

## Mediterranean diet and neuroprotection

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The Mediterranean diet is characterized by high consumption of fruits, vegetables and fishes with or without wine. It is also often associated with a consumption of edible vegetable oils, especially olive oil but also argan oil mainly by the Moroccan population. These different foods are rich in biologically active nutrients (lipids, polyphenols, terpenoids including carotenoids and vitamins). Lipids include omega-3 fatty acids (found in blue fishes) and omega-9 fatty acids found in olive and argan oils, as well as phytosterols. Fatty acids and phytosterols are involved in the control of lipid homeostasis. Polyphenols essentially flavonoids, terpenoids of which the carotenoids and the vitamins (such as  $\alpha$ -tocopherol, the main constituent of vitamin E) have antioxidant activities against lipid peroxidation and also anti-inflammatory properties. Some of these molecules ( $\omega$ -3 fatty acids,  $\alpha$ -tocopherol) are also able to prevent organelles (mitochondria, lysosome and peroxisome) dysfunctions and fight against cell death (autophagy, apoptosis) induced by intrinsic and extrinsic environmental factors (cholesterol oxidation products - named oxysterols - and pollutants). Several of the molecules present in the Mediterranean diet are mainly efficient to prevent the cytotoxic effects of 7-ketocholesterol, 7 $\beta$ -hydroxycholesterol and 24S-hydroxycholesterol which are found at increased levels in the brain, plasma and/or cerebrospinal fluids of patients with age-related diseases, including neurodegenerative diseases. Since neurodegenerative diseases have in common a RedOx equilibrium breakdown, inflammation and mitochondrial alterations (probably associated with peroxisomal abnormalities) that may affect the signaling pathways leading to autophagy and apoptosis, it is important to identify molecules that can oppose these various dysfunctions. As the Mediterranean diet contains many cytoprotective molecules ( $\omega$ -3 and -9 fatty acids, polyphenols, phytosterols, carotenoids, tocopherols) able to cross the blood-brain barrier, this diet could be beneficial to the proper functioning of the nervous system. In addition, new pharmacological approaches, enabling specific targeting of bioactive molecules associated with the Mediterranean diet using carriers, such as functionalized nanoparticles associated with natural products, could lead to development of new drugs to treat neurodegenerative diseases which are most often incurable. As there is also evidence that polyphenols are able to stimulate neurotrophic signaling pathways, promote neurogenesis and cognitive functions, these observations also reinforce the interest of compounds present in the Mediterranean diet to prevent neurodegeneration.