



Coordinate activation of lysosomal, Ca²⁺ and ATP-ubiquitin-dependent proteolytic pathways in the soleus muscle in hind-limb suspended rats

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► To cite this version:

Daniel Taillandier, E Aurousseau, A Obled, D Béchet, M Ferrara, et al.. Coordinate activation of lysosomal, Ca²⁺ and ATP-ubiquitin-dependent proteolytic pathways in the soleus muscle in hind-limb suspended rats. *Reproduction Nutrition Development*, 1994, 34 (6), pp.640-640. hal-00899725

HAL Id: hal-00899725

<https://hal.science/hal-00899725>

Submitted on 11 May 2020

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conditions studied so far [Attaix *et al* (1994) *op cit*], and could presumably be responsible for the breakdown of myofibrillar proteins.

Coordinate activation of lysosomal, Ca^{2+} - and ATP-ubiquitin-dependent proteolytic pathways in the soleus muscle in hind-limb suspended rats. D Taillandier¹, E Aourousseau¹, A Obled¹, D Béchet¹, M Ferrara¹, P Cottin², A Ducastaing², X Bigard³, CY Guézennec³, D Attaix¹ (¹INRA-Theix, Centre de Recherche en Nutrition Humaine et Unité d'Étude du Métabolisme Azoté, 63122 Saint-Genès-Champanelle; ²ISTAB et Université de Bordeaux I, 33405 Talence; ³Centre d'Études et de Recherches de Médecine Aéronautique, 91228 Brétigny-sur Orge, France)

During simulated weightlessness, increased protein breakdown is the major determinant of muscle atrophy and protein wasting in antigravity muscles, *ie* the soleus [Thomason and Booth (1990) *J Appl Physiol* 68, 1-12]. The aim of this study was to identify the proteolytic pathways responsible for these alterations in skeletal muscle.

Twenty male Wistar rats with an initial body weight of 120 ± 5 g were randomly assigned to a control and a non-weight-bearing group. The experimental group was suspended by the tail according to the protocol described by Taillandier [(1993) Thèse de Doctorat de l'Université Blaise-Pascal, Clermont-Ferrand II, France]. Animals were studied after 9 d of treatment. Isolated soleus muscles were incubated to measure protein synthesis and breakdown simultaneously, as described by Tischler *et al* [(1982) *J Biol Chem* 257, 1613-1621]. Two other groups of rats raised in identical conditions were used to measure either the rate of proteolysis after inhibiting both lysosomal and Ca^{2+} -dependent proteases [Wing and Goldberg (1993) *Am J Physiol* 264, E668-E676], or mRNA levels for multiple components of proteolytic systems, in the soleus muscle.

The soleus muscle atrophy was higher than 50% ($P < 0.001$) after 9 d treatment. Total protein breakdown of suspended rats was enhanced by 66% ($P < 0.001$), compared to control animals. By contrast, the rate of protein synthesis was not significantly modified by hindlimb suspension. The

lysosomal and Ca^{2+} -dependent proteolysis was greatly enhanced (254%, $P < 0.001$) in the soleus muscle of non-weight-bearing rats, but did not exceed 18% of total proteolysis. In addition, the inhibition of both lysosomal and Ca^{2+} -dependent proteases did not suppress increased proteolysis in the soleus muscle of suspended rats. Northern blot procedures revealed large increases in mRNA levels for lysosomal (cathepsins B, L and D), and Ca^{2+} -dependent (m-calpain) proteases, and for components of the ATP-ubiquitin-dependent proteolytic pathway (ubiquitin, 14-kDa ubiquitin carrier protein E2, C2 and C9 proteasome subunits) in the soleus muscle of non-weight-bearing rats. Similar data were observed in a phasic muscle, the extensor digitorum longus.

These data clearly demonstrate that the major proteolytic systems are coordinately activated in skeletal muscle during simulated weightlessness. Cathepsins, calpains and the proteasome could degrade different classes of proteins, the ATP-ubiquitin-dependent proteolytic pathway being presumably responsible for the breakdown of the major contractile proteins.

VII. Nutrition and pathology

Effects of moderate amounts of dietary fat on post-prandial lipemia in healthy human subjects. C Dubois¹, M Armand¹, P Borel¹, M Senft¹, H Portugal², AM Pauli², PM Bernard², V Azais-Braesco³, C Latge⁴, D Lairon¹ (¹Unité 130-INSERM (National Institute of Health and Medical Research), 18, avenue Mozart, 13009 Marseille; ²Hôpital Sainte-Marguerite, 13000 Marseille; ³Unité Vitamines, LNSA-INRA, 78000 Jouy-en Josas; ⁴Crealis, Brive, France)

There have been considerable developments in postprandial studies on human subjects during recent years. These experiments have generally studied blood postprandial responses to amounts of fat (70–140 g) greatly exceeding that usually ingested during a meal, even for a western high-fat diet (40–50 g per meal).

The present study therefore compares the post-prandial responses to 2 different and moderate amounts of dietary fat (30 and 40 g) in the form of well-defined dietary emulsions of sunflower oil (droplet size: 30–44 μm). The 30 g fat