Using nanoparticles to facilitate penetration of the blood-brain barrier for drug delivery

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Introduction

- The BBB is made up of a number of structures; endothelial cells bound together via tight junctions (TJs), parenchymal cells, astrocyte end-feet, and a basement membrane [1].
- Transport across the BBB can be broken down into two main types: paracellular and transcellular [2].
  - Paracellular: Between cells; mostly small ions/solutes
  - Transcellular: Through cells; hydrophobic molecules (diffusion), proteins/lipophic molecules (receptors)
- These transport mechanisms can be “hacked” by nanoparticles to facilitate delivery of therapeutics or other molecules.

Background

Nanoparticles can either be synthetic or natural: synthetic NPs can either be polymeric (ex/ polyactic acid, polyethenimine, dendrimers, etc.) or inorganic (ex/ gold, silica), while natural NPs are made from natural materials such as polysaccharides, amino acids, and proteins (ex/ albumin, chitosan).

NPs can be modified in a variety of different ways, which is what makes them useful and promising for the future of drug delivery. NPs can be made in specific shapes (rods, spheres, squares, disks, etc.) which can penetrate the BBB in different ways.

One study for example, found that polylystrene gold nanorods coated with anti-body showed a 7-fold increase of accumulation in brain tissue in mouse models when compared to their nanosphere counterparts [6]. Some other things that can be modified include the size, the charge of the NP, the method of drug delivery (ex/ covalent binding, adsorption, entrapment) and the ligands that can be bound to the surface of the NP to help it bypass the BBB.

<table>
<thead>
<tr>
<th>Source</th>
<th>Method</th>
<th>Results</th>
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<tr>
<td>PEGylated polyactic acid NPs</td>
<td>• Modified with a transferrin-like ligand (B6)</td>
<td>• Significant increase in brain accumulation, Decrease in peripheral accumulation</td>
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<td>[7] Poly lactic-co-glycolic acid (PLGA) NPs</td>
<td>• Loaded with dopamine for delivery across the BBB</td>
<td>• Allowed for controlled release and therefore reduced toxicity-related side-effects</td>
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<td>[10] Lactoferrin-modified NPs</td>
<td>• Loaded with a neurotrophic factor gene (hGDNF)</td>
<td>• Significant improvement in the locomotor activity of the PD mice models</td>
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Results

Quinoline-n-butyl-cyanoacrylate-based NPs
• Loaded with l-ICQ: a radiolabel β-amyloid affinity drug
• (Kulkarni et al)
• Significant increase in the penetration of the BBB when bound to the NPs

References


