Diagnostic and therapeutic challenges in neurodegenerative diseases.

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Nanotechnology will play a key role in developing new diagnostic and therapeutic tools. Nanotechnologies use engineered materials with the smallest functional organization on the nanometre scale in at least one dimension. Some aspects of the material can be manipulated resulting in new functional properties.

Neurodegenerative diseases of the elderly currently represent a major challenge to the health care system. With the increasing longevity of the general population, the predicted figures for the prevalence of these disorders and their global financial impact are truly staggering. For example, it has been estimated that by 2030 as many as 7.7 million people in the US will have Alzheimer's disease, and by 2050 this number will reach approximately 13.5 million, with total annual costs for care rising from $172 billion in 2010 to $1.08 trillion in 2050. This analysis does not take into account the value of unpaid care provided by families and others, estimated to have been $144 billion in 2009. In the UK, the cost of dementia is now estimated to exceed the combined cost of cancer, heart disease and stroke. The prevalence of Parkinson's disease is expected to double by the year 2030, and, given the greater risk of Parkinson's disease dementia in elderly individuals with Parkinson's disease, it is expected that the health care costs for this disorder will increase even more relative to the prevalence of the disease. These concerns highlight the urgent need for the development of effective disease-modifying therapies. Effective treatment would have a major influence on the economic and social burden of these age-related disorders. For example, in the case of Alzheimer's disease, it has been estimated that a delay in onset by 5 years would translate into a 50% decrease in disease prevalence, and a delay of 10 years would result in a virtual disappearance of the disease. Unfortunately, despite considerable investment, to date all attempts at developing such treatments have failed. In summary, there is an urgent need of developing reliable biomarkers of very early phases of the neurodegenerative process and to discover effective therapies directed at the core of the biological process in order to stop disease progression.

Besides this general and urgent need, there are many other key points in the diagnosis and tretatment of neurodegenerative diseases that can be targeted by nanotechnologies. Among them it is worth mentioning:

1.- Early diagnosis:

a) To monitor the rate of cell loss in brain nuclei and alert the defence system and the compensatory mechanisms systems (neurogenesis included) when the rate is exceeding the normal expected decline.
b) To monitor the state of defence and compensatory mechanisms.
c) To create biosensors to monitor neurotransmitter levels in precise locations within the brain which can be reduced long before the appearance of symptoms.
d) To improve image technologies (Fluorophores and quantum dots) which may also facilitate surgical approaches.
e) Systems to detect abnormalities in plasma, thus avoiding the need of invasive tools.

2.- Study of pathogenetic mechanisms. To increase our knowledge about the mechanisms of cell death, thereby opening the doors to new drug targets.

3.- Treatment

- To direct drugs to their target in a very specific way: Smart targeted drug delivery systems. Drugs can act on signalling pathways required for neurotransmission (symptomatic effect) or in signalling pathways involved in neurodegeneration (neuroprotection and neurorescue). (eg. Nanoparticles, drug encapsulation strategies, multifunctional nanotherapeutics, ablation of areas with nanoparticles, DNAbots to identify and destroy pathogenic proteins,...)
- To develop systems able to overcome the blood brain barrier (eg, biobar codes)
- To create biosensors to monitor neurotransmitter levels in precise locations within the brain.

- Intracellular manipulations and interventions: To repair DNA and other damages, cleaning of deposits of aggregated abnormal proteins,…
- To introduce genes and proteins required for normal functioning in a highly controlled way (durable and controlled expression of the gene) avoiding the needs of viral vectors and complex control systems or of infusion pumps (Eg organic silica particles)
- To create bridges between different nuclei affected by the degenerative process and to favour their development by blocking the expression of antireparative signals (no-go, etc)
- Creation of media to push the development of functional specific type of neurons from stem cells.

All these points can be considered as opportunities for nanotechnologies. Indeed, the NEURONANO era is here.