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Qiang Zhou, Drug Des 2016, 5:3(Suppl)
http://dx.doi.org/10.4172/2169-0138.C1.009

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Treating Alzheimer's disease How selective the targets need to be?

Decades of efforts have been devoted to investigate the pathological mechanisms underlying Alzheimer's disease (AD), in search of more effective therapeutic drugs and treatment. In this talk, by reviewing two of our recent works on drug targets in AD mouse models, I will discuss the bigger question of how selective AD targets is desirable. First, I will discuss whether GluN2B-containing NMDA receptors (GluN2B-NMDARs) are a good target, since no systematic study has been performed to evaluate this target in vivo. Acute injection of GluN2B-NMDAR antagonist did not improve the memory deficits in AD transgenic mice but rather impaired memory function in wt mice. Neither short-term (17 days) nor long-term (4 month) administration of these antagonists improved memory functions in AD mice. The above treatment did not rescue the reduction in spine density in AD mice, either given prior to or after the appearance of plaque in the brain. Second, I will discuss the effects of traditional Chinese medicine, xueshuantong (XST) which elevate cerebral blood flow, on AD mice. After systemic injection of XST for 30 days, AD mice showed better performance on rotarod and Morris water maze, suggesting improved motor and spatial learning and memory functions. Reduced density of amyloid plaques were seen in XST-treated AD mice in fixed brain sections, and two-photon time lapse imaging of the same plaques over 15 days revealed size reduction in pre-existing plaques. In addition, synapse density in the immediate vicinity of plaques was higher in XST-treated mice, suggesting enhanced synaptic function. Imaging of cerebral blood flow in the same microvessels demonstrated enhanced blood flow in XST-treated AD mice. Third, I will discuss implications from the above studies, that we need to target early pathological processes, consider targets outside the brain and select carefully the models used to evaluate the efficacy.

Biography

Qiang Zhou is a Professor of Chemical Biology and Biotechnology at Peking University Shenzhen Graduate School. He was trained as an Electrophysiologist and Neuroscientist. His research has evolved from studies in ion channels and receptors, to synaptic transmission and plasticity and further to neural network and behavioral analysis. His expertise also includes fluorescence imaging techniques and molecular biology approaches and he is one of the world's leading experts in combining electrophysiological recording with real time fluorescence imaging. He has worked in both academia and pharmaceutical industry. He is presently focusing on elucidating mechanisms underlying major central nervous system diseases (Alzheimer's disease, depression and schizophrenia) for new therapeutic interventions and prevention.

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