The V471A polymorphism in autophagy-related gene ATG7 modifies age at onset specifically in Italian Huntington disease patients

Submitted by Emmanuel Lemoine on Wed, 04/22/2015 - 16:53

Titre: The V471A polymorphism in autophagy-related gene ATG7 modifies age at onset specifically in Italian Huntington disease patients

Type de publication: Article de revue

Auteur: Metzger, S. [1], Walter, C. [2], Riess, O. [3], Roos, R. A [4], Nielsen, J. E [5], Craufurd, D. [6], Nguyen, H. P [7], REGISTRY investigators of the European Huntington's Disease Network [8]

Editeur: Public Library of Science

Type: Article scientifique dans une revue à comité de lecture

Année: 2013

Langue: Anglais

Date: 2013/07/31

Numéro: 7

Pagination: e68951

Volume: 8

Titre de la revue: PLoS One

ISSN: 1932-6203

Mots-clés: *Polymorphism, Single Nucleotide [9], Adolescent [10], Adult [11], Age of Onset [12], Aged [13], Autophagy/*genetics [14], Child [15], Child, Preschool [16], Cohort Studies [17], Gene Frequency [18], Genotype [19], Humans [20], Huntington Disease/*epidemiology/*genetics/pathology [21], Italy/epidemiology [22], Middle Aged [23], Ubiquitin-Activating Enzymes/*genetics [24], Young Adult [25]
The cause of Huntington disease (HD) is a polyglutamine repeat expansion of more than 36 units in the huntingtin protein, which is inversely correlated with the age at onset of the disease. However, additional genetic factors are believed to modify the course and the age at onset of HD. Recently, we identified the V471A polymorphism in the autophagy-related gene ATG7, a key component of the autophagy pathway that plays an important role in HD pathogenesis, to be associated with the age at onset in a large group of European Huntington disease patients. To confirm this association in a second independent patient cohort, we analysed the ATG7 V471A polymorphism in additional 1,464 European HD patients of the “REGISTRY” cohort from the European Huntington Disease Network (EHDN). In the entire REGISTRY cohort we could not confirm a modifying effect of the ATG7 V471A polymorphism. However, analysing a modifying effect of ATG7 in these REGISTRY patients and in patients of our previous HD cohort according to their ethnic origin, we identified a significant effect of the ATG7 V471A polymorphism on the HD age at onset only in the Italian population (327 patients). In these Italian patients, the polymorphism is associated with a 6-years earlier disease onset and thus seems to have an aggravating effect. We could specify the role of ATG7 as a genetic modifier for HD particularly in the Italian population. This result affirms the modifying influence of the autophagic pathway on the course of HD, but also suggests population-specific modifying mechanisms in HD pathogenesis.

**Liens**

[1] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=17917
[2] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=17918
[3] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=17919
[4] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=17920
[5] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=17921
[6] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=17857
[7] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=17922
[8] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=17862
[9] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=15935
[10] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=1214
[11] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=1002
[12] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=6086
[13] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=1072
[14] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=15932
[15] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=1216
[16] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=1534
[17] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=9910
[18] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=13392
[19] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=1698
[20] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=991
[21] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=15933
[22] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=15934
[23] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=5941
[24] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=15936
[25] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=6036
Publié sur Okina (http://okina.univ-angers.fr)