

**FRIEDREICH ATAXIA: 150 YEARS OF BENCH AND BEDSIDE STUDIES**

A. ANTENORA<sup>1</sup>, F.M. SANTORELLI<sup>2</sup>, G. DE MICHELE<sup>1</sup>, S. PELUSO<sup>1</sup>, F.SACCÀ<sup>1</sup>  
and A. FILLA<sup>1</sup>

*<sup>1</sup>Department of Neuroscience and Reproductive and Odontostomatological Sciences, Federico II University, Naples, Italy; <sup>2</sup>IRCCS Stella Maris, Pisa, Italy*

**Friedreich ataxia is the most frequent hereditary ataxia among Caucasians. Almost invariably, the disease is caused by homozygous GAA triplet repeat expansions in the first intron of the frataxin gene, *FXN*, whereas point mutations or deletions in conjunction with an expanded GAA tract account for the remaining cases. The expanded intronic alleles interfere with *FXN* transcription, decreasing the production of normally functioning frataxin protein to 5-20% of normal. Deficient frataxin levels result in excessive mitochondrial iron accumulation, reduced iron-sulfur clusters vital for mitochondrial energy production, and increased intracellular oxidative damage. To date, no cure has emerged and treatments remain largely supportive, despite extensive ongoing research and several rationale strategies have been attempted.**

*Corresponding author:* Alessandro Filla,  
Department of Neuroscience and Reproductive  
and Odontostomatological Sciences,  
Federico II University, Italy  
Via Pansini 5, 80131 Napoli  
Tel.: +390817462476  
e-mail: afilla@unina.it

## NF- $\kappa$ B UNBALANCE AND DYSFUNCTION IN ACUTE AND AGE-RELATED NEURODEGENERATIVE DISEASE

A. LANZILLOTTA<sup>1</sup>, V. PORRINI<sup>1,2</sup>, A. BELLUCCI<sup>1</sup>, M. BENARESE<sup>1</sup>,  
C. BRANCA<sup>1</sup>, E. PARRELLA<sup>1</sup>, PF. SPANO<sup>1,2</sup> and M. PIZZI<sup>1,2</sup>

<sup>1</sup>*Department of Molecular and Translational Medicine and National Institute of Neuroscience, University of Brescia, Italy;* <sup>2</sup>*IRCCS, San Camillo Hospital, Venice, Italy*

The mechanisms underlying the progressive loss of neurons in age-related neurodegenerative diseases remain unknown to date. NF- $\kappa$ B factors are cardinal transcriptional regulators of inflammation and apoptosis and have been involved in the brain programming of systemic aging as well as in the pathogenesis of brain ischemia. Studies focusing on the complexity of NF- $\kappa$ B transcriptional activity in neuronal cell death showed that the composition of NF- $\kappa$ B active dimers and epigenetic mechanisms modulating histone acetylation finely condition neuronal vulnerability to brain ischemia. The atypical activation of NF- $\kappa$ B RelA acetylated on lysine 310 (K310) residue can trigger the expression of apoptotic genes but also constitutes a target for a neuroprotective combination of epigenetic drugs. Conversely, activation of NF- $\kappa$ B/c-Rel promotes neuroprotective effects through the transcription of specific anti-apoptotic genes. In addition, the absence of c-Rel shatters the resilience of nigral dopaminergic (DA) neurons to aging and induces parkinsonian features in mice. Indeed, we found that c-Rel-deficient mice show an increased RelA activation in the basal ganglia, and develop an L-DOPA-responsive parkinsonism associated with loss of DA neurons in the substantia nigra, neuroinflammation, accumulation of alpha-synuclein and iron during aging. Here, we discuss the effect of unbalanced activation of RelA and c-Rel during aging and propose novel challenges for the development of potential therapeutic strategies for neurodegenerative diseases.

## BENEFICIAL EFFECTS OF HYDROGEN IN THE CNS AND A NEW BRAIN-STOMACH INTERACTION

M. NODA<sup>1</sup>, M. ITO<sup>2</sup>, I. OHSAWA<sup>3</sup> and K. OHNO<sup>4</sup>

<sup>1</sup>Laboratory of Pathophysiology, Graduate School of Pharmaceutical Sciences, Kyushu University, Fukuoka, Japan; <sup>2</sup>Research Team for Mechanism of Aging, Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan;

<sup>3</sup>Research Team for Functional Biogerontology, Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan; <sup>4</sup>Division of Neurogenetics, Center for Neurological Diseases and Cancer, Nagoya University Graduate School of Medicine, Nagoya, Japan

A new medical gas, molecular hydrogen (H<sub>2</sub>), has been reported to be effective for a variety of disorders and clinical trials have shown promising results. Though the precise mechanism is still unknown, it is obvious that H<sub>2</sub> has multiple effects. The first prominent effect of H<sub>2</sub> was as antioxidant or reactive oxygen species (ROS)-scavenger, though it blocks only hydroxyl radicals (•OH), which are the most toxic ROS, but not others. Then the possibility as a signal modulator was proposed and it became obvious that many protective effects of H<sub>2</sub> were not simply explained by antioxidant. Blocking reactive oxygen species (ROS) would be a rather direct anti-oxidative effect and if so, H<sub>2</sub> need to encounter ROS. However, long-term consumption of H<sub>2</sub> makes some unknown biological change which subsequently reveals resistance to ROS without any presence of H<sub>2</sub> itself. One of the ROS-resistant mechanisms of H<sub>2</sub> is due to brain-stomach interaction via ghrelin. The action of H<sub>2</sub> in the stomach seems to be quite specific; it activates β1 but not β2 adrenoceptor to increase the production and the release of ghrelin. Whether ghrelin secretion is a universal mechanism in all other protective effects induced by drinking H<sub>2</sub> water needs to be elucidated.

2279-5855 (2014)

Copyright © by BIOLIFE, s.a.s.

This publication and/or article is for individual use only and may not be further reproduced without written permission from the copyright holder.

Unauthorized reproduction may result in financial and other penalties

DISCLOSURE: ALL AUTHORS REPORT NO CONFLICTS OF INTEREST RELEVANT TO THIS ARTICLE.

## NEUROIMAGING SIGNATURES OF NEURODEGENERATION IN THE AMYOTROPHIC LATERAL SCLEROSIS - FRONTOTEMPORAL LOBAR DEGENERATION CONTINUUM

F. TROJSI<sup>1,2</sup>, M.R. MONSURRÒ<sup>1,2</sup> and G. TEDESCHI<sup>1,2</sup>

*<sup>1</sup>Department of Medical, Surgical, Neurological, Metabolic and Aging Sciences, Second University of Naples, Naples, Italy; <sup>2</sup>MRI Research Center SUN-FISM – Second University of Naples, Naples, Italy*

Brain imaging techniques, especially those based on magnetic resonance imaging (MRI), have been increasingly applied to study the structure and function of the human brain in health and disease. More recently, the combined investigation of genetic information and imaging data, both proposed as candidate endophenotypes or disease vulnerability markers, resulted to be considerably helpful to explore the structural and functional consequences of some genetic polymorphisms or mutations on brain connectivity, allowing to exploit the possible genotype-endophenotype associations in several neurological disorders. With regard to neurodegenerative diseases, amyotrophic lateral sclerosis (ALS), a multi-systemic neurodegenerative disease with early and prominent impairment of motor abilities, and frontotemporal lobar degeneration (FTLD), the second most common early-onset dementia, have been proven to share several clinical, neuropathological, genetic and neuroimaging features, and have been thought to belong to the same spectrum of disease. Specifically, both overlapping and diverging brain connectivity patterns, evaluated by diffusion tensor imaging (DTI), voxel- and surface-based morphometry (VBM) and resting-state functional MRI (RS-fMRI) analyses, have been described comparing several ALS and FTLD populations. In this article we review the current state of knowledge concerning the most advanced neuroimaging findings associated with clinical and genetic patterns of neurodegeneration across the ALS-FTLD continuum, underlying the usefulness of a multimodal approach to assess novel biomarkers of disease and more appropriate treatment strategies.

2279-5855 (2014)

Copyright © by BIOLIFE, s.a.s.

This publication and/or article is for individual use only and may not be further reproduced without written permission from the copyright holder.

Unauthorized reproduction may result in financial and other penalties

**DISCLOSURE: ALL AUTHORS REPORT NO CONFLICTS OF INTEREST RELEVANT TO THIS ARTICLE.**

**NERVE GROWTH FACTOR, SYNAPTIC PLASTICITY AND ALZHEIMER'S DISEASE**F. WEISZ<sup>1,2</sup>, E. DEL DUCA<sup>1</sup>, A. CATTANEO<sup>1</sup> and R. NISTICÒ<sup>1,2</sup>*<sup>1</sup>European Brain Research Institute, Rome, Italy; <sup>2</sup>Department of Physiology and Pharmacology 'Erspamer', Sapienza University of Rome, Rome, Italy*

**Nerve growth factor (NGF) modulates multiple signaling pathways to regulate neuronal survival, synaptic plasticity and cognitive processes. On the other hand, NGF has been implicated in the pathophysiology of a wide variety of neurological and psychiatric diseases and may serve as a potential therapeutic strategy for the treatment of neurodegenerative disorders. Here we explore the interactions between NGF, synaptic plasticity and Alzheimer's disease (AD), and highlight a novel NGF variant which might provide an innovative therapeutic option to restore neuroplasticity deficits in AD.**

2279-5855 (2014)

Copyright © by BIOLIFE, s.a.s.

This publication and/or article is for individual use only and may not be further reproduced without written permission from the copyright holder.

Unauthorized reproduction may result in financial and other penalties

**DISCLOSURE: ALL AUTHORS REPORT NO CONFLICTS OF INTEREST RELEVANT TO THIS ARTICLE.**