World Journal of Scientific Research and Reviews
Vol. 3, No. 2, March 2015, pp. 1-5, E-ISSN: 2334 - 0304
Available online at http://wjsrr.com/

Research article

AGING THROUGH NEURONAL DEATH

DI DONNA GIUSEPPE MD PhD , DI MURO ROSA MD

Brain Research Center, Via dei Cappellari 29 – 00186 Rome, Italy
E-mail: gdidonna01@gmail.com

ABSTRACT

The Authors, starting from the analysis of the different current theories about the causes determining the aging process, propose a different study hypothesis, which, by individuating the cause of the body functional activities deterioration in the progressive neuronal population death, considers this deterioration as the origin of the general progressive slow deterioration. **Copyright © WJSRR, all rights reserved.**

Keywords: aging, death, neuronal

INTRODUCTION

Aging theories

Many theories have been proposed in order to explain the molecular mechanism of aging:

- planned obsolence theory
- telomerase theory of aging
- neuroendocrine theory
- the mitochondrial decline theory
- the free radical theory
- the membrane theory of aging
- the Hayflick limit theory

ETIOLOGY

Cellular elements of all organs and apparatus, renovate continuously during the life, this happens through a cellular division process, which repeats in vivo more than the 50 cellular divisions observed by Hayflick in tissue culture, and that is commonly said to happen in the moment in which the mother cell gets aged.

The cell reproduction pathway goes along the cell division pathway, which does not happen as a consequence of a state of aging but in the moment in which the cell is in the full functional potentiality.

We are non speaking of a “mother” cell generating two “daughter” cells, but we are referring to a cell which divides and generates two new cells.

Cellular division is an answer to a need: the need of having cellular elements offering flexibility, plastic and reparative capabilities, essential for the organs which, because of their function, are prone to wear and tear.

The neuronal cell has instead different characteristics, due to the fact that this kind of cells is a perpetual element, present from birth to death.

NEURONAL NETWORKS

Neuronal cells can be divided in around 10.000 different types, and, even if they all have many characteristics in common, they do not connect each other indifferently forming random networks; every cell, instead, establishes specific connections at level of well defined synaptic contacts and just with selected postsynaptic target cells and not with some other cells.

An important characteristic of the cerebral organization is the fact that cells with characteristics similar, can carry out different functions, depending on the type of the connections they establish with sensory receptors and muscles.

In multipolar neurons, which are predominant in the vertebrate neural system, the number and the extension of the dendritic processes depends on the number of the synaptic contacts which other neurons establish with the cell itself.

A spinal motoneuron with dendrites which are relatively few and poorly developed, receives approximately 10.000 synaptic contacts, 2.000 on the cell body, 8.000 on the dendrites and 150.000 on the cerebellar Purkinje cells.

The complex neural network, along with the twisted dendrites, is part of a precise order which would be completely altered by a cellular division; in order to put the entire structure again, if would be necessary to use such a big expenditure of energy which would be against the physical principle of minimum energy. This explains why the neuron does not divide.

Therefore, the neuronal cell follows a fixed pathway: it remains always the same during the whole life, or, alternatively, it dies.

As a consequence of this process of neuronal death, which happens phyisiologically, in a constant and gradual way already after thirty years of age, or pathologically, as a consequence of a traumatic event, the initial patrimony of non removable neuronal cells depletes definitely, determining a cerebral cells deterioration and, consequently, a progressive aging.

Taking into account, as an exemplifying elementary model, a motoneuron pheriperially connected to its corresponding myofibril, the death of that motoneuron will determine, as a consequence, the death of the corresponding myofibril; the same thing happens inversely, because there is a close correlation between these two elements.

Therefore, the progressive cerebral deterioration of the neurons and the definitive death of the perpetual elements, will have, as a consequence, a progressive depletion of the corresponding elements and of all the connected functions, both from the strictly numeric side and from the side of the complex biophysical processes.

MATERIALS AND METHODS

The Authors' hypothesis about the cause of the aging is referred to the peculiarity of the neuron, as a unique perpetual cellular element, which is the fact that the neuron does not divide.

AGING

If we want to interpret all this complex organization from a physical point of view, we can consider the neural network and then the whole living organism, as a complex open biological system, which obeys thermodynamics laws, by dispersing energy and increasing its entropy.

Aging determines an increase both in the system's complexity and in its degree of disorder, therefore the state of equilibrium results altered.

From this point of view, aging should be detected where a bifurcation or a critical point happens in equilibrium dynamics (Van Geert 1994).

CENTRAL LIMIT THEOREM (CLT)

The aging theories proposed until now, are phenomenological conclusions which comply the Central Limit Theorem (CLT) – in the range of the probability theory – which states that the sum of a sufficient number of independent random variables, each which a well-defined mean and a well-defined variance, will be approximately normally distributed: in fact, quantities of dividing cells are often the balanced sum (weighted sum) of many unobservable random events.

The CLT expresses the fact that the sum of many, but, small, independent stochastic variables (random), tends to a Gaussian distribution. This means that all the active cells, including the dividing ones, cannot keep dividing forever and, as a consequence, are subject to deterioration and destined to conclude their life cycle.

The non-dividing cells also have inbound and outbound flows, and such activity produces and dissipates energy but, according to the CLT, this activity is destined to slow and then to stop.

The slowdown mechanism depends on the cellular population, because the deterioration or the end connected to it, causing their death.

The slowdown of the neuronal activity causes a delay in the start:

- the ion exchange activity is altered and this causes an alteration in the neuronal function (waiting time)
- the neuronal function falls, the neuron dies and with the entire neuronal population connected with it.

The death of the neuronal population causes the aging process.

CONCLUSIONS

The damage of the neuron and its death is hyphotized to be the cause of aging.

Many causes contribute to the wear and tear of the neuron.

An alteration of the function of the sodium-potassium pump, affects the energetic aspect, in particular the inflow of Ca++ ions is one of the first effects which causes part of the axonal injury, because it activates the Ca++

dependent proteases and determines the formation of peroxide-type radicals, which carry out a toxic effect on neurons.

The altered function of the sodium-potassium pump causes an alteration in energy production and the altered function of the neuronal cell, originating a cusp, it means that the dynamic equilibrium state of the organism is broken (Markow process), and, as a consequence of that, in the equilibria logic, the gradual progressive aging process happens.

The axonal injury determines the onset of other alterations in the injured neuron, at the end, also affects the cells which are synaptically connected with the injured neuron.

The neuronal degeneration phenomenon (chromatolysis) goes together with an increase in the number of the free polysomes in the cell body and an increase in the RNA and in the protein synthesis (this is an expression of the need of new proteins to build up the structure of the neuronal distal segment).

If the cell cannot restore its functional contacts it becomes atrophied and necrotic.

The transneuronal degeneration explains, at least in part, how injures which occurred in a certain part of the nervous system, can have effects in other parts of the nervous system itself, even far from the zone of injury, this fact is due to the high level of interdependence among the neurons, which is fundamental for their respective survival and the action of consequent progressive deterioration (aging).

Most of the theories of aging make hypothesis that include causes which are only secondary phenomena in relation to the aging process itself, which has its base, a cause which the logic, even the most simple one, recognizes: the progressive massive death of the perpetual cellular unit, the neuron, which leads and regulates all the functions of the organism-

G. DI DONNA R. DI MURO
DISCOVERED AND FORMULATED BY THE AUTHOR
MD PhD GIUSEPPE DI DONNA ON 27 FEBRUARY 1997

BIBLIOGRAPHY

[1] Ansado J. et al.: Coping with task demand in aging using neural compensation and neural reserve triggers primarily intra-hemispheric-base neurofunctional reorganization. Neurosc. Res, feb 2013

[2] Avila J. et al.: Tau and neuron aging. Aging dis. 2013, 4 (19); 23-28

[3] Bortz WM: Aging as entropy. Exp. Gerontol. 1986; 21 (4-5), 321-28

[4] Eissenberg J.C.: telomeres, cancer & aging: live long& prosper? Mo. Med., jan-feb 2013; 110 (1); 11-16

[5] Garrett D.D. et al.: Moment-to-moment brain signal variability: a next frontier in human brain mapping? Neurosc. Biobheav. Rev., copyright © 2013 Elsevier ltd

[6] Hopkins R.O.: The brain after critical illness: effects of illness and aging on cognitive function. Crit, care, feb 2013; 17 (1); 116

[7] Jacob K.D. et al.: Markers of oxidant stress that are clinically relevant in aging and age-related disease. Mech. Ageing Dev.; feb 2013

[8] Kawashima R.: Mental exercises for cognitive function: clinical evidence. J. Prev. Med. Public Health; jan 2013

[9] Kilmas A. et al.:Regional ADC measurements during normal brain aging in the clinical range of b values: a DWI study; Clin. Imaging; feb 2013

[10] Kushner J.A.: The role of aging upon beta cell turnover. J. Clin. Invest. 2013, 1; 123 (3); 990-95

[11] Lee D.C. et al.: Aging enhances classical activation but mitigates alternative activation in the central nervous system. Neurobiol. Aging; 2013, 34 (6), 1610-20

[12] Lövden M. et al.: Structural brain plasticity in adult learning and development. Neurosc. Biobehav. Rev.; feb 2013

[13] Maitre J. et al.: Discrepancy in the involution of the different neural loops with age. Eur. J. appl. Phyisiol.; feb 2013

[14] Merksmer Pl. et al.:The sirtuins, oxidative stress and aging: an emerging link. Aging (Albany, NY); 2013

[15] Mostany R. et al.: Altered synaptic dynamics during normal brain aging. J. Neurosc., 2013, 2; 33 (9) 4094-4104

[16] Nishiyama A. et al.: Systematic repression of transcription factors reveals limited patterns of gene expression changes in ES cells. Sci. rep. 2013, 3; mar 2013

[17] Nomura Y.: Neurochemical aspects of brain aging-neuronal death and decreased synaptic functions. Hokkaido Igaku Zasshi; may 1996

[18] Wang Y. et al.: Coordination of autophagy with other cellular activities. Acta Pharmacol. Sin.; mar 2013

[19] Wilson R.S. et al.: The influence of cognitive decline on well-being in old age. Psycho. Aging; feb 2013

[20] Yang L. et al.: Aging, culture and memory for categorically processed information. J. gerontol. Psychol. Sci. soc. Sci.; feb 3012