



## Cognitive frailty, a new target for healthy ageing



The increase in life expectancy is a global phenomenon, affecting both developed and under-developed countries. Data from the World Health Organisation (WHO) Regional Office for Europe show that, despite considerable differences between countries, there is a persistent trans-national increase in life expectancy at birth in the recent decades. The global figures in the continent jump from 71.74 to 76.31 years in the 1980–2010 period [1]. This success is the result of effective strategies against disease, advances in public health, and improvement in socioeconomic and living conditions.

Frailty is a new, crucial clinical condition associated with ageing. Frailty results from the age-related decay of physiological systems, which leads to increased vulnerability to stressors [2]. Frail individuals disproportionately decrease their buffering capacity in such a way that even minor insults condition unexpected deterioration in health. It is important to stress that the concept of frailty does not overlap with that of disease. There is, however, an association because frailty increases the risk for disease, and disease itself may increase the risk for an individual to become frail.

The pathophysiological basis of this more unfavourable impact of ageing in some subjects is still unclear. There is, however, the conviction that, as for many biological phenomena, both genomics and environment should play a role. Whichever the determinants, frailty results from an increased damage that leads to loss of homeostatic control in the cellular maintenance systems. Interestingly, this progressive deterioration does not seem to be specific of a particular organ or system. The brain has received particular attention, given the considerable burden imposed by cognitive decline. It is again the health agencies, like the WHO with the report on dementia [3], which have alerted of the magnitude of the threat in the actual context of worldwide ageing.

The progression of age-associated deterioration of brain functional reserve translates into cognitive deficits. Cognitive decline follows the pattern of several noncommunicable diseases, which exhibit clinical gradation. Dementia defines the final stage, which is often preceded by the less dramatic mild cognitive impairment (MCI). MCI involves the appearance of clinically recognised deficits in cognition that do not prevent independent performance of activities of daily living. The potential for reversibility of MCI has increased the interest towards this preliminary form and its early diagnosis. Also of high interest, the concept of brain frailty has gained momentum.

What do we know of cognitive frailty (CF)? Are we allowed to speak of CF as a clearly defined, even separate, entity? There is little

doubt in that ageing affects cellular performance and death in the brain. It is not only the advances provided by experimental models, but also the wealth of data that is being gathered from explorations with new functional imaging technologies in the human. There are now data about the association of ageing with accelerated death of neurons in crucial areas like the hippocampus, or changes in the microglia, the resident immune cell population in the brain, all of them providing the basis for decreased homeostatic reserve. Having said so, the identification of CF is limited by the proper lack of specific indicators. This is not only a limitation of brain frailty, but also that of other organs and systems, since the two most recognised models of frailty, the phenotypic model of Fried or the cumulative deficit model of Rockwood, use general functional indicators, as in the former, or an aggregate of deficits in clinical and laboratory parameters where only some assimilate to central nervous system functions, as in the latter.

Because of those limitations, clinical studies are focusing in taking standardised instruments assessing cognition, like the minimal state examination (MMSE), or the own diagnosis of MCI as a reference. Interestingly, several cross-sectional studies have shown correlation of frailty and cognitive deterioration. Of higher interest, longitudinal studies have reproduced the correlation between physical frailty and cognitive decline [4]. Based on those observations, a group of experts has recently issued a consensus defining CF [5]. According to them, CF is a clinical syndrome found in elderly individuals, which characterises by concurrent physical frailty and potentially reversible cognitive impairment [clinical dementia rating score (CDR)=0.5]. Importantly, subjects with Alzheimer's or other dementias are excluded.

To conclude, CF constitutes a new construct that underlines the use of the concept of frailty within the specific area of cognitive decline. It is not a totally new concept, since brain investigators have already considered frailty in the latter years; but it is operative because it reinforces the clinical association with physical frailty. That association may open the way for the use of strategies, lifestyle for example, which are being tested for the prevention of physical frailty. The finding of effective measures in the prevention of cognitive decline will deserve every effort.

### Conflict of interest

None.

### Author contribution

Prof. Antonio Cano has been the author. He has been involved in the design of the content, has written the manuscript and has decided the final version to be published.

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### References

- [1] [http://www.euro.who.int/\\_data/assets/pdf\\_file/0004/197113/EHR2012-Eng.pdf?ua=1](http://www.euro.who.int/_data/assets/pdf_file/0004/197113/EHR2012-Eng.pdf?ua=1) (accessed 27.07.15).
- [2] A. Clegg, J. Young, S. Iliffe, M.O. Rikkert, K. Rockwood, Frailty in elderly people, *Lancet* 381 (2013) 752–762.
- [3] [http://apps.who.int/iris/bitstream/10665/75263/1/9789241564458\\_eng.pdf?ua=1](http://apps.who.int/iris/bitstream/10665/75263/1/9789241564458_eng.pdf?ua=1) (accessed 27.07.15).
- [4] D.A. Robertson, G.M. Savva, R.A. Kenny, Frailty and cognitive impairment—a review of the evidence and causal mechanisms, *Ageing Res. Rev.* 12 (2013) 840–851.
- [5] Q. Ruan, Z. Yu, M. Chen, Z. Bao, J. Li, W. He, Cognitive frailty, a novel target for the prevention of elderly dependency, *Ageing Res. Rev.* 20 (2015) 1–10.

Antonio Cano (MD PhD)<sup>a,b,\*</sup>

<sup>a</sup> Service of Obstetrics and Gynecology,  
Clínico University Hospital,  
Av. Blasco Ibáñez 17,  
46010 Valencia,  
Spain

<sup>b</sup> Department of Pediatrics,  
Obstetrics and Gynecology,  
University of Valencia,  
Av. Blasco Ibáñez 15,  
46010 Valencia,  
Spain

\* Corresponding author at: Department of  
Pediatrics,  
Obstetrics and Gynecology,  
Facultad de Medicina Av. Blasco Ibáñez 15,  
46010 Valencia,  
Spain.

Fax: +34 96 386 48 15.

E-mail address: [antonio.cano@uv.es](mailto:antonio.cano@uv.es)

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