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Study on Diabetes Induced Dementia and the Mechanisms of Synaptic Plasticity in KK-Ay Mice

Diabetes mellitus (DM) may induce dementia, so-called diabetic encephalopathy. In the present study, the spontaneously obesity-induced Type 2 diabetic model, KK-Ay mice were used to study the relationship between spatial learning and memory deficits and the alteration of hippocampal synaptic plasticity.Our results showed that KK-Ay mice presented typical T2DM syndrome and deterioratedprogressivelyin Morris water maze from early stage (3 month old). Meanwhile, Aßdeposition and Tau phosphorylation increased in hippocampus. LTP (long term potentiation) was also impaired significantly. It is interesting that these deficits in KK-Ay mice could be relieved by diet intervention and anti-AD drugs. Further, we found that the underlying mechanisms of LTP impairment in KK-Ay mice might attribute to abnormal phosphorylation or expression of glutamate receptors subunits rather than alteration of basal synaptic transmission. The expression levels of NR1, NR2A and NR2B subunits of NMDA receptors (NMDARs) were unchanged while the Tyr-dependent phosphorylations of NR2A and NR2B subunits were significantly reduced in KK-Ay mice. The p-Src and CaMKII were also down regulated.In addition, AMPA receptor, GluR1 was decreased, and the GluR2 was significantly increased.In summary, ourresults suggest that deficits in learning and plasticity in KK-Ay mice may mainly arise from the abnormalof NR2 subunits, which were related to the activities of p-Src and CaMKII. It might be recovered by diet interventionand anti-AD treatment.

Biography

Wang,Xiaoliang has completed his MD from University of Essen, Germany in 1987. He returned to the Chinese Academy of Medical Sciences, Beijing in 1988 and promoted to full professor in 1993. He served as director of Institute of MateriaMedica, CAMS from 1997 to 2010. His research fields including neurodegenerative diseases, drug discovery and development. He has published 200 papers in reputed journals and has been serving as editorial board membersfor several journals.

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