Nose-to-brain delivery of polymeric nanoparticles

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The difficulties encountered in the treatment of brain diseases with conventional pharmacological tools have created the need for innovative strategies. The combination of nanocarriers and alternative administration routes could represent an efficient approach to reach the brain. Intranasal administration (IN) provides a non-invasive option to deliver drugs to the brain, bypassing the BBB, reducing the first-pass effect and enhancing patient compliance. The objective of the present study was to investigate the biodistribution and bioavailability to the brain of polymeric nanoparticles (PNPs) after IN administration in healthy mice. PNPs were prepared with poly-lactide-co-glycolide polymer using nanoprecipitation method. PNPs had a polymodal distribution around 350 nm. The biodistribution of DiR-loaded PNPs was evaluated by means of 3D fluorescence tomography imaging. Our results show that 3h after a single IN administration, more than 5% of the injected dose was detectable in the brain. PNPs were quickly cleared from the thorax and the abdominal cavity, while the brain fluorescence slowly decreased ranging from 3.7% to 2.3% between 24h and 96h. Repeated IN administrations (2 administrations, 24h apart) provided a significant increment of PNPs-associated fluorescence in the brain, without affecting PNPs accumulation in other organs. These findings support nose-to-brain translocation of PNPs as a noninvasive strategy to enhance the bioavailability of therapeutics to the brain.