


COMMENTARY

Malnutrition and neuropsychiatric symptoms (NPS) of dementia

Commentary on “Malnutrition and Neuropsychiatric Symptoms in Dementia: The Cache County Dementia Progression Study” by Kauzor *et al.*

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The term neuropsychiatric symptoms of dementia (NPS) is used to describe a constellation of noncognitive symptoms and behaviors that are reported in >90% of individuals with dementia (Tampi and Jeste, 2022). NPS are often unsafe, and they cause significant disruption in the care of the individual with dementia. The most common type of NPS that is noted among an individual with dementia varies depending on the etiology for dementia (Kolanowski *et al.*, 2017). Apathy is the most common NPS that is noted among individuals with Alzheimer’s disease (AD), whereas depression is the most common NPS identified among people with vascular dementia (VaD). Anxiety is the most common NPS seen among individuals with dementia with Lewy bodies (DLB), and agitation and aggression are the most common NPS reported among people with frontotemporal dementia (FTD) (Kolanowski *et al.*, 2017). NPS is often thought to be associated with a faster progression of the illness and is a common reason for the placement of people with dementia in acute care hospitals and nursing homes (NHs) (Tampi & Jeste, 2022). Additionally, NPS increases the morbidity and mortality rates among individuals with dementia (Gerlach & Kales, 2020). Due to the greater utilization of health services, NPS is responsible for one-third of the cost of caring for people with dementia (Beeri *et al.*, 2002). Furthermore, NPS often increases caregiver distress and depression and can be responsible for reduced caregiver employment (Gerlach and Kales, 2020).

The neurobiology of NPS indicates a complex interaction between various biological, psychological, social, and environmental factors (Tampi *et al.*, 2022). Biological factors include neuroanatomical (neuritic plaques and neurofibrillary tangles in the frontal and temporal cortices and atrophy of right frontal lobe being associated with delusional misidentification syndrome), neurochemical (damage to

cholinergic neurons in the frontal and temporal cortices and to the adrenergic and serotonergic systems; psychotic symptoms occurring due to higher levels of norepinephrine in the substantia nigra and the lower levels of serotonin in the presubiculum), neurophysiological (dysfunction of the frontal, temporal, and parietal cortices being associated with psychotic symptoms), and genetic factors (polymorphisms of serotonin (5-HT_{2A}) receptors being associated with hallucinations; apolipoprotein E4 (APOE4) allele being associated with earlier onset of symptoms and agitation; psychosis and aggression can occur due to the polymorphisms of dopamine receptors). Additional biological factors include underlying medical illnesses like hypothyroidism, urinary tract infection, pneumonia, constipation, and pain that can lead to or exacerbate NPS (Tampi and Jeste, 2022). Among the psychological factors, higher levels of neuroticism have been found to be associated with greater progression of affective symptoms, apathy/appetite symptoms, sleep disorders, and overall NPS symptoms (Rouch *et al.*, 2019). Greater conscientiousness is protective against evolution of psychotic, affective and apathy/appetite symptoms, and global NPS symptoms. Greater openness has been associated with lower affective symptom evolution, and higher extraversion has been associated with lower affective symptoms but higher behavioral dyscontrol. Social factors include mismatched expectations of the caregiver due to their lack of understanding of the illness, resulting in negative communication styles of harsh tone, anger, and yelling (Tampi and Jeste, 2022). Environmental factors that can result in or cause an exacerbation of NPS include an under or overstimulating environment, other general environmental changes, or changes to the daily routine.

Data from the Cache County Study in the United States indicated that women have greater tendency

toward developing anxiety [odds ratio (OR) = 2.22] and delusions (OR = 2.15) (Steinberg *et al.*, 2006). Greater dementia severity was found to be associated with a tendency to develop hallucinations and agitation (OR = 2.42) but was associated with a reduced risk of developing depression (OR = 0.75). In this study, positive APOE epsilon4 status was associated with an increased risk of developing aberrant motor behaviors (OR = 1.84). Later time of observation (being seen at 18-month follow-up vs at baseline visit) increased the chances for developing delusions (OR = 1.27) and aberrant motor behaviors (OR = 1.22). The presence of more serious general medical comorbidity increased the risk of developing agitation/aggression (OR = 1.76), irritability (OR = 1.75), disinhibition (OR = 1.98), and aberrant motor behaviors (OR = 1.94). A study conducted in Singapore found that older individuals (≥ 65 years) were found to be at greater risk of developing more severe NPS (OR = 1.89) (Yatawara *et al.*, 2018). There was also a trend noted for individuals with primary education experiencing greater NPS (OR = 2.24) when compared to individuals with tertiary education.

Social determinants of health (SDoHs) can be defined as conditions in the environments where individuals are born, live, learn, work, play, worship, and grow older that have an impact on health, functioning, and quality-of-life outcomes (Jeste and Pender, 2022). These include factors that are associated with early childhood development; access to education, job opportunities, and income; racial, ethnic, and other forms of discrimination; basic needs including housing, transportation, and neighborhoods; access to clean air and water; and access to affordable health care.

SDoHs for dementia include early-life adversity, which is associated with an increased risk of developing dementia (Majoka and Schimming, 2021). Lower socioeconomic status (SES) and lower levels of education are also associated with a greater risk of developing dementia. With regard to the type of employment, manual labor is associated with a higher risk of developing dementia. Greater food insecurity in early and later life is also associated with a higher risk of developing dementia. People who live in neighborhoods that are economically disadvantaged with fewer physical resources have a greater risk of developing dementia. Lower levels of social engagement and greater levels of stress are associated with a higher likelihood of developing dementia. Racial and other forms of discrimination also increase the risk of dementia as a direct effect of discrimination on the individual and indirectly through lower SES, reduced educational

level, decreased employment status, and residential segregation.

Studies indicate that both food insecurity and malnutrition are associated with cognitive decline among older adults (Portela-Parra and Leung, 2019; Yu *et al.*, 2021). Emerging evidence indicates that poor nutritional status/malnutrition is also associated with NPS especially verbal aggressiveness/emotional disinhibition and apathy (Kimura *et al.*, 2019; Kishino *et al.*, 2022).

A new paper being published in *International Psychogeriatrics* by Kauzor *et al.* evaluated the association between poor nutritional status and NPS from a population-based sample of individuals with dementia (Kauzor *et al.*, *in press*). In this study, the authors evaluate data from 292 individuals with dementia. To evaluate nutritional status and NPS, the investigators used the modified Mini-Nutritional Assessment and the Neuropsychiatric Inventory (NPI). They used age of onset of dementia, type of dementia, duration of diagnosis of dementia, medical comorbidities, sex, APOE genotype, and education as covariates for testing. The investigators found that higher nutritional status was associated with lower NPI total scores [-0.58 , 95% confidence interval (CI), -0.86 to -0.29] after controlling for age of onset of dementia, sex, and number of medical conditions. After controlling for sex and number of medical conditions, the investigators noted that individuals at risk of malnourishment had NPI total scores 1.76 points higher [95% CI, 0.04–3.48] when compared to well-nourished participants. They also noted that malnourished individuals had NPI total scores 3.20 points higher [95% CI, 0.62–5.78] when compared to well-nourished participants. The investigators also noted that better nutritional status was associated with lower scores on psychosis [-0.08 , 95% CI, -0.16 to -0.004], depression [-0.11 , 95% CI, -0.16 to -0.05], and apathy [-0.19 , 95% CI, -0.28 to -0.11] NPI domains.

In terms of risk factors for NPS, this study found that men scored 2–2.5 lower on the NPI total scores when compared to women (Kauzor *et al.*, *in press*). The domain scores for anxiety and aberrant motor behaviors were also 0.4 points lower among men when compared to women. A higher psychosis score of 0.75 points was associated with the APOE E4 allele. Individuals with VaD scored approximately 1.4 points lower on the psychosis domain when compared to other types of dementias. Individuals with longer dementia duration at baseline were found to have lower depression scores (-0.11) but higher psychosis (0.17) and aberrant motor behavior (0.12) domain scores. Additionally, lower psychosis (-0.09) and irritability (-0.07) scores were

associated with greater years of educational attainment. Individuals with ≥ 6 comorbid conditions had higher total NPI scores (by 3 points) and depression and irritability (by 0.5 points) when compared to individuals with 4–5 conditions. Individuals with 0–3 conditions had higher apathy domain scores (by 0.83 points) than individuals with 4–5 conditions. However, these individuals had lower irritability domain scores (by 0.56 points) when compared to individuals with ≥ 6 conditions.

The strength of the new study is that it used a population-based sample and it had a high participation rate. Additionally, the participants were identified relatively early in their course of dementia and were followed up for up to 6 years. Furthermore, the investigators examined individual NPS along with multiple other medical comorbidities, in addition to nutritional status. The limitations of the study include limited number of participants to evaluate the differences in outcomes for the different etiologies for dementia. The investigators were also unable to assess the impact of potential confounding factors such as race/ethnicity and SES on nutritional status and NPS. As most of the participants were living in private homes, the findings of the current study may not be generalizable to those living in institutions.

Social factors and societal problems play a crucial role in worsening mental health and increasing the risk of mental illnesses even in later life (Crompton, 2023). Research data also indicate that greater cumulative exposure to adverse events over the life course of an individual is associated with significantly lower well-being and greater odds of depressive symptoms among older adults (Richardson *et al.*, 2023). What is also interesting is that there is no greater correlation between adverse events occurring later in the life with negative well-being and depressive symptoms, when compared to adverse events occurring earlier in life. There is also a serious need to develop specific scales to assess SDoHs in mental health among culturally and ethnically diverse populations (Bagot, 2023).

The solutions to these social factors and societal problems are to support the development of resilience and reduce the risk of mental illness (Crompton, 2023). Policies at an organizational level, in local and state governments, and at a national and international level also are needed to help with health and well-being of all individuals.

The care of individuals with dementia including those living in NHs is complicated by polypharmacy, which may result in or worsen NPS. Available data indicate that one in three (33%) NH residents with dementia receive ≥ 2 psychotropic medications concurrently, whereas one in eight (13%) receive ≥ 3 psychotropic medications concurrently (Jester

et al., 2021). Male sex was associated with greater use of ≥ 2 psychotropic medications (adjusted odds ratio (OR) = 1.04, $p = 0.07$). Regular reviews of all the medications taken by individuals with dementia are needed to prevent injudicious polypharmacy and the occurrence of serious adverse effects including the risk of death. Emerging data indicate that it is feasible to develop and implement training programs to improve the overall quality of care of individuals with NPS in NH (Sampson *et al.*, 2021).

When accessing and managing individuals with NPS, it is important to pay close attention to SDoHs including food insecurity in addition to all the biological and psychosocial factors. As there is growing evidence that SDoHs can significantly affect the occurrence, type, and severity of NPS, any comprehensive management plan to address these symptoms should always include a strategy to mitigate and or treat the effects of SDoHs.

Conflict of interest

None.

References

- Bagot, K. S.** (2023). Need for culturally and ethnically specific measures and measures of social determinants of health in mental health research among indigenous populations. *International Psychogeriatrics*, 35, 225–227.
- Beeri, M. S., Werner, P., Davidson, M. and Noy, S.** (2002). The cost of behavioral and psychological symptoms of dementia (BPSD) in community dwelling Alzheimer's disease patients. *International Journal of Geriatric Psychiatry*, 17, 403–408.
- Compton, M. T.** (2023). Improving the well-being of older adults requires programs that enhance resilience as well as policies, across sectors, that promote health. *International Psychogeriatrics*, 35, 215–217.
- Gerlach, L. B. and Kales, H. C.** (2020). Managing behavioral and psychological symptoms of dementia. *Clinics in Geriatric Medicine*, 36, 315–327.
- Jeste, D. V. and Pender, V. B.** (2022). Social determinants of mental health: recommendations for research, training, practice, and policy. *JAMA Psychiatry*, 79, 283–284.
- Jester, D. J., Molinari, V., Zgibor, J. C. and Volicer, L.** (2021). Prevalence of psychotropic polypharmacy in nursing home residents with dementia: a meta-analysis. *International Psychogeriatrics*, 33, 1083–1098.
- Kauzor, K., et al.** (in press). Malnutrition and neuropsychiatric symptoms in dementia: the Cache County dementia progression study. *International Psychogeriatrics*.
- Kimura, A. et al.** (2019). Malnutrition is associated with behavioral and psychiatric symptoms of dementia in older women with mild cognitive impairment and early-stage Alzheimer's disease. *Nutrients*, 20, 1951.

- Kishino, Y. et al.** (2022). Longitudinal association between nutritional status and behavioral and psychological symptoms of dementia in older women with mild cognitive impairment and early-stage Alzheimer's disease. *Clinical Nutrition*, 41, 1906–1912.
- Kolanowski, A. et al.** (2017). Determinants of behavioral and psychological symptoms of dementia: a scoping review of the evidence. *Nursing Outlook*, 65, 515–529.
- Majoka, M. A. and Schimming, C.** (2021). Effect of social determinants of health on cognition and risk of Alzheimer disease and related dementias. *Clinical Therapeutics*, 43, 922–929.
- Portela-Parra, E. T. and Leung, C. W.** (2019). Food insecurity is associated with lower cognitive functioning in a national sample of older adults. *Journal of Nutrition*, 149, 1812–1817.
- Richardson, S., Carr, E., Netuveli, G. and Sacker, A.** (2023). Adverse events over the life course and later-life wellbeing and depressive symptoms in older people. *International Psychogeriatrics*, 35, 243–257.
- Rouch, I. et al.** (2019). Does personality predict behavioral and psychological symptoms of dementia? Results from PACO prospective study. *Journal of Alzheimer's Disease*, 69, 1099–1108.
- Sampson, E. L. et al.** (2021). Development, feasibility, and acceptability of an intervention to improve care for agitation in people living in nursing homes with dementia nearing the end-of-life. *International Psychogeriatrics*, 33, 1069–1081.
- Steinberg, M. et al.** (2006). Risk factors for neuropsychiatric symptoms in dementia: the Cache County study. *International Journal of Geriatric Psychiatry*, 21, 824–830.
- Tampi, R. R., Bhattacharya, G. and Marpuri, P.** (2022). Managing Behavioral and Psychological Symptoms of Dementia (BPSD) in the era of boxed warnings. *Current Psychiatry Reports*, 24, 431–440.
- Tampi, R. R. and Jeste, D. V.** (2022). Dementia is more than memory loss: neuropsychiatric symptoms of dementia and their nonpharmacological and pharmacological management. *American Journal of Psychiatry*, 179, 528–543.
- Yatawara, C., Hiu, S., Tan, L. and Kandiah, N.** (2018). Neuropsychiatric symptoms in South-East Asian patients with mild cognitive impairment and dementia: prevalence, subtypes, and risk factors. *International Journal of Geriatric Psychiatry*, 33, 122–130.
- Yu, W. et al.** (2021). Associations between malnutrition and cognitive impairment in an elderly Chinese population: an analysis based on a 7-year database. *Psychogeriatrics*, 2021, 80–88.