $\pm$ 7.3 ^e

^a Controls scored in the normal range for all measures.

^b p<.001 vs dementia

^c p=.007 vs. dementia

^d p<.05 vs dementia

^e p<.001 dementia vs. controls

^f p<.01 dementia vs. controls

Table 3. DRS-R98 item severities (mean scores $\pm$ SD) for the four groups; significance is for comparisons using Mann-Whitney U test.

DRS-R98 Item	Controls (n=40)	Delirium (n=40)	Comorbid delirium- dementia (n=40)	Dementia (n=20)
1. Sleep-wake cycle disturbance	0.7 $\pm$ 0.7	1.6 $\pm$ 0.8 ^b	1.5 $\pm$ 0.7 ^b	1.0 $\pm$ 0.6 ^e
2. Perceptual disturbances and hallucinations	0.1 $\pm$ 0.3	0.8 $\pm$ 1.2 ^a	0.7 $\pm$ 1.0 ^a	0.1 $\pm$ 0.3 ^e
3. Delusions	0.0 $\pm$ 0.0	0.2 $\pm$ 0.7	0.6 $\pm$ 1.0 ^a	0.1 $\pm$ 0.5 ^e
4. Lability of affect	0.2 $\pm$ 0.4	0.9 $\pm$ 0.8 ^c	0.7 $\pm$ 0.7 ^b	0.2 $\pm$ 0.4 ^e
5. Language	0.3 $\pm$ 0.5	1.3 $\pm$ 0.7	1.0 $\pm$ 0.8	0.9 $\pm$ 0.6
6. Thought process abnormalities	0.4 $\pm$ 0.5	1.9 $\pm$ 1.0 ^{cd}	1.1 $\pm$ 0.8 ^a	0.6 $\pm$ 0.9 ^e
7. Motor agitation	0.1 $\pm$ 0.4	1.6 $\pm$ 3.4 ^c	0.9 $\pm$ 0.8 ^c	0.2 $\pm$ 0.4 ^e
8. Motor retardation	0.4 $\pm$ 0.5	1.3 $\pm$ 0.8 ^c	0.9 $\pm$ 1.0 ^a	0.4 $\pm$ 0.5 ^e
9. Orientation	0.1 $\pm$ 0.2	1.4 $\pm$ 0.7 ^a	1.4 $\pm$ 0.7 ^a	0.9 $\pm$ 0.7
10. Attention	0.2 $\pm$ 0.4	2.2 $\pm$ 0.9 ^a	2.1 $\pm$ 0.9 ^a	1.6 $\pm$ 1.1
11. Short-term memory	0.2 $\pm$ 0.5	1.9 $\pm$ 1.0	2.0 $\pm$ 1.0	1.5 $\pm$ 1.2
12. Long-term memory	0.3 $\pm$ 0.5	1.3 $\pm$ 0.9	1.7 $\pm$ 1.0	1.1 $\pm$ 1.1
13. Visuospatial ability	0.3 $\pm$ 0.6	1.9 $\pm$ 1.0	2.3 $\pm$ 1.9	1.8 $\pm$ 1.0
14. Temporal onset of symptoms	0	1.5 $\pm$ 0.6 ^c	1.6 $\pm$ 0.7 ^c	0.1 $\pm$ 0.2 ^e
15. Fluctuation in symptom severity	0	1.1 $\pm$ 0.5 ^c	1.0 $\pm$ 0.6 ^c	0.0 $\pm$ 0.0 ^e
16. Physical disorder	1.0 $\pm$ 0.2	1.5 $\pm$ 0.5 ^c	1.7 $\pm$ 0.5 ^c	1.0 $\pm$ 0.1 ^e

^a More impaired than dementia at $p \leq .05$

^b More impaired than dementia at $p \leq .01$

^c More impaired than dementia at $p \leq .001$

^d More impaired than delirium-dementia at $p \leq .001$

^e No difference between dementia and controls

Table 4. CTD item scores for the four groups using Mann Whitney U test. Controls performed in the normal range for each item.

CTD Item	Controls (n=40)	Delirium (n=40)	Comorbid delirium-dementia (n=40)	Dementia (n=20)^c
Orientation	6.0 ± 0.0	4.5 ± 1.0	3.0 ± 2.3	4.3 ± 2.2
Attention ^a	4.5 ± 1.0	1.5 ± 1.6	1.7 ± 1.8	2.7 ± 1.6
Memory	5.3 ± 0.8	2.9 ± 2.3	2.3 ± 2.0	3.3 ± 2.0
Comprehension	5.6 ± 0.5	4.1 ± 1.6	3.9 ± 1.6	4.2 ± 1.6
Vigilance ^b	5.5 ± 1.0	1.4 ± 1.8	1.8 ± 2.2	2.6 ± 1.9

^a Delirium and delirium-dementia < dementia at p<0.05

^b Delirium < dementia at p<0.05

^c Dementia < controls on all items at p<0.001

Figure 1. Boxplots of distribution of Total DRS-R98 scores for diagnostic groups

Figure 2. Boxplots of distribution of scores on the CTD spatial span item forwards (SSF) and backwards (SSB) for diagnostic groups.



