Cerebrovascular dysfunctions are a common feature of several neurodegenerative disorders, including Alzheimer's disease (AD). Increasing evidence describes impairment of the brain vasculature as an early event in AD, possibly caused by oxidative stress and responsible for cerebral blood flow reduction and blood-brain barrier (BBB) alterations, that culminate in neurodegeneration. Damage to the vascular endothelium is further induced by β-amyloid (Aβ) peptides, a pathological hallmark of AD, toward the generation of reactive oxygen species (ROS) in endothelial cells. Therefore, oxidative stress has an important role in the pathophysiology and progression of AD. In this scenario, the use of cerium oxide nanoparticles (CNP) as ROS scavenging agents has gained increasing interest. Here we firstly investigated the ability of CNP to hinder ROS production by human cerebral microvascular endothelial cells (hCMEC/D3) exposed to Aβ oligomers. The results showed that treatment with CNP restored basal ROS levels in brain microvascular cells both after acute or prolonged exposure to Aβ. Then, we showed that the uptake of CNP increased after cell incubation with Aβ. To gain insight into this phenomena, cell surface modifications were investigated under Aβ treatment. We demonstrated that vascular pro-oxidant stimuli, i.e. cell exposure to Aβ and hydrogen peroxide, induced microvilli-like protrusions on the surface of endothelial cells, which enhance CNP binding to the cell surface. This allows the possibility to exploit endothelial microvilli formation under oxidative stress conditions to boost the uptake of anti-oxidant nanoparticles at the vascular level as potential therapy for ROS-mediated cerebrovascular dysfunction in brain disorders.