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Dietary plant derived omega-3 fatty acid alpha linolenic acid prevents age-dependent arterial stiffness and improves outcome after stroke in mice

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Background: A fundamental determinant of cardio- and cerebrovascular diseases is vascular aging, characterized by arterial stiffness. Arterial stiffness is an independent predictor of adverse cardio- and cerebrovascular events and mortality.

Fish-derived omega-3 fatty acids (n3-FA) have been described to decrease cardiovascular events in high risk populations. Little is known on the effects of the plant-derived n3 FA alpha-linolenic acid (ALA). More insight is urgently needed, because of the low costs and abundant global supply of ALA. Thus, we aimed to investigate the effects of a long-term dietary intervention with ALA on age-dependent arterial stiffness and the magnitude of these effects on a specific vascular endpoint – ischemic stroke – in a mouse model of aging.

Methods: C57BL/6 wildtype males were either fed an ALA-rich (high ALA, 7.3 g%) or a respective control (0.3 g%) diet for 12 months, starting from 6 months of age.

At 9, 15 and 18 months, arterial stiffness was assessed by measuring pulse wave velocity (PWV) in the right common carotid artery using a Vevo 3100 system (VisualSonics, Fig. 1A).

At 18 months, ischemic stroke was induced by transient middle cerebral artery occlusion (30 mins/48 h). Stroke size was assessed by triphenyl tetrazolium chloride staining and neurological function by a Bederson based score.

Results: Arterial stiffness steadily and significantly increased in controls over time, while ALA clearly and effectively prevented it (PWV at 9 vs. 18 months: controls + 95%; p<0,0001 vs. High ALA + 15%; ns) (Fig 1A).

Stroke size at 18 months was significantly decreased in ALA-fed animals compared to controls (28.39 mm^3 vs. 51.77 mm^3 p=0.0017) (Fig. 1B). In line with the morphological changes, controls performed significantly worse neurologically (Fig. 1C). Additionally, post-stroke survival at 48 h was improved in ALA-fed animals compared to controls, with 85% survival compared to 57% (Fig. 1D).

Conclusion: We demonstrate that long-term dietary supplementation with the plant-derived ALA fully prevents the development of age-dependent arterial stiffness.

The magnitude of this effect is clearly reflected in biologically relevant decreased stroke size, improved neurological performance and even post-stroke survival.

This study not only demonstrates vasoprotective effects of ALA, but also links them to improved outcome of a specific clinical endpoint. Future analyses will aim at delineating the molecular basis of the observed benefits. This will result in a better understanding of some ambiguous results from clinical trials and likely define the population which benefits from ALA.

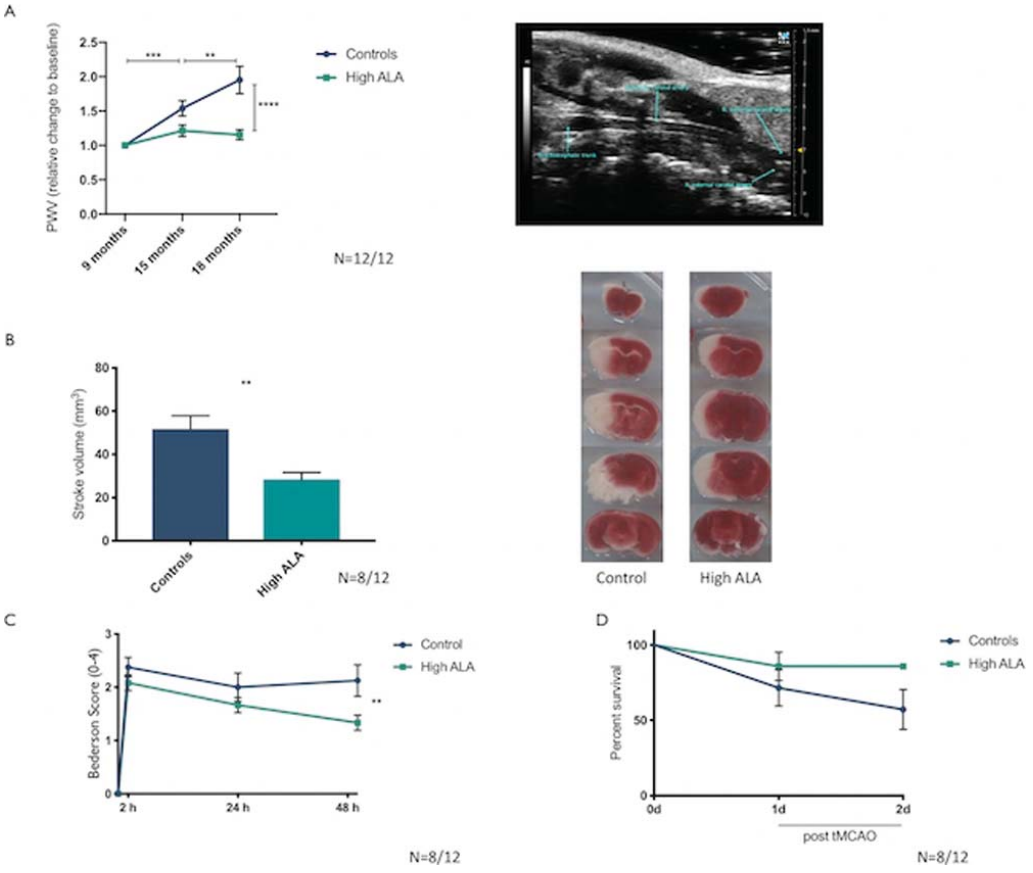

Figure 1