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LETTER TO THE EDITOR
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Late-Life Depression and Subjective Cognitive Decline: Risk Factors of Dementia

Dementia is a clinical syndrome resulting from diseases of the brain, typically of a chronic or progressive nature, and manifests through various high-level cortical dysfunctions. It is primarily characterized by gradual impairments in memory, learning, reasoning, spatial orientation, and language, including mental and behavioral symptoms.[1] In 2018, the worldwide incidence of dementia was reportedly 50 million, and this count is projected to increase to 152 million by 2050.[2] Regardless, it is noteworthy that dementia remains the sole disease among the top 10 causes of death, lacking a dependable approach for prevention, deceleration, or remedy. Consequently, attention has been redirected toward its prevention through the identification of modifiable risk factors in individuals at a heightened risk of developing dementia.

Late-life depression (LLD) refers to the manifestation of major depressive disorder (MDD) in individuals aged ≥60 years. Unlike MDD, which is prevalent in younger populations, LLD is often associated with age-related neurodegeneration, cognitive decline, or physical illnesses.[3] A previous meta-analysis showed a 2-fold higher risk of dementia in individuals with a history of depression.[4] Subjective cognitive decline (SCD) refers to an individual's self-perceived cognitive deterioration, emphasizing personal experience rather than impairment in neuropsychological evaluations.[5] Many patients with SCD exhibit indications of preclinical Alzheimer's disease (AD), and SCD has been prospectively associated with underlying AD pathology.[5] In older adults, SCD and depression often coexist, as demonstrated by Pavel et al's study,[6] which found that older adults with SCD experienced reduced levels of physical and emotional well-being. Reportedly, LLD and SCD alone were independent risk factors for dementia.[7] Nevertheless, the cumulative impact or additive risk of SCD and LLD on the development of dementia remains uncertain.

A nationwide longitudinal study conducted in Korea revealed that both LLD and SCD were independent risk factors for the onset of dementia.[8] In addition, the coexistence of depression within a year prior to study enrollment and SCD exhibited a cumulative effect on the likelihood of developing dementia. However, a recent meta-analysis discovered that while anxiety-related affective symptoms were associated with an increased risk of SCD progressing to mild cognitive impairment (MCI) or dementia, depressive symptoms did not exhibit the same association.[9] In addition to the timing of depression onset, this may be attributed to variances in etiology between individuals with SCD as a result of depressive symptoms and those with SCD as a result of being in the first phase of dementia and accompanied by depressive symptoms. Across various age groups, it is commonly observed that depressive symptoms independently exert a negative influence on cognitive functioning. In clinical practice, cognitive repercussions are mostly alleviated upon successful treatment or remission of depressive symptoms; however, this phenomenon does not necessarily indicate an underlying subclinical dementia in older adults. Moreover, individuals with higher levels of depressive symptoms may exhibit increased susceptibility to negative interpretation biases,[10] thereby intensifying their subjective experience and resulting in a greater frequency of self-reported SCD. In the future, studies should prioritize differentiating individuals who experience major depressive symptoms leading to SCD from those who experience major SCD and related depressive symptoms. This distinction could enhance comprehension regarding the potential additional risk posed to individuals with SCD in terms of cognitive progression when depressive symptoms coexist, albeit independently, with SCD.

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Furthermore, at present, there is a lack of consensus on the definition of SCD. For instance, in Pavel et al's study,[6] SCD was assessed based on a single question, "Do you perceive any difficulties with your memory?" with response options including "Yes and it bothers me," "Yes but it does not bother me," and "No". Participants who responded "Yes" were classified as having SCD, whereas those who responded "No" were included in the control group. In another study, Wang et al[8] utilized a 5-item self-report measurement method alongside the individual self-perception memory concerns employed by Pavel et al,[6] to examine 4 additional dimensions of memory-related issues. Recognizing the need to address this gap, the working group of the SCD Initiative proposed research criteria for early-stage SCD in MCI in 2014, along with a list of core features recommended for inclusion in SCD studies. Jessen et al[5] suggested that it is crucial to assess and document anxiety, depression, and SCD-related issues within the framework of SCD, as they may signify distinct facets of the condition.

Interventions often yield optimal outcomes when implemented at the earliest stages of dementia, which is characterized by minimal pathology and fewer manifestations of behavioral and cognitive symptoms. Given that AD is the most prevalent cause of dementia, it has gained increasing attention and has been subjected to extensive research. According to a recent study, SCD signified a phase of increased vulnerability to AD, making it an opportune period for early intervention.[9] Considering the acknowledged intricate association between SCD and depression, anxiety, and other psychiatric disorders, it is imperative that further research be conducted to ascertain whether SCD, as a subjective decline in memory, would exhibit a comparable heightened susceptibility to MCI and dementia. Such findings would help in the design of appropriate early intervention strategies for people with MCI.

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