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Invited Perspective

Insight into Potential Mechanisms Linking Loneliness and Cognitive Decline: Commentary on "Health Factors as Potential Mediator the Longitudinal Effect of Loneliness on General Cognitive Ability"

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Loneliness impacts mental and physical health in older adults, with health effects exceeding that of smoking 15 cigarettes per day or obesity.[1] Older adults are at particularly high risk for loneliness due to living alone, physical decline, and shrinking social networks.[2,3] Furthermore, the Covid-19 pandemic and physical distancing guidelines have increased social isolation and loneliness among older adults worldwide. Loneliness has also been linked to cognitive decline. Large-scale longitudinal studies have reported that lonely individuals are at increased risk of developing dementia at 3–4 years of follow-up.[4,5] Alzheimer's disease affects one in ten Americans over age 65, with the number of cases projected to double over the next thirty years.[6] However, there is a lack of definitive treatments and preventative strategies for

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Alzheimer's disease. While loneliness is a promising target of intervention for cognitive health, the underlying physiological, psychological, and social pathways by which loneliness affects cognitive functioning are unknown.

In their study, Kim et al[7] examine the mediating role of physiological risk, functional ability, self-rated health, depressive symptoms, and social participation in the association between loneliness and cognitive decline in older adults. The study used data from three waves (baseline, 5 year and 10 year follow-up) of the National Social Life, Health, and Aging Project (NSHAP). The total sample included 3,005 Americans who were born between 1920 and 1947, ranging in age from 58 to 86 years at recruitment. Cognitive ability at 5- and 10-year follow-up was assessed with the Chicago Cognitive Function Measure (CCFM; an abbreviated version of the Montreal Cognitive Assessment). Baseline loneliness was assessed using the 3-item UCLA Loneliness Scale. Physiological risk was evaluated through an index comprised of blood pressure, pulse rate, BMI, as well as biomarkers of metabolic, inflammatory, and immune functioning. Functional ability was assessed by self-report on instrumental activities of living. Self-rated health was assessed by a single-item question. Depressive symptoms were assessed by the 10-item Center for Epidemiologic Studies Depression (CES-D) Scale. Social participation was assessed using a 4-item scale about informal and formal group social activities.

The study found that there was a small but significant correlation between baseline loneliness and 10-year cognitive functioning ($r = -0.08$). Functional ability, self-rated health, and depressive symptomatology fully mediated effects of loneliness on cognition, while social participation was a partial mediator. These models controlled for age, sex, race/ethnicity, annual household income, and 5-year cognitive functioning score. When these models were corrected for multiple comparisons, only functional ability remained a significant mediator. Physiological risk did not mediate the effects of loneliness on 10-year cognitive functioning scores.

Overall, these findings reflect how the link between loneliness and cognition may be mediated through mood, functioning, and health. While studies have shown that there are effects of loneliness on cognition that are independent of depression, depression and loneliness are strongly linked in older adults.[8,9] Loneliness predicts trajectories of depression, and depressed individuals are often lonely. Similarly, while loneliness can impact daily functioning, functional impairments can affect engagement in social interactions in return. Similarly, loneliness influences subjective and objective health and vice versa. Thus, these complex psychosocial processes of aging are important factors to consider in older adults, especially as part of the interrelated downstream consequences of loneliness.

Surprisingly, physiological risk was not found to be a significant mediator. Dysregulated stress response to social threats has long been a hypothesized mechanism of the downstream health consequences of loneliness, with impacts on immune, neuroendocrine, and cardiovascular function.[10] Indeed, lonely individuals have elevated basal inflammatory biomarker levels as well as blunted cortisol and elevated cytokine responses to psychosocial stressors and inflammatory responses.[11–13] However, the multisystem risk assessment at Year 5 used in this study did not mediate the loneliness-cognition relationship. Future studies should consider how longitudinal trajectories of physiological functioning and risk influence trajectories of loneliness and cognition. More studies using longitudinal and targeted assessments of basal inflammatory and cortisol levels as well as psychosocial and biological challenges are needed in older adults to fully understand these biological processes.

Fundamentally, loneliness research may need more nuanced ways to assess loneliness. The UCLA Loneliness Scale[14] has long been the most valid and popular scale used in empirical research, avoiding the gender bias associated with a single direct question that explicitly uses the word "loneliness."[15] However, due to the lack of temporal boundaries on the questions, the UCLA scale fails to differentiate between chronic and persistent loneliness and situational or temporal loneliness. Prior findings from ecological momentary assessment (EMA) studies have demonstrated diurnal rhythms for positive affect and social activities in older adults.[16] One study of children found that state and trait loneliness had different impacts on diurnal cortisol and sleep patterns.[17] Studies that use EMA in combination with the UCLA scale to assess patterns of social behaviors, as well as biomarkers of stress and inflammatory processes may allow researchers to distinguish between different subtypes of loneliness.

The underlying mechanism by which loneliness affects cognitive functioning is unknown, though examination of sleep has promise. Studies in animals and in the general population have described how poor sleep has been associated with annual decline in global cognitive performance,[18] accelerated brain atrophy,[19] and increased β-amyloid deposition.[20] Additionally, self-reported sleep disturbances partially mediated the link between baseline loneliness and poor self-reported health (assessed by a single question) at 8-year follow-up in a large cohort study of older adults (65+ years), while controlling for depression and social isolation.[21] Thus, sleep may be a crucial link between loneliness and cognition, though its role is yet to be fully defined. As loneliness research continues to evolve, multimodal approaches will ultimately advance our understanding of the ubiquitous, impactful, and slippery concept of loneliness.

DISCLOSURE

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