The effect of interferon beta 1a and polyphenolic extracts on autophagy, apoptosis and oxidative stress in patients with multiple sclerosis: an in vitro study

M. Ruggieri[1], L. Savino[1], D. Centonze, S. Scacco[1], G. Matarese, A. Uccelli, R. Mechelli, M. Salvetti, D. Paolicelli[1], M. Trojano[1] *on behalf of MS RUN group.*

[1]Department Basic Medical Sciences, Neurosciences and Sense Organs. University of Bari, Bari, Italy

Background

Accumulation of aberrant proteins and inclusion bodies, hallmarks of neurodegenerative diseases such as Multiple Sclerosis (MS), have toxic effects, resulting in overproduction of reactive oxygen species and oxidative stress.
Autophagy, considered an alternative apoptosis, is a significant intracellular mechanism that removes damaged organelles and misfolded proteins in order to maintain cell homeostasis (1). Excessive or insufficient autophagic and apoptotic activity leads to altered homeostasis causing neurodegeneration (2,3).

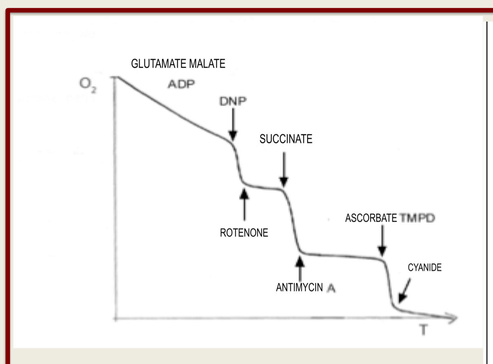
Objective

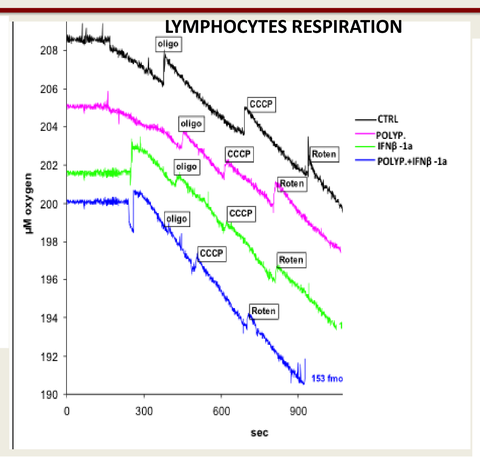
In this study, we evaluated the “in vitro” effects of IFN-β 1a and polyphenolic extracts on the induction of apoptosis and autophagy , as well as their relation to oxidative stress trough respirometric analysis measuring oxygen consumption .

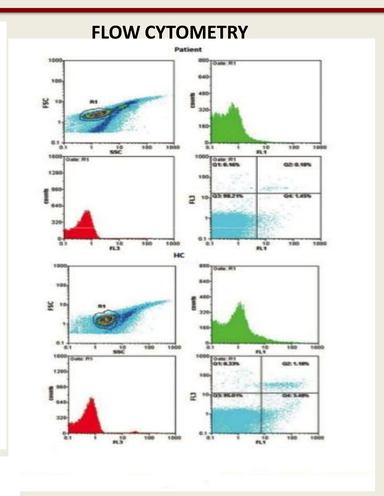
Material and Methods

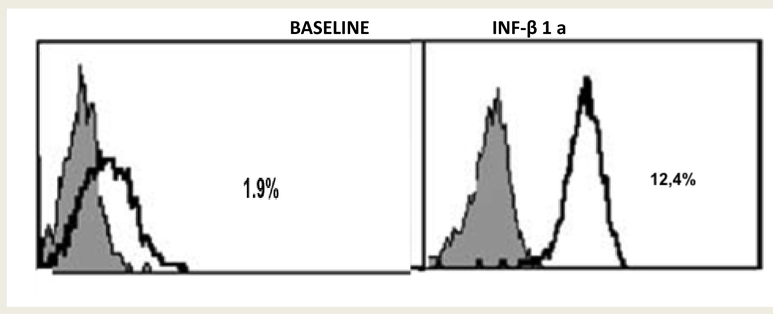
Peripheral and cerebrospinal fluid lymphocytes of 50 RR-MS patients were included into the study. Fifty healthy controls (HCs) serum samples , age and sex matched, were used in the same experiments. Autophagic (ATG5 and LC3b), apoptotic (Bax and Bcl2) molecules, and oxygen consumption were studied. Respirometric analysis, Western blot-, flow cytometry, and cell culture were used.

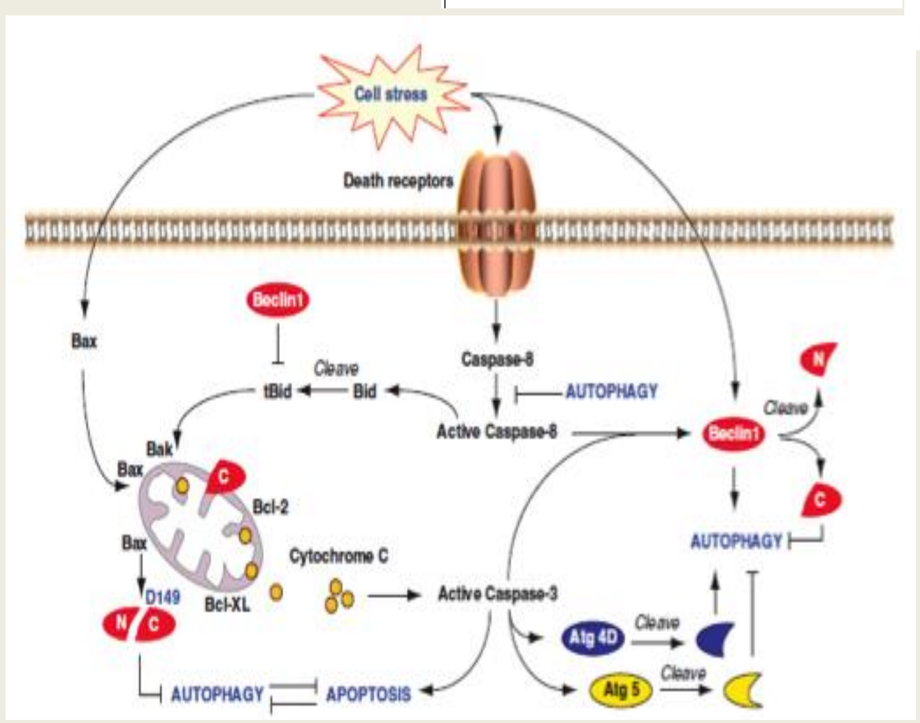
Results

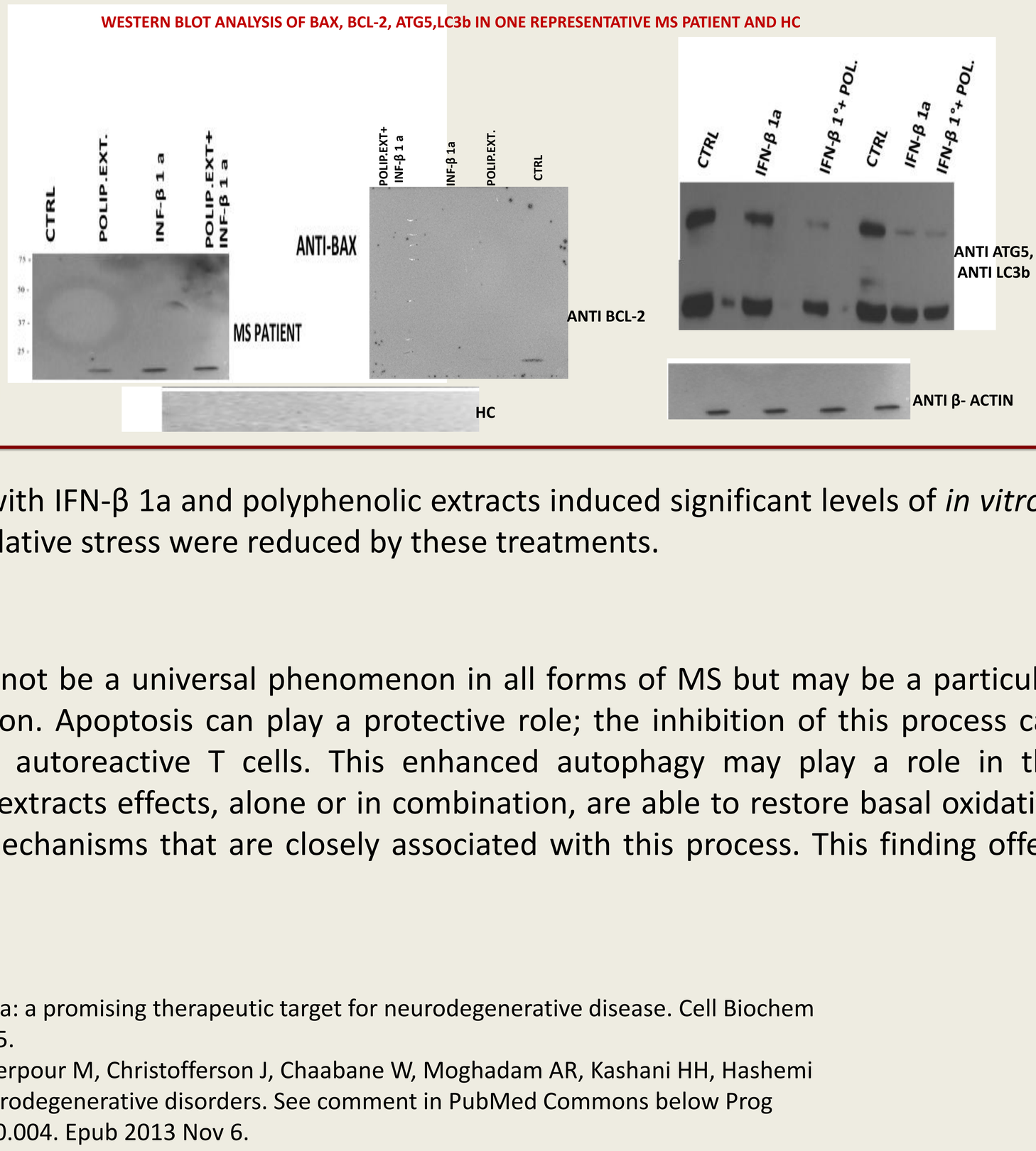












Treatment of peripheral and CSF lymphocytes with IFN-β 1a and polyphenolic extracts induced significant levels of *in vitro* apoptosis induced in, while autophagy- and oxidative stress were reduced by these treatments.

Conclusions

These finding suggest that oxidative stress may not be a universal phenomenon in all forms of MS but may be a particular manifestation of inflammatory neurodegeneration. Apoptosis can play a protective role; the inhibition of this process can significantly enhance growth –and perpetuate autoreactive T cells. This enhanced autophagy may play a role in the pathogenesis of MS. IFN-β 1a and polyphenolic extracts effects, alone or in combination, are able to restore basal oxidative stress as well as the apoptotic or autophagic mechanisms that are closely associated with this process. This finding offers insights into a possible cure for MS.

References

1. Kamat PK, Kalani A, Kyles P, Tyagi N. Autophagy of mitochondria: a promising therapeutic target for neurodegenerative disease. Cell Biochem Biophys.2014 Nov;70(2):707-19. doi: 10.1007/s12013-014-0006-5.
2. Ghavami S, Shojaei S, Yeganeh B, Ande SR, Jangamreddy JR, Merpour M, Christofferson J, Chaabane W, Moghadam AR, Kashani HH, Hashemi M, Owji AA, Los MJ. Autophagy and apoptosis dysfunction in neurodegenerative disorders. See comment in PubMed Commons below Prog neurobiol. 2014 Jan;112:24-49. doi: 10.1016/j.pneurobio.2013.10.004. Epub 2013 Nov 6.
3. Kesidou E, Lagoudaki R, Touloumi O, Poulatsidou KN, Simeonidou C. Autophagy and neurodegenerative disorders.Neural Regen Res 2013 Aug 25;8(24):2275-83. doi: 10.3969/j.issn.1673-5374.2013.24.007.