



## Commentary

## The injured brain might need more fat!



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One of the benefits of medical and technological advances is the increase in life expectancy and thus, an increase in the proportion of the “oldest ( $\geq 80$  years)” individuals in the general population [1]. The increase in number and proportion of “oldest” individuals has resulted in an increase in the incidence and prevalence of dementia and other age-related cognitive impairment [1]. A common observation in the brains of individuals with dementia, especially vascular cognitive dementias (VCIDs), are microinfarcts [9, 10]. Cerebral microinfarcts result from the loss of blood flow through cortical-penetrating micro-vessels (arteriole or venule) supplying or draining a neurovascular unit [3, 4]. These microinfarcts are usually asymptomatic until cognitive symptoms develop decades later when the individual is much older. As such, identifying at-risk individuals and providing neuroprotective protective molecules is required to reduce the impact, and thus complications resulting from the presence and burden of cerebral microinfarcts.

Studies have suggested a neuroprotective role for the omega-3 polyunsaturated fatty acids (PUFAs) (Lo Van [5]). A recently published study [6] hypothesized that omega-3 PUFAs will protect against the development of cerebral microinfarcts and association symptoms. This study utilized an endogenous and exogenous model/approach and showed that omega-3 PUFAs not only protected the development and severity of cerebral microinfarcts but also ameliorated cerebral microinfarct-associated neurological symptoms such as learning and anxiety. A potential mechanism proposed by the authors was that omega-3 PUFAs inhibit and thus prevented receptor-interacting serine/threonine protein kinase 1 (RIPK1)-dependent apoptosis of neurons after a cerebral microinfarction [6].

While preclinical and some clinical studies indicate that omega-3 PUFAs have a health benefit with regards to neuroprotection and/or cardio-protection, the overall evidence has been inconclusive. For instance, in a systematic review and meta-analysis, Rizos et al. [8] reported that use of omega-3 PUFAs was not associated with significant reduction in all-cause mortality, reduction in the incidence of stroke or cardiovascular endpoint. But a recent report issued by the American Heart Association (AHA), indicated otherwise, reporting a benefit in reduction of cardiovascular and cerebrovascular outcomes with consistent intake (at least once-a-week consumption of seafood) of omega-3 PUFAs [7]. The conclusions from this AHA report [7] directly contradicted Rizos et al. [8], but supports the findings of the study recently published by Luo et al. [6]. The exact reason for this inconsistency in results and thus conclusions from these studies is unclear. But the report from the AHA indicates that the benefits of omega-3 PUFAs might be dependent on a consistent intake. Furthermore, although omega-3 PUFAs and their derivatives make up an integral portion of neural and other cellular membranes, they cannot be endogenously synthesized by humans and thus have to be consumed in the diet. In two separate clinical studies which also agreed with the conclusion of Luo et al., the benefits of omega-3 PUFAs on neuroprotection evidenced by improvement in cognition and reduction in the burden of subclinical microinfarcts [2, 11] were dependent on daily intake. This strict regimen might be responsible for some of the inconsistent result since it is well understood that medications requiring daily intake tend to be associated with significant non-compliance, which affects efficacy and thus the overall therapeutic benefits of the medication. Most omega-3 PUFAs are available over the counter with little to no information on how to use them for maximum benefit. It is the conclusion of the editorial commentary that more education is needed for both doctors and consumers in the most effective way to use medications containing omega-3 PUFAs.

## Disclosure

The author declares no conflict of interest.

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