

Alzheimer e ácido alfa lipóico

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Lembremos que o ácido lipóico ativando a piruvato desidrogenase é uma das substâncias que abre as portas das mitocôndrias para o piruvato citoplasmático caminhar para a fosforilação oxidativa. O aumento de produção de ATP melhora a função dos neurônios.

Lipoic acid as a novel treatment for Alzheimer's disease and related dementias

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Alzheimer's disease (AD) is a progressive neurodegenerative disorder that destroys patient memory and cognition, communication ability with the social environment and the ability to carry out daily activities. Despite extensive research into the pathogenesis of AD, a neuroprotective treatment - particularly for the early stages of disease - remains unavailable for clinical use. In this review, we advance the suggestion that lipoic acid (LA) may fulfil this therapeutic need. A naturally occurring precursor of an essential cofactor for mitochondrial enzymes, including pyruvate dehydrogenase (PDH) and alpha-ketoglutarate dehydrogenase (KGDH), LA has been shown to have a variety of properties which can interfere with pathogenic principles of AD. For example, LA increases acetylcholine (ACh) production by activation of choline acetyltransferase and increases glucose uptake, thus supplying more acetyl-CoA for the production of ACh. LA chelates redox-active transition metals, thus inhibiting the formation of hydroxyl radicals and also scavenges reactive oxygen species (ROS), thereby increasing the levels of reduced glutathione. Via the same mechanisms, downregulation redox-sensitive inflammatory processes is also achieved. Furthermore, LA can scavenge lipid peroxidation products such as hydroxynonenal and acrolein. The reduced form of LA, dihydrolipoic acid (DHLA), is the active compound responsible for most of these beneficial effects. R-alpha-LA can be applied instead of DHLA, as it is reduced by mitochondrial lipoamide dehydrogenase, a part of the PDH complex. In this review, the properties of LA are explored with particular emphasis on how this agent, particularly the R-alpha-enantiomer, may be effective to treat AD and related dementias.

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Lipoic acid as an anti-inflammatory and neuroprotective treatment for Alzheimer's disease

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Alzheimer's disease (AD) is a progressive neurodegenerative disorder that destroys patient memory and cognition, communication ability with the social environment and the ability to carry out daily activities. Despite extensive research into the pathogenesis of AD, a neuroprotective treatment - particularly for the early stages of disease - remains unavailable for clinical use. In this review, we advance the suggestion that lipoic acid (LA) may fulfil this therapeutic need. A naturally occurring cofactor for the mitochondrial enzymes pyruvate dehydrogenase and alpha-ketoglutarate dehydrogenase, LA has been shown to have a variety of properties which can interfere with the pathogenesis or progression of AD. For example, LA increases acetylcholine (ACh) production by activation of choline acetyltransferase and increases glucose uptake, thus supplying more acetyl-CoA for the production of ACh. LA chelates redox-active transition metals, thus inhibiting the formation of hydroxyl radicals and also scavenges reactive oxygen species (ROS), thereby increasing the levels of reduced glutathione. In addition, LA down-regulates the expression of redox-sensitive pro-inflammatory proteins including TNF and inducible nitric oxide synthase. Furthermore, LA can scavenge lipid peroxidation products such as hydroxynonenal and acrolein. In human plasma, LA exists in an equilibrium of free and plasma protein bound form. Up to 150 µM, it is bound completely, most likely binding to high affinity fatty acid sites on human serum albumin, suggesting that one large dose rather than continuous low doses (as provided by "slow release" LA) will be beneficial for delivery of LA to the brain. Evidence for a clinical benefit for LA in dementia is yet limited. There are only two published studies, in which 600 mg LA was given daily to 43 patients with AD (receiving a standard treatment with choline-esterase inhibitors) in an open-label study over an observation period of up to 48 months. Whereas the improvement in patients with moderate dementia was not significant, the disease progressed extremely slowly (change in ADAScog: 1.2 points=year, MMSE: -0.6 points=year) in patients with mild dementia (ADAScog<15). Data from cell culture and animal models suggest that LA could be combined with nutraceuticals such as curcumin, (-)-epigallocatechin gallate (from green tea) and docosahexaenoic acid (from fish oil) to synergistically decrease oxidative stress, inflammation, Aβ levels and Aβ plaque load and thus provide a combined benefit in the treatment of AD.

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