

Review articles

Defining delirium for the *International Classification of Diseases, 11th Revision*

David J. Meagher^{a,b,c,*}, Alasdair M.J. MacLulich^d, Jouko V. Laurila^e

^aDepartment of Adult Psychiatry, Midwestern Regional Hospital, Limerick, Ireland

^bHealth Systems Research Centre, University of Limerick, Limerick, Ireland

^cMilford Care Hospice, Castletroy, Limerick, Ireland

^dGeriatric Medicine/MRC Centre for Cognitive Ageing and Cognitive Epidemiology, University of Edinburgh, Queen's Medical Research Institute, Edinburgh, Scotland, UK

^eDepartments of Internal Medicine and Geriatrics, Helsinki University Central Hospital, Helsinki, Finland

Received 21 February 2008; received in revised form 11 May 2008; accepted 15 May 2008

Abstract

Objective: The development of ICD-11 provides an opportunity to update the description of delirium according to emerging data that have added to our understanding of this complex neuropsychiatric syndrome. **Method:** Synthetic article based on published work considered by the authors to be relevant to the definition of delirium. **Results:** The current *DSM-IV* definition of delirium is preferred to the ICD-10 because of its greater inclusivity. Evidence does not support major changes in the principal components of present

Keywords: Delirium; Classification; Diagnosis; Dementia

definitions but a number of key issues for the updated definition were identified. These include better account of non-cognitive features, more guidance for rating contextual diagnostic items, clearer definition regarding the interface with dementia, and accounting for illness severity, clinical subtypes and course. **Conclusion:** Development of the ICD definition of delirium can allow for more targeted research and clinical effort.

© 2008 Published by Elsevier Inc.

Introduction

Acute disturbance of mental status in the context of illness, stress, or drug intoxication has been recognized as an entity for millennia. However, only with the development of clear definitions and diagnostic criteria has delirium begun to receive the clinical and research attention that it warrants. The syndromal nature of delirium means that diagnostic criteria are subject to testing and refinement as new data emerge. The past decade has witnessed considerable research activity relevant to delirium and as a consequence the task of updating the existing *International Classification of Diseases (ICD)* definition by the World Health Organization [1] provides an opportunity to develop the concept and address the short-

comings of the present definition according to data rather than mere expert opinion. This process must be sensitive to the current definition, so that existing research maintains generalisability, as well as allow closer alignment to the *Diagnostic and Statistical Manual of Mental Disorders (DSM)* systems. Moreover, developments in relation to the dementias also require that the interface between these connected disorders be addressed. Finally, an updated definition must be operationalized such that delirium can be reliably detected in clinical practice as well as research. The purpose of this article was to consider evidence that can inform the revision process for the definition of delirium for *ICD-11 which is planned for publication in 2011*.

Delirium does not have any pathognomic feature and instead the diagnosis is based upon characteristic symptoms occurring in a context that is highly suggestive. The definition of delirium must therefore combine key clinical symptoms and signs with required contextual items. Delirium is

* Corresponding author. Department of Adult Psychiatry, Midwestern Regional Hospital, Limerick, Ireland.

E-mail address: david.meagher@ul.ie (D.J. Meagher).

frequently comorbid with preexisting cognitive problems and occurs in the context of precipitating illness, other forms of stress (e.g., postoperatively), and drug intoxication. A challenge in definition is to account for this complex clinical picture that varies with causation and across treatment settings. Although delirium is a complex disorder, clinicians and researchers need criteria that are robust, reliable, objective, and as simple as possible. It is essential to have criteria that have utility in real-world settings, make diagnosis of milder and less obvious forms easy, but can identify those with poor outcome across different populations.

International Classification of Diseases, 10th Revision

The existing *ICD-10* definition of delirium [1] includes different criteria for clinical and research use both of which include a broad range of features that capture the phenomenological complexity of the syndrome. It therefore contrasts with the *DSM-IV* [2] definition which does not mention characteristic features such as disturbances of sleep–wake cycle and motor activity. However, the *ICD-10* criteria for delirium have not been preferred by researchers, *partly reflecting the sizeable contribution of psychiatrists (who tend to be highly familiar with DSM) to the field but also because ICD-10 requires the presence of so many features, some of which are highly variable in their frequency (e.g. emotional disturbances)*. This shortcoming has been highlighted by a number of studies indicating that the *ICD-10* criteria lack sensitivity and exclude many patients that would be classified as delirious by *DSM* systems and which have similar clinical profiles and prognosis as delirium [3–5]. This lack of inclusivity could be addressed by simplifying the definition to emphasize the distinction between required (invariable) features vs. suggestive features that are typically present but that are not mandatory for the diagnosis.

Sources of information in determining delirium caseness

Making a diagnosis of delirium usually requires gathering information from multiple sources. A patient's mental status can be assessed by observation, interview, and formal cognitive testing. Further information regarding the course of any deficits is gleaned from the observer's knowledge of the patient, clinical notes, other staff, carers, etc. Specifying the type and quality of this information is important. Delirium presents special challenges here. Because delirium symptoms fluctuate, a patient can be orientated to time, person, and place when formally assessed at the bedside, for example on a morning ward round, while the clinical notes indicate that the patient was disorientated, paranoid, and agitated just hours earlier during the night. This raises the question of whether patients can be diagnosed with *current* delirium if they do not exhibit inattention and cognitive deficits in a single, brief assessment. Revised criteria might

address the timeframes over which delirium can be diagnosed, and the extent to which third-party information contributes to the diagnosis.

Another important issue with respect to information gathering relates to the status of information derived from patient interviews. Patients who are drowsy may not be able to answer questions regarding their symptoms, and patients with memory impairment may not recall disturbances of perception or thought content. Positive features of delirium derived from patients' account of their symptoms would appear to be specific, but not a sensitive indicator of delirium, and so cannot be relied upon as core diagnostic or severity markers.

Revised diagnostic criteria must address these issues. In particular, the status of different sources of information needs to be made explicit so that clinicians and researchers can use a standardized approach to the diagnosis of patients where particular information is unavailable or less reliable. A standardized dataset for delirium assessment could include measurement of cognition and arousal, and eliciting of neuropsychiatric symptoms and signs via interview and collateral history.

Attention as the core sign of delirium

For many centuries, the concept of delirium has included altered consciousness with generalized disturbance of higher cortical function. The extent to which all measurable elements of cognition should be affected and whether a primary cognitive domain is disproportionately impaired is less clear. Historically, clouding of consciousness has been emphasized, but this is a concept that lacks precision. Disturbed attention has become a cardinal feature of diagnostic criteria for delirium since *DSM III* [6], partly because of its high frequency and relative ease of measurement. The description of primary cognitive elements in *ICD-10* has created some confusion where it has been unclear whether a diagnosis requires *both* clouding of consciousness *and* reduced attention or whether either will suffice or whether clouding of consciousness is deemed present *as evidenced by* reduced ability to focus, sustain, or shift attention. Recent work addressing the relationship between the various elements of delirium indicates disproportionate disturbance of attention but with high correlation with other cognitive elements of delirium [7]. Moreover, the few phenomenological studies that have included serial assessment suggest that it is a consistent feature during the course of a delirious episode, further supporting the position of attention as a dominant element for definition [8].

However, given the central role of inattention in delirium diagnosis, the nature of the attentional deficits and how these are measured requires clarification. For example, attentional deficits vary considerably in severity: some patients are barely able to converse, whereas others have subtle deficits that are best detected by formal cognitive testing. *The*

minimal required severity of attentional disturbance that is consistent with delirium is also unclear but could be defined according to the impact upon ability to engage with immediate environment. Another important issue is that the assessment of attention is complicated by the frequent presence of low arousal; whether attention can really be separated from arousal in these circumstances is a major point of debate. Currently, in clinical practice and research, attention is assessed by clinical observation and also by using cognitive tests, such as digit span, serial sevens test, or recitation of the months of the year in reverse order. However, the validity of cognitive test criteria for inattention has not been tested thoroughly; an important issue given that attentional deficits are common in the dementias [9,10] while milder disturbances of attention are extremely common in most if not all neuropsychiatric disorders. These issues will only be resolved by additional research.

Cognitive deficits in delirium

Delirium diagnosis currently also requires the demonstration of generalized cognitive disturbance which allows distinction from disorders with more discrete neuropsychological disruptions (e.g., dysmnestic syndromes, mood disorders, attention deficit disorders, etc.). *ICD-10* mandates that disturbances of *both* memory and orientation be evident. Specifically, a disproportionate disturbance of immediate recall and recent memory with relatively intact remote memory is required. Phenomenological studies indicate that this pattern is not always evident in delirium and that orientation in particular is prone to great fluctuation during the course of an episode [8]. This impacts considerably upon detection especially where lucidity is equated with absence of disorientation. Disturbances of memory are notoriously difficult to attribute to delirium in populations with dementia. The demonstration of generalized cognitive deficit may be better achieved by requiring that disturbances be evident in *any of a range* of readily testable cognitive domains (e.g., comprehension, visuospatial function, orientation, vigilance, executive abilities, or memory). However, there is a fundamental lack of exploratory studies which have examined multiple symptoms and signs of mental status change without the constraint that patients have delirium or not. Therefore, it is not known whether certain elements of cognitive deficits change in isolation, or whether there are always deficits in complex cognition or attention when mental status change occurs. Moreover, considering cognition alone, the extent to which deficits in elements of attention and other cognitive domains, e.g., executive function, occur separately is unknown. The evidence suggests a complex picture [11–15].

Another approach that would allow for discrimination between cognitive deficits in delirium and dementia is where emphasis is placed on cognitive deficits that are

disproportionately affected in delirium. Two recent studies provided information about the symptom frequencies in patients with delirium without dementia, dementia without delirium, and comorbid delirium and dementia [16,17]. These studies indicate that impaired attention, disturbed consciousness, and disorganized thinking are significantly more common in delirium, whereas memory and orientation are similarly affected in both delirium and dementia. Comprehension, visuospatial function, vigilance, and executive abilities are less well studied, but some evidence suggests that testing in these cognitive domains may show some discrimination between delirium and dementia [18]. The emphasis on certain cognitive elements that are more impaired in delirium could be achieved by *excluding* memory problems and disorientation as key elements in patients with documented or suspected dementia, or by requiring evidence that disturbances in these domains represent a clear deterioration from a recent baseline.

Arousal and motor activity in delirium

Another important differentiating feature between delirium and dementia is arousal. Marked variations in arousal are a defining feature of dementia with Lewy bodies [19], but are not a common feature of other forms of dementia of mild to moderate severity. In contrast, patients with delirium are frequently drowsy or stuporous. When reduced arousal occurs in the context of acute illness, delirium is a likely diagnosis. In such circumstances the patient is usually not amenable to cognitive testing, so the defining feature of the syndrome becomes reduced arousal of acute onset. Whether this pattern of features is the same syndrome as one where there are deficits in cognition without altered arousal is an important matter for further investigation. It can be argued that revised criteria for delirium must find a clearer way of incorporating this common clinical phenomenon, without the constraint of requiring further diagnostic features that depend upon the patient being able to undergo an interview or cognitive testing. Current criteria do not explicitly allow for this. *DSM-IV* stipulates that the disturbance of consciousness is demonstrable via attentional deficits. *ICD-10* is broader, stating that there must be an “impairment of consciousness and attention (ranging from clouding and coma; reduced ability to direct, focus, sustain and shift attention).” However, the requirement for deficits in consciousness *and* attention means that the status of patients in whom attention cannot be assessed is not entirely clear. Substituting ‘conscious level *or* attention’ might remedy this, at the risk of losing some specificity.

Other neuropsychiatric features

Delirium typically includes a range of noncognitive neuropsychiatric symptoms. Some are almost invariably present (i.e., disturbances of motor activity and sleep–wake

cycle occur in over 90% of cases of delirium) [7,20]. However, these are relatively nonspecific symptoms that occur with great frequency across a range of neuropsychiatric syndromes and in nondelirious hospitalized elderly. For *DSM-IV* [21], it was concluded that the inclusion of sleep and motor disturbances would not add to the specificity of diagnosis. Moreover, because many of the drugs used to treat the symptoms of delirium and dementia have substantial effects on these domains, the assessment of their role is further complicated. However, given that delirium detection is such a key issue for clinical and research populations, items that might add *sensitivity* are also important *and were specificity to be applied as the sole criterion, the resulting criteria would lack face validity due to the exclusion of many of the most prevalent features*. More detailed study of the character and frequency of disturbances in these domains is needed so that we can have a better understanding of how particular patterns (e.g., more severe disturbances of sleep–wake reversal or fragmentation may be relatively specific to delirium—Meagher et al. [7] found that 73% of delirious patients had at least moderate disorganization of sleep–wake cycle).

Similarly, affective changes, thought process abnormalities, thought content, and perceptual disturbances are common in delirium but not invariably present and therefore lack utility as essential diagnostic features. The character of these symptoms may assist in the distinction from other neuropsychiatric disorders (e.g., dementia) [21,22]. For example, perceptual disturbances are significantly more common in delirium whether or not concomitant dementia is evident [16,17]. More detailed studies can clarify their usefulness in this regard.

The context of delirium symptoms

Although individual symptoms and signs are not specific to delirium, their combination and context are highly characteristic and are an important pointer when attempting to distinguish delirium from more chronic disorders such as dementia. Delirium is typically of acute onset and symptoms fluctuate over the course of the day. In *ICD-10* diagnostic criteria for research, Criterion E mandates that “symptoms have rapid onset and show fluctuations over the course of the day.” However, many cases are more gradual in onset and the degree of symptom fluctuation within 24 h may be less for quieter (so-called hypoactive) presentations and often includes a prodromal phase of 2–4 days characterized by nonspecific symptoms (e.g., general malaise) and/or subsyndromal delirium [23–25]. *DSM-IV* criteria suggest fluctuation over “hours to days.” Moreover, the emphasis on short time frames for onset and fluctuation serves to bias definitions against hypoactive forms of delirium which are more difficult to identify, have poor prognosis, and need to be better accounted for (even emphasized) in new definitions.

Another aspect of delirium presentation is that although symptoms that fluctuate are necessary for the diagnosis, those particular symptoms are by definition less useful for detection due to their inherent variability. As a consequence, while symptoms that are required for a diagnosis should be less prone to fluctuation and reliably demonstrable throughout the course of delirium episode, other more variable symptoms confer the fluctuation required for diagnosis.

Aetiological attribution

Delirium is highly heterogeneous in its causation with typically three to four significant causes operating in parallel and/or sequentially over the course of an episode [7,26,27]. As such, single aetiology delirium is the exception rather than the rule. Although many accept that the aetiology of delirium contributes to clinical profile, convincing evidence that aetiology impacts upon phenomenological presentation and/or treatment needs remains lacking. Moreover, existing studies do not adequately account for the multifactorial nature of delirium aetiology and are predominantly cross-sectional in nature. The attribution of delirium to single aetiological categories fails to capture this complexity. It may also contribute to the tendency to attribute causation to the first or most obvious aetiology identified rather than encourage detailed and sustained investigation of causes throughout an episode. Moreover, in around 10% of cases no clear aetiology is identified and it is not necessary for a single ‘cause’ to be identified for every case but rather that the relevant physical morbidity is acknowledged. The current *ICD-10* guidance regarding attribution of causation requires that the manifestations of delirium can be presumed to be related to an aetiology identified by evidence from history, examination, or investigation.

In other recent classifications, delirium related to alcohol or psychoactive substances has been classified separately from delirium due to other causes. While this distinction has relevance to pathophysiological underpinnings (e.g., different electroencephalogram patterns) and treatment needs (e.g., benzodiazepine use as first-line treatment), it is not sensitive to the likelihood that delirium due to substance use may also be multifactorial and may contribute to an overly simplistic conceptualization of delirium causation in such cases. The relevance of the role of genetic factors identified in studies of alcohol-related delirium [28] has yet to be considered in non-alcohol-related cases but will provide important insights into the degree to which similar neurobiological vulnerabilities underlie delirium due to differing primary aetiologies.

Delirium and dementia

A major challenge is to create a delirium definition that improves recognition in clinical practice. A principal reason

for poor detection is that delirium and dementia commonly co-exist especially in elderly patients where delirium is frequently misattributed to dementia symptoms [29]. In *ICD-10*, the presence of underlying dementia is emphasized as a subtype of delirium but the diagnosis of each is made separately. According to the *ICD-10*, the diagnosis of dementia cannot be established *before* the duration of symptoms has exceeded 6 months and where assessment is complicated by superimposed delirium “the diagnosis of dementia should be deferred.” In *DSM-IV*, there is a circularity in delirium–dementia differentiation with delirium the suggested diagnosis where cognitive changes “are not better accounted for by a pre-existing, established or evolving dementia” and dementia diagnosed where “deficits do not occur exclusively during the course of a delirium.”

Where patients are known or suspected of having prior cognitive impairment, it is essential that a deterioration from baseline is used to identify symptoms that reflect delirium. This is especially important in hypoactive presentations where acuteness of onset and fluctuating course may be less evident. These quieter presentations are more common in patients with comorbid dementia. With hyperactive presentations, the behavioral and psychological symptoms of dementia (BPSD) represent an important differential, but delirium as a medical emergency should take diagnostic precedence and the possibility of acute physical aetiologies ruled out.

Greater clarity regarding symptoms that suggest delirium over dementia is needed. Studies that have compared phenomenology of ‘pure’ delirium with comorbid delirium and dementia indicate that the symptom profile of delirium is not greatly altered by concomitant dementia and that delirium symptoms dominate where both occur but with more impaired cognitive scores [30] or more disorganized thinking and disorientation [16]. Unfortunately, the diagnosis of delirium is often missed in these comorbid patients [29] such that specific guidance is needed for delirium diagnosis in those with preexisting cognitive problems and where the overlap is especially challenging, in the case of dementia with Lewy bodies (DLB). Studies to date suggest that disturbances of attention, disorganized thinking, consciousness, altered arousal, motor activity, and perceptual changes are significantly more common in delirium (either with or without comorbid dementia) while other delirium symptoms are less helpful diagnostically when comorbid dementia is present, i.e., disorientation and memory problems occur at similar or greater frequency to delirium in patients with ‘pure’ dementia [16,17].

The relationship between superimposed delirium and the so-called BPSD is not well studied, but clearly there is considerable phenomenological overlap. Existing diagnostic schemes offer little assistance in this distinction but the provision of clear diagnostic criteria for BPSD that are sensitive to the possibility of delirium would assist in developing studies that might illuminate this complex area. Clinical need warrants that delirium, as a medical emer-

gency, should take diagnostic precedence. The context of disturbances can be a key element in distinction, but the presence of a suspected potential physical aetiology is less useful in elderly populations in whom medical problems that can contribute to delirium are extremely common. The presence of altered consciousness and inattention supports a delirium diagnosis but is common where dementia is of the Lewy body variant [10]. In contrast with DLB, autonomic dysfunction (e.g., orthostatic hypotension, postural instability, constipation) and extrapyramidal symptoms are relatively uncommon in delirium even where neuroleptic agents are utilized and this may assist in differentiation [31,32]. Other work has highlighted that the content of psychotic symptoms can assist in differentiation, but more detailed studies of the character of thought content abnormalities, perceptual disturbances, and formal thought disorder are required [22]. The presence of a physical precipitant(s) and marked symptom fluctuation also favors a diagnosis of delirium over BPSD. Greater collaboration between researchers in these fields is needed.

One suggestion would be for BPSD to be confined to patients in whom a diagnosis of dementia is established and delirium, a medical emergency, is ruled out. For BPSD, disturbances of thinking, perception, motor behaviors, and sleep–wake cycle should occur without prominent inattention or altered consciousness, except where patients have end-stage dementia where distinction on these grounds is less useful.

The duration, course, and severity of delirium

The course of delirium is highly variable, ranging from a short-lived disturbance lasting hours to days to a more persistent and often more severe deterioration that overlaps with dementia [23,33]. The classical concept of delirium includes reversibility as a key element, although studies have highlighted that this is not the course for many elderly medical patients that develop delirium [34,35]. The extent to which this reflects delirium’s role as a harbinger of a previously silent evolving dementia remains uncertain, but in many cases persistent cognitive decline occurs in patients experiencing delirium who were apparently previously cognitively intact [36–39]. There is no clarity regarding the minimum time frame for diagnostic criteria to be met but diagnosable delirium frequently occurs in intensive care unit patients as part of the transition from coma back to recovered consciousness [40]. Given the prognostic and management implications, subclassification of delirium according to course would emphasize the potential for persistence and allow for clear distinction of differing illness trajectories for further research. There is a paucity of research, however, which has defined the phenomenology of delirium over weeks and months. Given the present state of knowledge, the various durations might be described as brief (48 h or less) vs. short-term (2–7 days) vs. more sustained (1–4 weeks) vs.

relapsing and remitting vs. persistent (more than 1 month). In the absence of new data, the present cut-off of 6 months could be maintained but with the recognition that where a period of sustained recovery has occurred, further delirium should be considered as a new episode.

Another potential parameter of delirium to be included in revised criteria is severity. Several scales used largely in research quantify severity including the Delirium Rating Scale [41], Delirium Rating Scale–Revised [42], and Memorial Delirium Assessment Scale [43]. Severity grading is meaningful, because greater severity is associated with poorer outcome [44,45]. However, neither *ICD-10* nor *DSM-IV* allows for grading of delirium severity. It may be useful for clinical practice and research to introduce a measure of episode severity based on both frequency and severity of key symptoms, perhaps adopting that used in other conditions, i.e., mild, moderate, and severe.

Clinical subtypes

Delirium is a highly heterogeneous syndrome and as such there may be utility in allocation of cases according to clinical subtypes. To date, most interest has involved subtyping according to motor activity alterations partly because of their high visibility and frequency (over 90% of deliria). Agitated-hyperalert vs. quiet-hypoactive variants of acute cognitive disturbances have been noted since ancient times as *phrenitis* and *lethargicus*, respectively. In more recent times, three motor variants have been studied—hyperactive, hypoactive, and mixed. The usefulness of motor-based subtyping was considered prior to *DSM-IV*, but it was concluded that there was a need to determine whether these subtypes could be reliably defined and whether they implied meaningful clinical differences [46]. There are now multiple studies of motor subtypes which suggest significant differences in relation to frequency and severity of nonmotoric symptoms [47], aetiology [48,49], pathophysiology [50,51], treatment experience [52–54], duration of episode, and outcome [54–56]. However, the area is fraught with problems in definition of subtypes, and this limits the generalisability of findings across studies. More recent work appears to be identifying a more consistent approach to definition emphasising motor disturbances that are relatively specific to delirium (rather than associated psychomotoric symptoms) [57]. The formal recognition of these subtypes of delirium would emphasize the different challenges they pose and promote more consistent recognition of less obvious presentations of delirium. Other approaches to subtyping of delirium, for example, psychotic vs. nonpsychotic, have not yet been sufficiently studied to determine their usefulness.

Syndromal vs. subsyndromal delirium

Recent studies have suggested that the presence of some features of delirium, but without sufficient features to meet

DSM or *ICD* criteria or at a severity below diagnostic cut-off for delirium on diagnostic scales, may be associated with adverse outcomes [58–60]. These findings along with studies that have linked prognosis to individual symptoms [61] suggest that further clarification of the significance of individual features is required. In particular, these findings raise the question of whether a less restrictive, or at least a more differentiated (e.g., in terms of severity, features, time course), definition of delirium is justified. Formal recognition of subsyndromal illness would facilitate research efforts to address these issues, but this requires clarity regarding definition of the concept.

Conclusions

DSM-IV descriptions of delirium have good acceptance among both clinicians and researchers and future descriptions within *ICD* need to be better aligned. Where possible, changes should be according to available research rather than to expert opinion or other factors. There does not appear to be strong, formal evidence to support major changes in the key features outlined in current *DSM* definitions, but some elements of the syndrome could be better accounted for, especially disturbances of sleep–wake cycle and motor behavior. The status of reduced arousal of acute onset needs to be clarified since it commonly impacts upon the ability to demonstrate impairment in cognition. The requirement for acuity of onset and fluctuation of symptoms in relatively hypoactive presentations could be lessened to require subacute onset with or without symptom fluctuation. The increasing evidence that patients with delirium experience a number of distinct courses and severities and for clinically relevant (motoric) subtypes supports the inclusion of subclassification according to these attributes. Specific guidance is required around diagnosis where dementia is present (or suspected) especially as to the cognitive elements that best constitute generalized impairment. In general, patients should have evidence of deterioration in cognitive abilities with inattention as a core element and evidence of impairment in a combination of either memory, orientation, visuospatial function, or comprehension, but where dementia is suspected disorientation and memory disturbances are less helpful. There is a particular need for studies exploring the delirium–dementia interface, improved clarity as to the features that assist in definition of clinical subtypes, and closer examination of the relevance of subsyndromal illness and the importance of individual delirium symptoms present in such cases.

The field of delirium has seen considerable advances in the last few years. *ICD-11* offers the possibility for an improved definition of delirium which addresses the many complexities of this conditions as well as providing a workable set of criteria applicable in clinical and research settings. However, it is likely that the definition of delirium will continue to evolve well beyond even *ICD-11* as the evidence base grows.

Acknowledgments

AM was supported by an MRC Clinician Scientist Fellowship. The UK Medical Research Council and the University of Edinburgh provide core funding for the MRC Centre for Cognitive Ageing and Cognitive Epidemiology which supported AM.

References

- [1] World Health Organization. Mental and behavioral disorders (F00–F99). The International Classification of Diseases, 10th rev.: ICD-10. Geneva: World Health Organization, 1992.
- [2] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4th ed. Washington (DC): American Psychiatric Association, 1994.
- [3] Laurila JV, Pitkala KH, Strandberg TE, Tilvis RS. Impact of different diagnostic criteria on prognosis of delirium: a prospective study. *Dement Geriatr Cogn Disord* 2004;18:240–4.
- [4] Cole MG, Dendukuri N, McCusker J, et al. An empirical study of different diagnostic criteria for delirium among elderly medical inpatients. *J Neuropsychiatry Clin Neurosci* 2003;15:200–7.
- [5] Liptzin B, Levkoff SE, Cleary PD, Pilgrim DM, et al. An empirical study of diagnostic criteria for delirium. *Am J Psychiatry* 1991;148:454–7.
- [6] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 3rd ed. Washington (DC): American Psychiatric Association, 1980.
- [7] Meagher DJ, Moran M, Raju B, Gibbons D, Donnelly S, Saunders J, Trzepacz PT. Phenomenology of 100 consecutive adult cases of delirium. *Br J Psychiatry* 2007;190:135–41.
- [8] Leonard M, Donnelly S, Conroy M, Saunders J, Trzepacz P, Meagher D. A longitudinal study of phenomenological profile in delirium. Proceedings of European Delirium Association Second Annual meeting, 2007. <http://www.europeandeliriumassociation.com>.
- [9] O'Keefe ST, Gosney MA. Assessing attentiveness in older hospitalized patients: global assessment vs. test of attention. *J Am Geriatr Soc* 1997;45:470–3.
- [10] Calderon J, Perry RJ, Erzincinoglu SW, Berrios GE, Denning TR, Hodges JR. Perception, attention, and working memory are disproportionately impaired in dementia with Lewy bodies compared with Alzheimer's disease. *J Neurol Neurosurg Psychiatry* 2001;70:157–64.
- [11] Bailie R, Christmas L, Price N, Restall J, Simpson P, Wesnes K. Effects of temazepam premedication on cognitive recovery following alfentanil-propofol anesthesia. *Br J Anaesth* 1989;63:68–75.
- [12] Dale MT, Naik R, Williams JP, Lloyd AJ, Thompson JP. Impairment of sustained attention after major gynaecological surgery. *Eur J Anaesthesiol* 2005;22:843–7.
- [13] McCrimmon RJ, Deary IJ, Huntly BJP, MacLeod KJ, Frier BM. Visual information processing during controlled hypoglycaemia in humans. *Brain* 1996;119:1277–87.
- [14] Sommerfield AJ, Deary IJ, McAulay V, Frier BM. Short-term, delayed, and working memory are impaired during hypoglycemia in individuals with type 1 diabetes. *Diabetes Care* 2003;26:390–6.
- [15] Silverstein JH, Steinmetz J, Reichenberg A, Harvey PD, Rasmussen LS. Postoperative cognitive dysfunction in patients with preoperative cognitive impairment—Which domains are most vulnerable? *Anesthesiology* 2007;106:431–5.
- [16] Cole MG, McCusker J, Dendukuri N, Han L. Symptoms of delirium among elderly medical inpatients with or without dementia. *J Neuropsychiatry Clin Neurosci* 2002;14:167–75.
- [17] 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? *Int J Geriatr Psychiatry* 2004;19:271–7.
- [18] 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.
- [19] McKeith I, Mintzer J, Aarsland D, Burn D, Chiu H, Cohen-Mansfield J, Dickson D, Dubois B, Duda JE, Feldman H, Gauthier S, Halliday G, Lawlor B, Lippa C, Lopez OL, Machado JC, O'Brien J, Playfer J, Reid W. Dementia with Lewy bodies. *Lancet Neurology* 2004;3:19–28.
- [20] Rockwood K. The occurrence and duration of symptoms in elderly patients with delirium. *J Gerontol Med Sci* 1993;48:M162–6.
- [21] Liptzin B, Levkoff SE, Gottlieb GL, Johnson JC. Delirium: background papers for DSM-IV. *J Neuropsychiatry Clin Neurosci* 1993;5:154–60.
- [22] Meagher DJ, Trzepacz PT. Phenomenological distinctions needed in DSM-V: delirium, subsyndromal delirium and dementias. *J Neuropsychiatry Clin Neurosci* 2007;19:468–70.
- [23] Levkoff SE, Liptzin B, Evans DA, Cleary PD, et al. Progression and resolution of delirium in elderly patients hospitalised for acute care. *Am J Geriatr Psychiatry* 1994;2:230–8.
- [24] Fann JR, Alfano CM, Burington BE, Roth-Roemer S, Katon WJ, Syrjala KL. Clinical presentation of delirium in patients undergoing hematopoietic stem cell transplantation. *Cancer* 2005;103:810–20.
- [25] De Jonghe JFM, Kalisvaart KJ, Dijkstra M, van Dis H, et al. Early symptoms in the prodromal phase of delirium: a prospective cohort study in elderly patients undergoing hip surgery. *Am J Geriatr Psychiatry* 2007;15:112–21.
- [26] Lawlor PG, Gagnon B, Mancini IL, et al. Occurrence, causes and outcome of delirium in patients with advanced cancer. *Arch Intern Med* 2000;160:786–94.
- [27] Laurila JV, Laakkonen M-L, Strandberg TE, Tilvis RS, Pitkala KH. Predisposing and precipitating factors for delirium in a frail geriatric population. *J Psychosom Res* 2008;65:249–54.
- [28] Trzepacz P, Meagher D. Neuropsychiatric aspects of delirium. In: Yudofsky S, Hales R, editors. *American Psychiatric Association Textbook of Neuropsychiatry*. 5th ed. Washington (DC): American Psychiatric Publishing Press, 2007. pp. 445–517.
- [29] Inouye SK, Foreman MD, Mion LC, et al. Nurses' recognition of delirium and its symptoms: comparison of nurse and researcher ratings. *Arch Intern Med* 2001;161:2467–73.
- [30] Trzepacz PT, Mulsant BH, Dew MA, Pasternak R, Sweet RA, Zubenko GS. Is delirium different when it occurs in dementia? A study using the Delirium Rating Scale. *J Neuropsychiatry Clin Neurosci* 1998;10:199–204.
- [31] McKeith I, Mintzer J, Aarsland D, Burn D, et al. Dementia with Lewy bodies. *Lancet Neurol* 2004;3:19–28.
- [32] Meagher D, Leonard M. Active management of delirium across treatment settings. *Adv Psychiatr Treat* [in press].
- [33] Rudberg MA, Pompei P, Foreman MD, Ross RE, Cassel CK. The natural history of delirium in older hospitalized patients: a syndrome of heterogeneity. *Age Ageing* 1997;26:169–74.
- [34] Marcantonio ER, Simon SE, Bergmann MA, Jones RN, Murphy KM, Morris JN. Delirium symptoms in post-acute care: prevalent, persistent, and associated with poor functional recovery. *J Am Geriatr Soc* 2003;51:4–9.
- [35] Sylvestre MP, McCusker J, Cole M, et al. Classification of patterns of delirium severity scores over time in an elderly population. *Int Psychogeriatr* 2006;18:667–80.
- [36] Rockwood K, Cosway S, Carver D, et al. The risk of dementia and death after delirium. *Age Ageing* 1999;28:551–6.
- [37] Rahkonen T, Luukkainen-Markkula R, Paanila S, Sivenius J, Sulkava R. Delirium as a sign of undetected dementia among community dwelling elderly subjects: a 2 year follow up study. *J Neurol Neurosurg Psychiatry* 2000;69:519–21.
- [38] Gruber-Baldini AL, Zimmerman S, Morrison RS, et al. Cognitive impairment in hip fracture patients: timing of detection and longitudinal follow-up. *J Am Geriatr Soc* 2003;51:1227–36.

- [39] Lundstrom M, Edlund A, Bucht G, Karlsson S, Gustafson Y. Dementia after delirium in patients with femoral neck fractures. *J Am Geriatr Soc* 2003;51:1002–6.
- [40] McNicoll L, Pisani MA, Zhang Y, et al. Delirium in the intensive care unit: occurrence and clinical course in older patients. *J Am Geriatr Soc* 2003;51:591–8.
- [41] Trzepacz PT, Baker RW, Greenhouse J. A symptom rating scale for delirium. *Psychiatry Res* 1988;23:89–97.
- [42] Trzepacz PT, Mittal D, Torres R, et al. Validation of the Delirium Rating Scale–Revised-98: comparison to the Delirium Rating Scale and Cognitive Test for Delirium. *J Neuropsychiatry Clin Neurosci* 2001;13:229–42.
- [43] Breitbart W, Rosenfeld B, Roth A, et al. The Memorial Delirium Assessment Scale. *J Pain Symptom Manage* 1997;13:128–37.
- [44] Adamis D, et al. Recovery and outcome of delirium in elderly medical inpatients. *Arch Gerontol Geriatr* 2006;43:289–98 (sort ref).
- [45] Wada Y, Yamaguchi N. Delirium in the elderly: relationship of clinical symptoms to outcome. *Dementia* 1993;4:113–6.
- [46] Liptzin B. What criteria should be used for the diagnosis of delirium? *Dement Geriatr Cogn Disord* 1999;10:364–7.
- [47] Meagher DJ, O'Hanlon D, O'Mahony E, Casey PR, Trzepacz PT. Relationship between symptoms and motoric subtype of delirium. *J Neuropsychiatry Clin Neurosci* 2000;12:51–6.
- [48] Ross CA, Peyser CE, Shapiro I, et al. Delirium: phenomenologic and etiologic subtypes. *Int Psychogeriatr* 1991;3:135–47.
- [49] Meagher DJ, O'Hanlon D, O'Mahoney E, Casey PR, Trzepacz PT. Relationship between etiology and phenomenological profile in delirium. *J Geriatr Psychiatry Neurol* 1998;11:146–9.
- [50] Balan S, Leibowitz A, et al. The relation between the clinical subtypes of delirium and the urinary level of 6-SMT. *J Neuropsychiatry Clin Neurosci* 2003;15:363–6.
- [51] Van der Cammen TJM, Tiemeier H, Engelhart MJ, Fekkes D. Abnormal neurotransmitter metabolite levels in Alzheimer patients with a delirium. *Int J Geriatr Psychiatry* 2006;21:838–43.
- [52] Meagher DJ, O'Hanlon D, O'Mahony E, et al. Use of environmental strategies and psychotropic medication in the management of delirium. *Br J Psychiatry* 1996;168:512–5.
- [53] Breitbart W, Tremblay A, Gibson C. An open trial of olanzapine for the treatment of delirium in hospitalized cancer patients. *Psychosomatics* 2002;43:175–82.
- [54] Liptzin B, Levkoff SE. An empirical study of delirium subtypes. *Br J Psychiatry* 1992;161:843–5.
- [55] O'Keeffe ST. Clinical subtypes of delirium in the elderly. *Dement Geriatr Cogn Disord* 1999;10:380–5.
- [56] Kiely DK, Jones RN, Bergmann MA, Marcantonio ER. Association between psychomotor activity delirium subtypes and mortality among newly admitted postacute facility patients. *J Gerontol* 2007;62A:174–9.
- [57] Meagher DJ, Moran M, Raju B, Gibbons D, Donnelly S, Saunders J, Trzepacz PT. A new data-based motor subtype schema for delirium. *J Neuropsychiatry Clin Neurosci* 2008;20:185–93.
- [58] Levkoff SE, Liptzin B, Cleary P, Wetle T, Evans D, Rowe J, Lipsitz L. Subsyndromal delirium. *Am J Geriatr Psychiatry* 1996;4:320–9.
- [59] Cole M, McCusker J, Dendukuri N, Han L. The prognostic significance of subsyndromal delirium in elderly medical inpatients. *J Am Geriatr Soc* 2003;51:754–60.
- [60] Marcantonio ER, Simon SE, Orav EJ, et al. Outcomes of elders admitted to post-acute care facilities with delirium, subsyndromal delirium, or no delirium. *J Am Geriatr Soc* 2002;50:S168.
- [61] Cole MG, McCusker J, Ciampi A, Dyachenko A. An exploratory study of diagnostic criteria for delirium in older medical inpatients. *J Neuropsychiatry Clin Neurosci* 2007;19:151–6.