

3rd International Conference on**CENTRAL NERVOUS SYSTEM DISORDERS AND THERAPEUTICS**

October 02-03, 2017 Vienna, Austria

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Metabolism of myelin in health and pathology

Myelin is a site of active aerobic energy metabolism, producing ATP through the oxidative phosphorylation (OXPHOS) machinery, which contributes to the acceleration of nervous impulse. This innovative view simplifies current ideas about the physical chemical mechanisms that ensures the advancement of the action potential (CAP) as such basic mechanisms are unchanged in the passage of the CAP from the non-myelinated to myelinated axon. The ATP produced in myelin sheath is transferred to the axon through the Gap Junctions, which are abundant in myelin sheath. The OXPHOS proteins expressed in myelin is closely related to that of mitochondria and hence there must be some process still to be defined, which guarantees the transfer of OXPHOS machinery from mitochondria to myelin; overall the mitochondria-myelin link is known since many mitochondrial pathologies primarily affect myelin. For perfect functioning, OXPHOS requires an active synthesis of the heme group, considering that it is a fundamental component of several subunits of respiratory complexes, and interestingly, myelin sheath displays a higher heme group synthesis in comparison with other districts. In particular, proper functioning of myelin is closely linked to an efficient biosynthetic pathway of the heme and the crucial passage is catalyzed by the enzyme ALA dehydratase (EC 4.2.1.24) that requires zinc as cofactor. Lead poisoning (Saturnism) results in an imbalance of this enzyme and myelin degeneration. Moreover, analyzing the OXPHOS metabolism in myelin isolated from autopsy specimens of multiple sclerosis (MS) patients, we have observed a defective energy/respiratory capacity. With this knowledge, the hypothesis that MS is not an autoimmune disease, but a disease triggered by myelin degeneration following a malfunction of some process related to its energy function and heavy metal pollution seems confirmed, also considering the historical link between industrialization and the MS onset.

Biography

Alessandro M Morelli carried out research in varied fields of biology, focusing in those areas most directly linked to medicine. He investigated on the enzyme Glucose-6-P-dehydrogenase and on its molecular mechanism of senescence. He has been working in the phototransduction molecular events in photoreceptor cells of vertebrate retina. He has discovered the protein FX, a NADP dependent enzyme, catalyzing synthesis of GDP-L-fucose. He has been working on the effects of electromagnetic fields of extremely low frequency on the activity of enzymes involved in phototransduction in retinal cells of vertebrates. Moreover, he has put in evidence the reversible effects of electromagnetic fields on lipid-linked enzymes such as acetylcholinesterase of retinal synaptosomes. Recently, with Isabella Panfoli, Silvia Ravera, Daniela Calzia, he has discovered the brain myelin energetic function and the ATP extramitochondrial synthesis operating in it, involving new paradigms for neurobiology, with application in the study of multiple sclerosis and other neurodegenerative diseases.

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