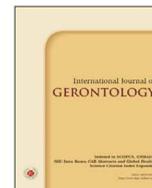




International Journal of Gerontology

journal homepage: <http://www.sgecm.org.tw/ijge/>



Editorial Comment

Delirium in the Elderly: Neurobiology and Trend in the Intervention

The rate of the elderly in Taiwan is expected to exceed 20% by 2025, making it a Super-Aged Society¹ and correspondent medical issues become serious in our health care systems. One of those problems in medical care is delirium in the Emergency room and at admission. Delirium is a syndrome of cognitive impairments often presented by a fluctuating course marked with disturbances in attention, awareness, circadian rhythm, and behavioral disturbance. According to the behavioral manifestations, it can be categorized as hypoactive, hyperactive and mixed types. Origins of delirium often reflect the pathophysiological consequences of various medical conditions, including acute infectious illnesses, serious medical complications, or drug adverse effects etc. The early detection and ensuring preventive treatment of delirium are becoming pivotal in the hospital. However, delirium is commonly underestimated and neglected in the critical care units, particularly at the early stage and hypoactive type.² Its neurobiological mechanisms and updated clinical interventions are not well recognized by the clinical staff, even though neuroscientific evidence has been well-documented over the past years.^{3,4}

In our journal, we have ever published 5 articles featuring the associated pictures of delirium, including post-operative conditions and post-COVID syndrome in the elderly.^{2,5–8} The inflammatory reactions, such as cytokine profiles, is one of the major cause in the development of delirium among the elderly.⁸ Of those studies, one tried to early detect delirium and handle the underlying causes or clinical symptoms accordingly at admission to improve the clinical outcomes.² At the intervention of delirium, to identify underlying causes is fundamental, but at commonplace clinical situations, symptomatic managements are administered when the etiologies are not well known or complicated. The common pathophysiological mechanisms of delirious symptoms have evolved from the interactions among neurotransmitters, such dopamine and acetylcholine, to the balance of glutamate and GABA interneuron.³ The serotonergic system, especially a combined functioning of 5_{1a}, 5_{2a/2c} and 5₇ receptors, also becomes the potential intervention target for balancing excitation and inhibition neuronal functionings.⁹ Neuroanatomical areas of delirium are associated with ascending activating system, thalamus, suprachiasmatic nucleus and cortical area for awareness,^{3,4} implying that modification of circadian rhythm might play a role on treating the delirium.

In the future, we may need to apply those new neurobiological mechanisms for the intervention of symptoms in delirious states to improve the outcome of those patients. Instead of using highly sedative agents to resolve the nocturnal agitation, such as giving zolpidem with action on the GABA α 1 subunit,¹⁰ clinicians may try to utilize the more specific medicines to regulate the circadian rhythm, like the melatonin receptor agonist or orexin receptor antagonist. When antipsychotics with dopamine type 2 receptor blockade are considered, those also with strong effects on antihistamine receptor 1 might not be considered as the treatment of first choice.

At another hand, we can choose the medications with more actions on serotonin receptor 1_a, 2_{a/2c}, and 7 to modify the excitation-inhibition balance, such as brexpiprazole or lurasidone.⁹ In this issue, we once again highlight the issue of delirium by presenting the post-operative cognitive outcomes in older patients with cardiovascular surgery from the Yang YJ's team. Hopefully, our clinical staff will identify this pivotal issue actively and precisely.

In conclusion, delirium in the elderly is a complicated and emergent condition, resulting serious impacts on the therapeutic outcome. We need to detect the problem as early as possible and handle it promptly. Previous common ways at using medicines for delirious symptoms commonly arised from clinical experience instead of neurobiological knowledges. Updated mechanism based on pathophysiology and neuroanatomical dysfunction should be applied for appropriate managements of this serious issue.

References

1. Lin YY, Huang CS. Aging in Taiwan: Building a society for active aging and aging in place. *Gerontologist*. 2016;56(2):176–183. doi:10.1093/geront/gnv107
2. Buterakos R, Keiser M. Implementing a delirium admission protocol in the emergency department. *Int J Gerontol*. 2021;15(2):150–153. doi:10.6890/IJGE.202104_15(2).0012
3. Wilson JE, Mart MF, Cunningham C, et al. Delirium [published correction appears in *Nat Rev Dis Primers*. 2020 Dec 1;6(1):94]. *Nat Rev Dis Primers*. 2020;6(1):90. doi:10.1038/s41572-020-00223-4
4. Saper CB, Scammell TE, Lu J. Hypothalamic regulation of sleep and circadian rhythms. *Nature*. 2005;437(7063):1257–1263. doi:10.1038/nature04284
5. Xing C, Yan C. Effects of dexmedetomidine on the incidence of postoperative delirium and plasma S-100 β protein levels following hip surgery in the elderly population. *Int J Gerontol*. 2021;15(3):207–211. doi:10.6890/IJGE.202107_15(3).0004
6. Jeon EJ, Sohng KY. Risk factors and clinical outcomes of delirium after hip fracture surgery in Korean older adults: A retrospective study. *Int J Gerontol*. 2021;15(1):25–29. doi:10.6890/IJGE.202101_15(1).0005
7. Ha YC, Yoo JI, Park KS, Kim RB, Seo SH. Delirium in patient with hip fracture is related high mortality: A national cohort study. *Int J Gerontol*. 2021;15(1):45–48. doi:10.6890/IJGE.202101_15(1).0009
8. Chang CP, You CH, Tseng LY, Cheng YJ, Tseng HK. COVID-19 in older adults: A focus on clinical characteristics and frail status. *Int J Gerontol*. 2020;14(4):256–259. doi:10.6890/IJGE.202011_14(4).0001
9. Hernández-Vázquez F, Garduño J, Hernández-López S. GABAergic modulation of serotonergic neurons in the dorsal raphe nucleus. *Rev Neurosci*. 2019;30(3):289–303. doi:10.1515/revneuro-2018-0014
10. Rudolph U, Knoflach F. Beyond classical benzodiazepines: novel therapeutic potential of GABA α receptor subtypes. *Nat Rev Drug Discov*. 2011;10(9):685–697. doi:10.1038/nrd3502

Chau-Shoun Lee ^{a,b}

^a Department of Medicine, MacKay Medical College, New Taipei City, Taiwan

^b Department of Medical Education and Department of Psychiatry, MacKay Memorial Hospital, Taipei, Taiwan