Poisoning from industrial compounds can cause similar effects to ALS

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Researchers from the Bellvitge Biomedical Research Institute (IDIBELL) at the University of Barcelona (UB) have coordinated a research into how the IDPN nitrile causes neurological syndromes similar to those of the amyotrophic lateral sclerosis (ALS), a severe neuromuscular degenerative disease. The study, led by Jordi Llorens, has been recently published in *Neuropathology and Applied Neurobiology* journal.

Nitriles, chemical compounds containing the cyano (-CN) group, are ubiquitous in nature and have diverse applications in industry. In nature they appear as cyanogenic glycosides, for example in bitter almonds, and as aminonitriles, in some legumes. In industry they are used as solvents and intermediates in the synthesis of plastics, synthetic fibers, resins and pharmaceutical products, among others. The consumption by humans or animals of certain nitriles can cause symptoms similar to cyanide poisoning. This fact suggests that the release of this compound is responsible for acute intoxication. Some nitriles realease less cyanide or do it more slowly, causing neurotoxicity and neurological syndromes.

In a variety of diseases of the nervous system appears abnormal accumulation of neurofilaments, fibers that confer stiffness to neurons. Specifically, in amyotrophic lateral sclerosis (ALS) are observed protrusions formed by a large number of neurofilaments in the axons of motor neurons.

In the study, researchers have observed accumulations of neurofilaments

strikingly similar to those occurring in ALS, in laboratory rats exposed to IDPN (3.3'-iminodipropionitril). Because of this similarity, the researchers have studied the effect of IDPN to understand the biology of neurofilaments in ALS disease. The disease and the IDPN poisoning cause axonopathy, an injury to axons. The novelty of this study is the observation that the axonopathy causes a marked loss of neurofilaments in the terminals of motor neurons. This observation is relevant because the refraction of the terminals is the critical factor in the degeneration of the motor neuron.

The research coordinator explained that "the lack of neurofilaments in the area of the neuromuscular junction can have an impact on the function or stability of the union, contributing to its retraction and subsequent regeneration of the neuron".

Potential clinical applications

Due to the similarity between the proximal accumulations of neurofilaments between the animal model of IDPN and ALS, the researchers predict that the neuromuscular junctions of patients with amyotrophic lateral sclerosis show a lack of neurofilaments similar to that observed in the animal model. The loss of neurofilament terminals could be a pathogenic factor in the disease.

It is increasingly clear that ALS is a multifactorial disease in which genetic and environmental influences cause proximal axonopathy. These factors could alter the neuromuscular junction through the emptying mechanism of neurofilaments observed in IDPN intoxication. In addition, the data indicate that IDPN seems a useful tool for inclusion in multivariate animal models of disease.

More information: Soler-Martin C, U Vilardosa, Saldana-Ruiz S, Garcia N, Llorens J. Loss of neurofilaments in the neuromuscular

junction in a rat model of proximal axonopathy. *Neuropathology and Applied Neurobiology* 2012 Feb, 38 (1):61-71.