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Review article

Bio-inspired nano tools for neuroscience

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ABSTRACT

Research and treatment in the nervous system is challenged by many physiological barriers posing a major hurdle for neurologists. The CNS is protected by a formidable blood brain barrier (BBB) which limits surgical, therapeutic and diagnostic interventions. The hostile environment created by reactive astrocytes in the CNS along with the limited regeneration capacity of the PNS makes functional recovery after tissue damage difficult and inefficient. Nanomaterials have the unique ability to interface with neural tissue in the nano-scale and are capable of influencing the function of a single neuron. The ability of nanoparticles to transcend the BBB through surface modifications has been exploited in various neuro-imaging techniques and for targeted drug delivery. The tunable topography of nanofibers provides accurate spatio-temporal guidance to regenerating axons. This review is an attempt to comprehend the progress in understanding the obstacles posed by the complex physiology of the nervous system and the innovations in design and fabrication of advanced nanomaterials drawing inspiration from natural phenomenon. We also discuss the development of nanomaterials for use in Neuro-diagnostics, Neuro-therapy and the fabrication of advanced nano-devices for use in opto-electronic and ultrasensitive electrophysiological applications. The energy efficient and parallel computing ability of the human brain has inspired the design of advanced nanotechnology based computational systems. However, extensive use of nanomaterials in neuroscience also raises serious toxicity issues as well as ethical concerns regarding nano implants in the brain. In conclusion we summarize these challenges and provide an insight into the huge potential of nanotechnology platforms in neuroscience.

Contents

Abbreviations: AD, Alzeihmer's disease; ADDL, amyloid derived diffusible ligands; BBB, Blood-Brain-Barrier; BMEC, brain micro-vascular endothelium cell; CNS, central nervous system; CSF, cerebro-spinal fluid; CT, computerised tomography; GFP, green fluorescent protein; HIV, human immunodeficiency virus; IL, interleukin; MRI, magnetic resonance imaging; PD, Parkinson's disease; PEG, poly ethylene glycol; PET, positron emission tomography; PLA, poly-lactic acid; PLGA, poly(lactic-co-glycolic acid); PNS, peripheral nervous system; RGD, arginine glycine-aspartic acid; SPION, super-paramagnetic iron oxide nanoparticles; TEER, trans-endothelial electrical resistance; Tf, transferrin.

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1. Introduction

The attempt to understand the brain and its functions is quite old, starting from the Egyptians who believed the brain to be mere "cranial stuffing" and assumed the heart to be the seat of consciousness and intelligence. This concept was challenged by Greek philosophers like Alcameon of Croton (470B.C.) and Hippocrates (400 B.C) who hypothesized the brain to be the centre of human intellect. The importance of the brain in governing all aspects of human intelligence and sensation has been mentioned in ancient Vedic scriptures (1000B.C.).

Detailed anatomical study of the human brain was first conducted by Greek anatomist Galen and later carried forward and published by Thomas in his book *Cerebri anatome* (1664). His work lead to the beginning of a new branch of medicine called Neurology. Galvani's experiments with the frog (1786), Golgi's staining procedure in the late 1890s and Cajal's study of the neuron are some of the pivotal events that laid the foundation for modern neuroscience. The anatomical location of the brain and spinal cord along with the delicate nature of the nervous tissue has always been a major challenge in exploring the nervous system. Initial indirect routes of measuring brain activity comprised of thermal recordings and estimating cerebral blood flow. The advancement of technology and advent of non-invasive imaging techniques like computerised tomography (CT), positron emission tomography (PET) and magnetic resonance imaging (MRI) has made possible challenging projects like the human brain mapping which was nearly inconceivable a few decades ago.

The quest for exploring the sub-microscopic elements of the nervous system and developing theranostic technologies capable of interacting at the sub-neuronal level (molecular neuroscience) have led to the application of nanotechnology in neurosciences. It is noteworthy that the technology to develop nanomaterials and manipulate material properties in the atomic scale has existed for thousands of years.

Nanoparticle loaded drug delivery dates back to the Charak Samhita (100 BC) that describes unique metallic-mineral formulations called "*Bhasmas*" which have now been reported to be biologically prepared nanoparticles (Chaudhary, 2011; Pal et al., 2014). Carbon nanotubes used for fabrication of neural electrodes were used by Indian craftsmen more than 2000 years ago for making Damascus steel. The swords made from this steel had cementite nanowires encapsulated by carbon nanotubes which lead to its exquisite sharpness and ultralight weight (Reibold et al., 2006).

Materials engineered to the nanometer scale exhibit high surface-to-volume ratio along with unique optical, magnetic, and electrical properties. Nanotechnology is being extensively

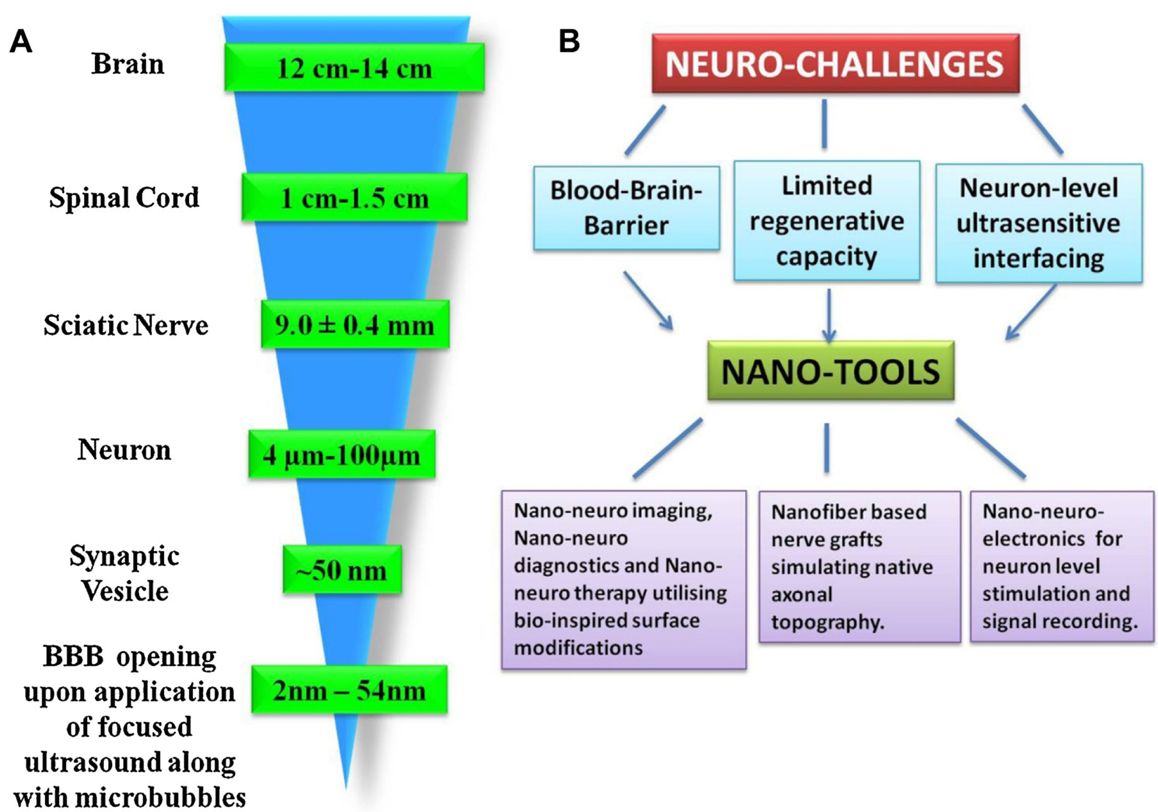

Fig. 1. Nano in Neuro—(A) The figure illustrates the nano-scale with respect to the human nervous system. (B) Brief summary of the significant role played by nanotechnology in addressing neurological challenges.