



Roles of selenium in cognition

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Dementia, a clinical syndrome with progressive and diffuse brain dysfunction, affects approximately 55.2 million people worldwide. The global cost of dementia will increase from \$1.3 trillion in 2019 to \$1.7 trillion in 2030 [1]. Therefore, it is imperative to prevent and treat dementia. Currently, both a couple of available drugs for dementia and their adverse reactions including nausea, vomiting, diarrhea, syncope and bradycardia have severely impeded their clinical use [2]. Fortunately, nutrients are found to be beneficial to dementia [1].

Selenium (Se), an essential trace element, has a great potential in the prevention and treatment of dementia [3]. Se exerts vital functions in dementia through selenoproteins, including antioxidation, anti-inflammation, regulation of calcium homeostasis, improvement of synaptic plasticity, and inhibition of ferroptosis [4]. Unfortunately, Se deficiency often occurs in the healthy elderly, the elderly with mild cognitive impairment and Alzheimer's disease (AD) largely due to the reduction of selenoproteins in the brain [3]. After Se supplementation, a significant improvement of learning and memory capabilities was observed in AD model mice [5] and participants aged 45–60 years receiving 100 µg Se/day for 9 years in a double-blind, placebo-controlled, randomized trial [6], demonstrating that Se supplementation was beneficial to cognitive performance.

Effects of Se on cognition mainly depend on its intake and speciation [7]. The recommended nutrient intake and tolerable upper intake of Se are between 55 and 75 and 400 µg, respectively. Se deficiency caused cognitive deficits in children [8], and chronic high Se exposure also significantly led to cognitive impairment [9]. Bioavailability of Se is closely associated with Se speciation, *i.e.*, organic species including selenomethionine and Se-enriched yeast, and inorganic species consisting of selenite and selenate. Compared to inorganic Se, organic Se shows higher bioavailability and less toxicity [10], and therefore is more widely used in Se supplementation. Furthermore, sodium selenite nanoparticles with an average particle size of 8 ± 0.34 nm have been developed to obtain higher bioavailability and minimal toxicity, and finally improve cognitive disorder in rats by inhibiting A β aggregation and regulating gut

microbiota [11]. Additionally, the synergistic effects of serine and Se on cognitive function were achieved by the promotion of selenoprotein synthesis [12].

In conclusion, Se plays an important role in cognition and its effects mainly depend on intake and speciation of Se. The exact association and mechanism between Se and cognition need to be further explored in future studies, including Se intake, Se speciation, Se dosage form, comprehensive evaluation parameters, randomized controlled trials, and large-scale human studies.

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History

Received August 26, 2023

Accepted September 3, 2023

Published online September 15, 2023

Conflict of interest

The authors declare that there are no conflicts of interest.

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