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WHAT'S NEW IN INTENSIVE CARE

Updated nomenclature of delirium and acute encephalopathy: statement of ten Societies

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Segregation of published research

Patients with an acute illness frequently acquire an acute, global disturbance in cognition variably referred to as *delirium*, *encephalopathy*, *acute confusional state*, *acute brain dysfunction*, *acute brain failure*, *and altered mental status* [1]. Although these different terms may have been perceived as distinct clinical entities [2], evidence to support such distinctions is lacking.

Acute disturbances in cognition are particularly prevalent among individuals admitted to the intensive-care unit [3]. These disturbances have been linked to predisposing and triggering factors [4], and have been independently associated with adverse short- and long-term outcomes, including higher mortality and chronic cognitive impairment [5, 6]. While progress has been made in the detection of this problem, research is needed to identify effective interventions for prevention and treatment. A rational approach to nomenclature represents an important basis to enable such advances.

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Societies: American Academy of Neurology (AAN), American Delirium Society (ADS), European Academy of Neurology (EAN), European Delirium Association (EDA), European Geriatric Medicine Society (EuGMS), European Society of Anaesthesiology (ESA), European Society of Intensive Care Medicine (ESICM), Neurocritical Care Society (NCS), Society of Critical Care Medicine (SCCM), and Società Italiana di Anestesia Analgesia Rianimazione e Terapia Intensiva (SIAARTI)

A definition of delirium is provided in the 5th version of the Diagnostic and Statistical Manual (DSM-5) of the American Psychiatric Association [7] and in the 11th edition of the International Statistical Classification of Diseases and Related Health Problems (ICD-11) [8]. Encephalopathy is a generic term that has been used to describe a global disturbance in brain function. However, the terms *acute encephalopathy, acute confusional state, acute brain dysfunction, acute brain failure,* and *altered mental status* lack uniform definitions and are not present in formal diagnostic systems. Our analysis focuses on delirium and acute encephalopathy, as these are the most frequently used terms.

We hypothesized that published research on delirium and encephalopathy is highly segregated, and that this segregation would be linked to the clinical discipline of investigators. We conducted a systematic search (see details in the Supplementary Materials) which led to three findings. First, journals on clinical neurology, neurosciences, or general or internal medicine published significantly more articles with 'encephalopathy' in the title, whereas journals associated with geriatrics, gerontology, psychiatry, psychology, intensive-care medicine, or anaesthesiology published significantly more delirium-titled articles ($P<0.001$). Second, articles with 'encephalopathy' in the title rarely (1%, $n=1$ of 100 randomly selected articles) mentioned 'delirium' in the text, and conversely articles with 'delirium' in the title used the word 'encephalopathy' in not more than 2% of publications ($n=2$ out of 100). Third, almost all citations in the delirium and encephalopathy literature (98.77%, $n=36{,}729$) were between papers with matching terms in the titles (i.e., delirium-titled articles citing other delirium-titled articles

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and encephalopathy-titled articles citing other encephalopathy-titled articles). Only a small proportion (0.53%, $n=197$) of citations were from encephalopathy-titled articles citing delirium-titled papers, or from delirium-titled articles referencing papers with the term 'encephalopathy' in the title (0.70%; $n=259$). It should, however, be noted that almost all articles on 'acute encephalopathy' use the term 'encephalopathy' in isolation; therefore, it is possible that segregation of the literature could be driven, in part, by the inclusion of articles on chronic encephalopathy.

These findings confirmed our hypothesis on the existence of segregated literatures, and suggest conceptual or semantic disparities across different medical disciplines. We believe that the lack of a uniform nomenclature represents a significant barrier to scientific progress and has implications for clinical management that might influence patient outcome. For example, use of the term 'delirium' may trigger specific management, whereas 'septic encephalopathy' may overlook mechanisms other than sepsis, such as metabolic alterations or drug side-effects. Additional factors, such as differences in billing and reimbursement between patients diagnosed with encephalopathy (versus delirium), may be a factor driving the selective use of terms in some countries, such as the USA.

Consensus recommendations on nomenclature

To generate expert consensus, we convened an international, interdisciplinary panel of leading experts with expertise in intensive-care medicine, neurology, geriatrics, rehabilitation medicine, pharmacy, anaesthesiology, and psychiatry. Panellists were tasked with generating recommendations on the nomenclature of delirium, acute encephalopathy, and related terms. The definitions were created, refined, and voted on using the modified Delphi method (see Supplementary Materials).

The panel recommends the term *acute encephalopathy* to describe a rapidly developing (in less than 4 weeks) pathobiological brain process which is expressed clinically as either subsyndromal delirium, delirium or coma and may have additional features, such as seizures or extrapyramidal signs (Box). The term acute encephalopathy is not recommended as a descriptor of clinical features that can be observed at the bedside. Instead, the panel recommends the term *subsyndromal delirium* for acute cognitive changes that are compatible with delirium, but do not fulfil all DSM-5 delirium criteria, *delirium* for a clinical state defined according to the criteria of the DSM-5 [6], and *coma* for a state of severely depressed responsiveness defined using diagnostic systems such as the Glasgow Coma Score (GCS) or the Full Outline of UnResponsiveness (FOUR) score (Box) [9, 10]. The panel further recommends against use of the terms *acute confusional state, acute brain dysfunction, acute brain failure*, or *altered mental status* in clinical practice or research (Box). Although these terms might have relevance for educational purposes, the panel felt that they lacked face or construct validity.

The recommendations in this manuscript have been endorsed by ten key professional societies (see Supplementary Materials), and this terminology is congruent with the recent recommendations for the nomenclature of cognitive change associated with anaesthesia and surgery [11]. Delayed neurocognitive recovery after anaesthesia and surgery can be regarded as consequence of prolonged postoperative acute encephalopathy.

In conclusion, current literature on delirium and acute encephalopathy is highly segregated, presenting an obstacle for clinical care and research. We recommend a consensus-based, pragmatic nomenclature which we expect will establish a foundation for advances in the field. Following dissemination of these recommendations, future research should evaluate the impact of this revised nomenclature on clinical practice and research.

Box: Recommendations for the nomenclature of delirium, acute encephalopathy, and related terms

1. The term *acute encephalopathy* refers to a rapidly developing (over less than 4 weeks, but usually within hours to a few days) pathobiological process in the brain. **This is a preferred term**
2. *Acute encephalopathy* can lead to a clinical presentation of subsyndromal delirium, delirium, or in case of a severely decreased level of consciousness, coma; all representing a change from baseline cognitive status
3. The term *delirium* refers to a clinical state characterized by a combination of features defined by diagnostic systems such as the DSM-5. Delirium according to the DSM-5 is defined if criterium A-E are fulfilled: A. Disturbance in attention (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment). B. The disturbance develops over a short period of time (usually hours to a few days) represents a change from baseline attention and awareness, and tends to fluctuate in severity during the course of the day. C. An additional disturbance in cognition (e.g., memory deficit, disorientation, language, visuospatial ability, or perception). D. The disturbances in criteria A and C are not explained by another pre-existing, established, or evolving neurocognitive disorder, and do not occur in the context of a severely reduced level of arousal, such as coma. E. There is evidence from the history, physical examination, or laboratory findings that the disturbance is a direct physiologic consequence of another medical condition, substance intoxication or withdrawal (i.e. because of a drug of abuse medication), or exposure to a toxin, or is because of multiple etiologies. **This is a preferred term**
4. The term *coma* refers to a clinical state of severely depressed responsiveness defined by diagnostic systems such as the GCS or FOUR score. **This is a preferred term**
5. The term *acute confusional state* **should not be used** in addition to the terms delirium and acute encephalopathy
6. The term *acute brain dysfunction* **should not be used** in addition to the terms delirium and acute encephalopathy
7. The term *acute brain failure* **should not be used** in addition to the terms delirium and acute encephalopathy
8. The term *altered mental status* is not synonymous with *delirium* and **should not be used**

DSM-5 means the Diagnostic and Statistical Manual (DSM-5) of the American Psychiatric Association. GCS refers to Glasgow Coma Score; the FOUR score means the Full Outline of UnResponsiveness score.

Electronic supplementary material
The online version of this article (https://doi.org/10.1007/s00134-019-05907-4) contains supplementary material, which is available to authorized users.

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