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Research Progress on the Correlation Between Delirium and Dementia

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Abstract

Delirium is an acute confusional state characterized by inattention, altered level of consciousness, and cognitive dysfunction, whereas dementia is an insidious, chronic, and progressive loss of previously acquired cognitive abilities. The occurrence of delirium is an independent risk factor for subsequent dementia, and conversely, patients with dementia have a significantly higher risk of developing delirium compared to the general population. Although the close relationship between the two is recognized, the specific mechanisms underlying their interaction remain unclear. In daily life and clinical practice, timely assessment of cognitive function and effective intervention in individuals experiencing delirium may potentially slow cognitive decline and even prevent the onset or progression of dementia. This article reviews the research on the correlation between delirium and dementia, exploring ways to mitigate or even reverse further cognitive deterioration in delirious patients.

Keywords

Delirium, Dementia, Cognitive Dysfunction

Background

According to the World Health Organization, with societal aging, costs related to dementia are projected to reach US$2.8 trillion by 2030, and the global number of people living with dementia is expected to reach 139 million by 2050. Dementia impacts individuals, families, and economies, with an estimated annual global cost of approximately US$1 trillion. Improving population cognitive function and preventing dementia through various interventions have become a major societal issue [1,2].

The relationship between delirium, cognitive decline, and dementia is highly significant. The risk of delirium increases 2–5 times in patients with dementia, and the onset of delirium may reveal previously unrecognized dementia [3]. Delirium reflects brain vulnerability, reduced cognitive reserve, and an increased risk of long-term dementia. Simultaneously, the experience of delirium itself leads to long-term cognitive impairment and dementia. Growing evidence from epidemiological studies to tissue culture and animal research strongly suggests that delirium causes, mediates, or both, permanent cognitive impairment [4].

Many patients experience delirium during hospitalization. Rates among internal medicine patients are 11%–14% in general internal medicine, 20%–29% in geriatric wards, and 19%–82% in intensive care units (ICUs). For surgical patients, postoperative delirium

rates are 11%–46% after cardiac surgery, 13%–50% after non-cardiac surgery, and 12%–51% in orthopedic surgery patients [4]. The cumulative incidence of delirium reportedly reaches 85% at the end of life. Despite being a common condition, 55%–80% of cases are not recognized or documented during clinical diagnosis and treatment [5].

In 2014, the U.S. Preventive Services Task Force stated that there was insufficient evidence to assess the balance of benefits and harms of universal screening for cognitive impairment in community-dwelling adults aged 65 and older using formal screening tools [6]. Under current conditions, identifying delirium and implementing cognitive function-related interventions may help guide resource allocation and improve patient care. Prevention and treatment strategies for delirium offer a valuable opportunity for early intervention, preservation of cognitive reserve, and prevention of irreversible cognitive decline during aging [3].

Definition and Diagnosis of Delirium and Dementia

According to the International Classification of Diseases, 11th Revision (ICD-11) definition, delirium is characterized by an acute or subacute onset of attention disorder (i.e., reduced ability to direct, focus, sustain, and shift attention) and consciousness disorder (i.e., reduced orientation to the environment). Symptoms often fluctuate within a day and are accompanied by other cognitive impairments (such as memory, language, visuospatial function, or perceptual disturbances). It may affect the sleep–wake cycle, and its etiology is often attributed to non-psychiatric behavioral disorders, substance intoxication, or withdrawal from certain medications. The diagnosis of delirium is based entirely on history and physical examination. Unlike most conditions where history is primarily obtained from the patient, the history for delirium is mainly provided by caregivers and nursing staff.

Many scales are used for screening and diagnosing delirium. The Confusion Assessment Method (CAM) is the most widely used tool in the US for identifying delirious patients, requiring special training for correct use. The CAM-ICU, derived from the CAM, relies on non-verbal responses to assess attention, thinking, and level of consciousness, making it suitable for critically ill ICU patients. There are two simplified versions of CAM: the 3-Minute Diagnostic Interview for CAM (3D-CAM) and the brief CAM (bCAM), both used to rate the four core CAM features. An ultra-brief two-item test (assessing ability to state the day of the week and recite the months of the year backwards) may be a reasonable screening tool with 93% sensitivity and 64% specificity. The 4 'A's Test (4AT) is another simple scale suggested for initial delirium screening, usable clinically without special training, with a sensitivity of 76% and specificity of 94% [5].

The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) diagnostic criteria for dementia (Major Neurocognitive Disorder) are as follows:

1. Evidence of significant cognitive decline from a previous level of performance in one or more cognitive domains (complex attention, executive function, learning and memory, language, perceptual-motor, or social cognition).
2. The cognitive deficits interfere with independence in everyday activities.
3. The cognitive deficits do not occur exclusively in the context of delirium.
4. The cognitive deficits are not better explained by another mental disorder [7].

Assessing possible dementia requires a brief history, cognitive, and neurological examination. History should be obtained from the patient and a close family member or friend, describing the affected cognitive domains (e.g., memory, language), severity (whether it affects daily life), and progression (speed and pattern, e.g., fluctuating or stepwise worsening). Cognitive examination determines the presence, severity, and nature of cognitive impairment, considering cultural, linguistic, educational, and other factors (e.g., anxiety, sleep deprivation). Common screening tools include the Montreal Cognitive Assessment (MoCA) and the Mini-Mental State Examination (MMSE). The MoCA takes about 10 minutes and is useful for early detection of cognitive impairment, including Mild Cognitive Impairment (MCI) with executive dysfunction; a score <24 suggests need for further assessment. The MMSE,

developed over 40 years ago, is less sensitive for MCI and less thorough in assessing executive function, advanced language skills, and complex visuospatial processing. Additional assessment, such as detailed neuropsychological testing evaluating a wider range of cognitive abilities, may be needed, especially in highly educated individuals with clear historical decline but "normal" screening scores [6].

The most critical distinction between delirium and dementia is that delirium onset is usually sudden, lasting hours to days, while dementia onset is insidious and progressive, lasting months to years. In delirium, attention and level of consciousness are reduced and fluctuating; in dementia, they are impaired only in late stages. Differentiating the two relies on caregivers noting acute changes in mental status or behavior relative to baseline, or retrospective diagnosis based on symptom resolution after precipitating factors are removed or the acute illness is treated [8].

The Link Between Delirium and Cognitive Decline/Dementia

Global cognitive impairment is a well-established risk factor for delirium; pre-existing cognitive impairment is the primary predisposing factor for delirium [5,9]. Studies show a linear increase in delirium risk as baseline cognitive ability declines [10]. A 2024 retrospective cohort study in *JCA*, developing a prediction model for postoperative delirium after non-cardiac surgery using data from 51,677 patients, identified pre-existing dementia as one of the strong predictors [11].

Delirium occurring in the context of dementia is termed Delirium Superimposed on Dementia (DSD) [12]. A 2017 large prospective cohort (n=1,409) of hospitalized adults over 60 found a DSD prevalence of 31%, while a 2021 meta-analysis of 81 studies (including 81,536 dementia patients) reported a DSD prevalence of 48.9% during hospitalization [13,14].

Simultaneously, patients experiencing delirium often suffer cognitive deterioration. In a study of critically ill adults, 74% developed delirium during hospitalization. Three months later, 40% of survivors had global cognition scores more than 1.5 standard deviations below the population mean, and a quarter were more than 2 standard deviations below [15]. A 2021 meta-analysis in *JAMA Neurology* showed that patients who experienced delirium had 2.3 times the odds of cognitive decline compared to those who did not [16]. A large retrospective study by Emily H. Gordon et al. observed that patients without dementia at baseline who had at least one delirium episode had approximately three times the risk of a new dementia diagnosis over five years of follow-up compared to those without delirium; among those with at least one episode, each additional episode increased this risk by 20% [17].

Despite extensive research confirming the close relationship between delirium and dementia, the specific mechanisms underlying their interaction remain unclear. Several mechanisms have been hypothesized to explain how delirium leads to permanent neuronal damage and dementia, including neurotoxicity (e.g., drugs, anesthetics, endotoxins), inflammation, chronic stress, neuronal injury (e.g., prolonged ischemia, hypoglycemia, shock, sepsis), accelerated dementia pathology (e.g., amyloid beta [Aβ] and tau pathology), and reduced cognitive reserve.

Certain insults, such as metabolic disturbances or specific drugs (e.g., anticholinergics), may directly cause neuronal dysfunction via altered neurotransmitter concentrations (e.g., acetylcholine deficiency or dopamine excess). Hypoxia or cerebral ischemia may directly cause brain dysfunction via impaired cerebral blood flow and metabolism. Some anesthetics may directly promote accelerated Aβ deposition, leading to apoptosis and cholinergic dysfunction, further accelerating or triggering Aβ pathology. Infection or the response to stressors (e.g., surgery, acute illness) can activate inflammatory mechanisms, causing neuronal damage through altered neurotransmission, apoptosis, microglial or astrocyte activation, and the production of free radicals, complement factors, glutamate, and nitric oxide.

While specific mechanisms are complex, some clinical consequences in delirious patients make their increased dementia risk understandable. For instance, hypoactive delirium can lead to complications such as aspiration pneumonia, pressure sores, UTIs, DVT, and pulmonary

embolism; hyperactive delirium can lead to falls, injuries, and forced use of antipsychotics, sedatives, and physical restraints. These can trigger a cascade of harmful stimuli adversely affecting the brain, further contributing to dementia [9]. A large prospective study of 53,417 participants suggested that circadian rhythm disruption may be associated with delirium susceptibility and dementia progression [18].

Furthermore, many studies seek common biomarkers for delirium and Alzheimer's disease (AD). Fong TG's team proposed a novel conceptual model, examining established AD biomarkers in delirium research and emerging neuronal injury and microRNA biomarkers in both delirium and AD research, potentially revealing shared and complex pathophysiology. Their review found that, in some studies, the cerebrospinal fluid (CSF) Aβ42/Tau ratio decreased in postoperative delirium patients, and the presence of the Apolipoprotein E (ApoE) ε4 allele was associated with delirium, although other studies reported conflicting conclusions. In addition, specific microRNAs were observed to be up- or down-regulated in both AD and delirium patients, supporting the potential role of miRNAs in understanding shared pathophysiology [19].

An observational cohort study by Cunningham EL found that CSF Aβ1–42 concentration predicted delirium following elective joint replacement surgery [20]. Recently, Professor Zhongcong Xie's team, based on the close AD–postoperative delirium relationship, conducted a prospective observational cohort study showing that patients with higher preoperative plasma concentrations of AD-related biomarkers Tau-PT217 or Tau-PT181 were more likely to develop delirium and had higher delirium severity [21].

Even if current research has not fully elucidated the mechanisms linking delirium and dementia - and given their complex etiology, it is unlikely that future research will attribute this relationship to a single mechanism - it is crucial for clinicians to recognize that once delirium is identified, measures to prevent further cognitive decline are urgent and necessary.

Management Following Delirium Identification

While considerable research summarizes delirium screening and emphasizes prevention, systematic research on managing patients after delirium has occurred—specifically how to maximally slow or even reverse cognitive deterioration—is still lacking. First, delirium can be a harbinger of medical emergencies. All delirious patients should be screened for acute physiological disturbances such as hypoxia, hypoglycemia, and hypercapnia. In older adults, delirium can be a subtle or atypical presentation of disease; for example, myocardial infarction may present as delirium rather than chest pain or shortness of breath in octogenarians [5].

After excluding critical conditions, modifiable factors contributing to delirium should be sought. Factors are categorized as predisposing and precipitating. Predisposing factors and some precipitating factors (e.g., undergoing surgery or anesthesia) cannot be changed after delirium onset. However, some precipitating factors are reversible, such as use of psychoactive medications, infection, and pain. Medication classes highly associated with delirium include benzodiazepines, sedative-hypnotics, drugs with strong anticholinergic properties, opioid analgesics, and pro-dopaminergic drugs. Discontinuing relevant psychoactive drugs is a key reversible factor after delirium onset [5].

Current evidence indicates that no single medication truly treats delirium. Antipsychotics such as haloperidol are most commonly used to control symptoms. However, both atypical and typical antipsychotics have potential side effects, including excessive sedation, QTc prolongation, aspiration risk, and increased mortality. Their use is generally considered only when patients are in hyperactive states posing a risk of self-harm or harm to others [5,22,23]. Non-pharmacological management is the first-line treatment, especially for hypoactive delirium. It includes providing a suitable environment (orientation cues, cognitive stimulation, family presence); monitoring fluid balance and bowel function; optimizing oxygenation in hypoxic patients; early mobilization with walking aids; prompt removal of invasive or restraining devices; medication review; ensuring adequate nutrition; correcting visual or hearing impairments; and restoring circadian rhythms.

Delirious patients require ongoing monitoring of medical, cognitive, and functional status until return to baseline. Frequency depends on the case but should be at least daily during hospitalization, weekly shortly after discharge, and monthly after return to the community. Activities of daily living should be assessed to monitor functional recovery post-delirium. Patients not returning to baseline cognitive or functional status within 1-2 months should be considered for comprehensive geriatric assessment and/or neuropsychological testing. Patients with delirium persisting beyond 2 weeks are much less likely to recover baseline function [5].

Furthermore, multi-component, long-term follow-up post-delirium is necessary. Adopting management strategies used for dementia may benefit cognitive recovery and prevent deterioration in post-delirium patients. In the Systematic Multi-domain Alzheimer's Risk Reduction Trial (SMARRT) by Kristine Yaffe et al., personalized risk reduction via health coaching and nurse visits led to significantly greater improvement in a composite cognitive score after 2 years in the intervention group (82 participants) compared to the control group (90 participants), representing a 74% greater improvement. Targeted risk factors included physical inactivity, uncontrolled hypertension, poor sleep quality, use of potentially cognitively adverse medications, high depressive symptoms, uncontrolled diabetes, social isolation, and current smoking [24].

This provides a feasible approach for managing post-delirium patients: enrolling those who experienced delirium during care into a unified management program and providing individualized interventions based on their specific dementia risk factors to improve long-term outcomes. A 2019 *JAMA* review summarized non-pharmacological approaches for dementia, which are also worth considering for cognitive recovery and prevention of deterioration in post-delirium patients. These include cognitive stimulation activities (e.g., reading, games); physical exercise (aerobic and anaerobic); social interaction (e.g., family gatherings); healthy diet (nuts, berries, leafy greens, fish); adequate sleep (uninterrupted, sufficient duration); appropriate personal hygiene (e.g., regular bathing); safe environments (indoor, e.g., kitchen utensils; outdoor, e.g., driving); medical and advanced care directives; long-term healthcare planning (e.g., late-stage dementia living arrangements); assistance with financial planning and management; effective communication; and mental well-being through engagement in meaningful activities [6].

Conclusion

In summary, the further management of delirious patients can be divided into three parts: monitoring cognitive function, non-pharmacological interventions, and pharmacological treatment when necessary. The active participation of the patient, friends, family, and healthcare providers in creating conditions conducive to cognitive recovery and preventing further deterioration is crucial. Improving cognitive function is a process requiring multi-party involvement and long-term persistence, with potentially slow or minimal results. However, its significance for the individual patient, their family, and society as a whole is immense, deserving of collective attention and effort.

Conflict of Interest

The author has read and approved the final version of the manuscript. The author has no conflicts of interest to declare.

References

[1] Long S, Benoist C, Weidner W. World Alzheimer Report 2023: Reducing dementia risk: never too early, never too late. London, England: Alzheimer's Disease International; 2023. Available from: https://www.alzint.org/u/World-Alzheimer-Report-2023.pdf

[2] Livingston G, Huntley J, Sommerlad A, Ames D, Ballard C, Banerjee S, Brayne C, Burns A, Cohen-Mansfield J, Cooper C, Costafreda SG, Dias A, Fox N, Gitlin LN, Howard R, Kales HC, Kivimäki M, Larson EB, Ogunniyi A, Orgeta V, Ritchie K, Rockwood K, Sampson EL, Samus Q, Schneider LS, Selbæk G, Teri L, Mukadam N. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. Lancet. 2020 Aug 8;396(10248):413-46. Erratum in: Lancet. 2023 Sep 30;402(10408):1132. [**PMID**: 32738937]

[3] Fong TG, Davis D, Growdon ME, Albuquerque A, Inouye SK. The interface between delirium and dementia in elderly adults. Lancet Neurol. 2015

Aug;14(8):823-32. Erratum in: Lancet Neurol. 2015 Aug;14(8):788. [**PMID**: 26139023]

[4] Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. Lancet. 2014 Mar 8;383(9920):911-22. [**PMID**: 23992774]

[5] Mattison MLP. Delirium. Ann Intern Med. 2020 Oct 6;173(7):ITC49-ITC64. [**PMID**: 33017552]

[6] Arvanitakis Z, Shah RC, Bennett DA. Diagnosis and Management of Dementia: Review. JAMA. 2019 Oct 22;322(16):1589-99. [**PMID**: 31638686]

[7] Sachdev PS, Blacker D, Blazer DG, Ganguli M, Jeste DV, Paulsen JS, Petersen RC. Classifying neurocognitive disorders: the DSM-5 approach. Nat Rev Neurol. 2014 Nov;10(11):634-42. [**PMID**: 25266297]

[8] Fong TG, Inouye SK. The inter-relationship between delirium and dementia: the importance of delirium prevention. Nat Rev Neurol. 2022 Oct;18(10):579-96. [**PMID**: 36028563]

[9] Ghezzi ES, Ross TJ, Sharman R, Davis D, Boord MS, Thanabalan T, Thomas J, Keage HAD. The neuropsychological profile of delirium vulnerability: A systematic review and meta-analysis. Neurosci Biobehav Rev. 2022 Jan;132:248-59. [**PMID**: 34863781]

[10] Wilson JE, Mart MF, Cunningham C, Shehabi Y, Girard TD, MacLullich AMJ, Slooter AJC, Ely EW. Delirium. Nat Rev Dis Primers. 2020 Nov 12;6(1):90. Erratum in: Nat Rev Dis Primers. 2020 Dec 1;6(1):94. [**PMID**: 33184265]

[11] Cai S, Li J, Gao J, Pan W, Zhang Y. Prediction models for postoperative delirium after cardiac surgery: Systematic review and critical appraisal. Int J Nurs Stud. 2022 Dec;136:104340. [**PMID**: 36208541]

[12] Morandi A, Davis D, Bellelli G, Arora RC, Caplan GA, Kamholz B, Kolanowski A, Fick DM, Kreisel S, MacLullich A, Meagher D, Neufeld K, Pandharipande PP, Richardson S, Slooter AJ, Taylor JP, Thomas C, Tieges Z, Teodorczuk A, Voyer P, Rudolph JL. The Diagnosis of Delirium Superimposed on Dementia: An Emerging Challenge. J Am Med Dir Assoc. 2017 Jan;18(1):12-18. [**PMID**: 27650668]

[13] Avelino-Silva TJ, Campora F, Curiati JA, Jacob-Filho W. Association between delirium superimposed on dementia and mortality in hospitalized older adults: A prospective cohort study. PLoS Med. 2017 Mar 28;14(3):e1002264. [**PMID**: 28350792]

[14] Han QYC, Rodrigues NG, Klainin-Yobas P, Haugan G, Wu XV. Prevalence, Risk Factors, and Impact of Delirium on Hospitalized Older Adults With Dementia: A Systematic Review and Meta-Analysis. J Am Med Dir Assoc. 2022 Jan;23(1):23-32.e27. [**PMID**: 34648761]

[15] Kosar CM, Thomas KS, Inouye SK, Mor V. Delirium During Postacute Nursing Home Admission and Risk for Adverse Outcomes. J Am Geriatr Soc. 2017 Jul;65(7):1470-75. [**PMID**: 28338215]

[16] Goldberg TE, Chen C, Wang Y, Jung E, Swanson A, Ing C, Garcia PS, Whittington RA, Moitra V. Association of Delirium With Long-term Cognitive Decline: A Meta-analysis. JAMA Neurol. 2020 Nov 1;77(11):1373-81. Erratum in: JAMA Neurol. 2020 Nov 1;77(11):1452. [**PMID**: 32658246]

[17] Gordon EH, Ward DD, Xiong H, Berkovsky S, Hubbard RE. Delirium and incident dementia in hospital patients in New South Wales, Australia: retrospective cohort study. BMJ. 2024 Mar 27;384:e077634. [**PMID**: 38537951]

[18] Gao L, Li P, Gaykova N, Zheng X, Gao C, Lane JM, Saxena R, Scheer FAJL, Rutter MK, Akeju O, Hu K. Circadian Rest-Activity Rhythms, Delirium Risk, and Progression to Dementia. Ann Neurol. 2023 Jun;93(6):1145-57. [**PMID**: 36808743]

[19] Fong TG, Vasunilashorn SM, Libermann T, Marcantonio ER, Inouye SK. Delirium and Alzheimer disease: A proposed model for shared pathophysiology. Int J Geriatr Psychiatry. 2019 Jun;34(6):781-89. [**PMID**: 30773695]

[20] Cunningham EL, McGuinness B, McAuley DF, Toombs J, Mawhinney T, O'Brien S, Beverland D, Schott JM, Lunn MP, Zetterberg H, Passmore AP. CSF Beta-amyloid 1-42 Concentration Predicts Delirium Following Elective Arthroplasty Surgery in an Observational Cohort Study. Ann Surg. 2019 Jun;269(6):1200-205. [**PMID**: 31082921]

[21] Liang F, Baldyga K, Quan Q, Khatri A, Choi S, Wiener-Kronish J, Akeju O, Westover MB, Cody K, Shen Y, Marcantonio ER, Xie Z. Preoperative Plasma Tau-PT217 and Tau-PT181 Are Associated With Postoperative Delirium. Ann Surg. 2023 Jun 1;277(6):e1232-38. [**PMID**: 35794069]

[22] Hughes CG, Boncyk CS, Culley DJ, Fleisher LA, Leung JM, McDonagh DL, Gan TJ, McEvoy MD, Miller TE; Perioperative Quality Initiative (POQI) 6 Workgroup. American Society for Enhanced Recovery and Perioperative Quality Initiative Joint Consensus Statement on Postoperative Delirium Prevention. Anesth Analg. 2020 Jun;130(6):1572-90. [**PMID**: 32022748]

[23] Devlin JW, Skrobik Y, Gélinas C, Needham DM, Slooter AJC, Pandharipande PP, Watson PL, Weinhouse GL, Nunnally ME, Rochwerg B, Balas MC, van den Boogaard M, Bosma KJ, Brummel NE, Chanques G, Denehy L, Drouot X, Fraser GL, Harris JE, Joffe AM, Kho ME, Kress JP, Lanphere JA, McKinley S, Neufeld KJ, Pisani MA, Payen JF, Pun BT, Puntillo KA, Riker RR, Robinson BRH, Shehabi Y, Szumita PM, Winkelman C, Centofanti JE, Price C, Nikayin S, Misak CJ, Flood PD, Kiedrowski K, Alhazzani W. Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU. Crit Care Med. 2018 Sep;46(9):e825-73. [**PMID**: 30113379]

[24] Yaffe K, Vittinghoff E, Dublin S, Peltz CB, Fleckenstein LE, Rosenberg DE, Barnes DE, Balderson BH, Larson EB. Effect of Personalized Risk-Reduction Strategies on Cognition and Dementia Risk Profile Among Older Adults: The SMARRT Randomized Clinical Trial. JAMA Intern Med. 2024 Jan 1;184(1):54-62. [**PMID**: 38010725]