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Comparison of diagnostic classification systems for delirium with new research criteria that incorporate the three core domains

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ABSTRACT

Objective: Diagnostic classification systems do not incorporate phenomenological research findings about the three core symptom domains of delirium (Attentional/Cognitive, Circadian, Higher Level Thinking). We evaluated classification performances of novel Trzepacz, Meagher, and Franco research diagnostic criteria (TMF) that incorporate those domains and ICD-10, DSM-III-R, DSM-IV, and DSM-5.
Methods: Primary data analysis of 641 patients with mixed neuropsychiatric profiles. Delirium (n = 429) and nondelirium (n = 212) reference standard groups were identified using cluster analysis of symptoms assessed using the Delirium Rating Scale-Revised-98. Accuracy, sensitivity, specificity, positive and negative predictive values (PPV, NPV), and likelihood ratios (LR+, LR−) are reported.
Results: TMF criteria had high sensitivity and specificity (87.4% and 89.2%), more balanced than DSM-III-R (100% and 31.6%), DSM-IV (97.7% and 74.1%), DSM-5 (97.7% and 72.6%), and ICD-10 (66.2% and 100%). PPV of DSM-III-R, DSM-IV, and DSM-5 were <90.0%, while PPV for ICD-10 and TMF were >90%. ICD-10 had the lowest NPV (59.4%). TMF had the highest LR+ (8.06) and DSM-III-R the lowest LR− (0.0). Overall, values for DSM-IV and DSM-5 were similar, whereas for ICD-10 and DSM-III-R were inverse of each other. In the pre-existing cognitive impairment/dementia subsample (n = 128), TMF retained its highest LR+ though specificity (58.3%) became less well balanced with sensitivity (87.9%), which still exceeded that of DSM.
Conclusions: TMF research diagnostic criteria performed well, with more balanced sensitivity and specificity and the highest likelihood ratio for delirium identification. Reflecting the three core domains of delirium, TMF criteria may have advantages in biological research where delineation of this syndrome is important.

1. Introduction

Research using symptom rating instruments has advanced the phenomenological understanding of delirium and found that delirium has three core symptom domains [1]. These domains are Cognitive (attention with other cognitive abilities), Higher Level Thinking (thought process, semantic language and executive function) and Circadian (sleep–wake cycle and motor activity patterns). These were delineated from studies using descriptive, regression, and exploratory and confirmatory factor analyses [2–8]. These domains are also consistent with findings from delirium research on sleep–wake cycle, motor activity and attention [9–14]. Further, these core domain symptoms are likely generated from associated underlying neural disturbances implicated in delirium. As a state of impaired consciousness, delirium alters functioning of highly distributed neural networks for information processing across all higher cerebral cortical regions, as well as gating and circadian rhythm in diencephalic regions (thalamus and hypothalamus) [15–17].

Different versions of the Diagnostic and Statistical Manual of Mental Disorders (DSM) and International Classification of Diseases (ICD) have been employed over recent decades for delirium diagnosis, but comparison studies indicate that these systems vary in their identification of delirium [18–25]. Though their cardinal criterion involves inattention, inclusion of other symptoms varies. Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) [26] and Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5) [27] require the fewest symptoms of any classification system to obtain a diagnosis of delirium, therefore capturing cases that could be termed subsyndromal [18–25]. Further, none requires nor recommends that at least one symptom be present from each of delirium's three core domains.

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When diagnostic criteria are loose in their requirements they may increase detection rates by nonspecialists, where false positives are better tolerated than false negatives given the prognostic implications of delirium. However, research benefits from a more accurate classification system that increases certainty regarding delirium presence, especially critical for translational and treatment research.

More specific delirium diagnostic criteria are needed because of the inconsistencies among current classification systems that are principally derived through expert consensus. Our proposed Trzepacz, Meagher, and Franco (TMF) Research Diagnostic Criteria for delirium (see Box 1 below, and Supplemental Box 1 in e-component for Spanish version) capture and require elements from all three core domains with the intent that researchers seeking to understand phenomenology, pathophysiology, treatment and translational relationships have criteria that would be more enduring and rigorous (see Table 1 for comparisons across classification systems). Requiring presence of core domains should also enhance clinical diagnosis of delirium. In fact, Kean et al. (2010) developed a 3-item delirium diagnostic tool for nonspecialists that only assessed symptoms representing each core domain (sleep–wake cycle, vigilance and comprehension) in acute traumatic brain injury patients and found a very strong relationship using receiver operating characteristic analysis with an independent DSM-IV diagnosis, performing similarly to the Delirium Rating Scale-Revised-98 (DRS-R98) [6].

Box 1
TMF Research Diagnostic Criteria. Delirium core domains are reflected by criteria as follows: Cognitive by B and C1, Higher level thinking by C2, and Circadian by D1 and D2.

Trzepacz, Meagher, and Franco (TMF)
Research Diagnostic Criteria for Delirium©
Delirium is an impaired state of consciousness reflected by the following criteria being met:

A. Acute or subacute change from baseline that may fluctuate in severity over minutes or hours.
B. Impaired attentional ability (such as reduced attention span and/or focus).
C. Cognitive and higher level thinking impairment evidenced by both:
1. Deficits in at least one other cognitive domain such as orientation, memory, and/or visuospatial ability.
2. Disorganized thinking, diminished capacity to comprehend, and/or less meaningful and coherent communication.
D. Circadian abnormalities as evidenced by either or both:
1. Sleep–wake cycle disturbance including disruptions, sleeplessness and/or excessive drowsiness and napping.
2. Motor activity alteration inappropriate to the time of day or circumstance (hyperactive, hypoactive or mixed).
E. Symptoms are not solely attributable to another Neurocognitive disorder such as dementia or mild cognitive impairment, nor better explained by coma, stupor or sedation.
F. Symptoms are temporally related to one or more identifiable physiological or pharmacological potential etiologies and may occur on a background of other cognitive impairment such as dementia.

Associated features may be present but are not required for diagnosis:

a. Labile affect that is often incongruent to the context and under poor self-control.
b. Perceptual disturbances including illusions, hallucinations or misidentifications that are commonly visual but may be auditory, tactile, olfactory or gustatory.
c. Abnormal thought content that may reach delusional proportions and is more often persecutory or grandiose.

Table 1
Comparison of required delirium symptoms in DSM-III-R, DSM-IV, DSM-5, ICD-10, and the proposed Trzepacz, Meagher, and Franco (TMF) Delirium Research Criteria classification systems. Symptoms are color-coded to denote their respective domain — either the three core domains of delirium (purple, green or blue) or the noncore domain (orange). Beige-shaded cells denote contextual characteristics or exclusions designated in the criteria. Additionally, an R denotes a symptom that is required and listed in its own criterion. S denotes where at least one symptom is required within the same domain. D denotes where at least one symptom is required within a criterion but is listed along with symptoms from a different domain.

	Classification system				
	ICD–10	DSM–III–R	DSM–IV	DSM–5	TMF
Symptom					
Attention	R	R	R	R	R
Orientation	D	D	D	D	S
Memory	D	D	D	D	S
Visuospatial				D	S
Language			D	D	S
Thought process		R			S
Thought content					
Sleep–wake cycle	S	D			S
Motor activity	S	D			S
Affect					
Perception		D	D	D	
Characteristic					
Onset					
Fluctuation					
Causative factor					
Not attributable to dementia					
Not due to coma					

Our study aim is to compare the discriminant capacity of existing delirium diagnostic systems with our proposed TMF research diagnostic criteria. In order to evaluate the TMF criteria in an unbiased fashion we could not rely on an existing system as the reference standard. Therefore, we first developed an agnostic reference standard using cluster analysis of DRS-R98 items from a prospectively collected pooled research database of 641 neuropsychiatric cases to determine delirium and nondelirium groups. These delirium and nondelirium clusters (groups) provided the independent reference standard against which we compared the discriminant performances of DSM, ICD and our proposed TMF criteria for delirium status.

2. Materials and methods

2.1. Study population and design

This report includes cross-sectional data prospectively collected during research assessments of delirium in 8 patient cohorts from 5 interrelated studies of delirium phenomenology conducted in Ireland and India as part of a collaborative consortium, the Cognitive Impairment Research Group at the University of Limerick, in Ireland. Data collection and rater training were standardized and consistent across all studies where all collaborators were experienced delirium researchers (DM, ML, FJ, KC, ST, JF). All raters were trained by an expert (DM) in the use of the DRS-R98, who is also a member of a group that developed the DRS-R98 Administration Guide (that can be obtained by request at pttrzepacz@outlook.com).