

## Vascular Dementia 2019: Obesity impairs memory and hippocampal post-synaptic structure in chronic cerebral hypoperfusion in rats : failure of compensatory mechanism?

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Obesity is continuously increasing worldwide, and this trend is considered as obesity pandemic. The reason for focusing on obesity as a major health problem is that it causes various diseases such as metabolic diseases and cardiovascular diseases. As one of them, vascular dementia, was reported to be high prevalence in obese population, which was associated with obesity-related insulin resistance or oxidative stress. Thus, previous studies focused on the obesity as a risk factor, however, there were few researches the effect of obesity on disease progression. To confirm the pathological changes in obese vascular dementia, obesity was induced by high-fat diet(HFD) feeding and then, vascular dementia model was proceeded with biliateral common carotid artery occlusion(BCCAO) procedure in rats. After 6 weeks of the procedure, HFD+BCCAO exhibited worse memory performances in Morris water maze test( $p<.05$ ) and radial arm maze test( $p<.05$ ) than BCCAO. In addition, post-synaptic density-95 in hippocampus were significantly decreased in HFD+BCCAO than BCCAO( $p<.05$ ). We confirmed that obesity aggravated memory impairment with disruption of post-synaptic proteins. On the other hand, brain-derived neurotrophin factor, phospho-extracellular signal-regulated kinase(p-ERK) and phospho-cAMP response element binding protein(p-CREB) was respectively increased in BCCAO(all  $p<.05$ ) more than Sham, but HFD+BCCAO(all  $p<.05$ ) showed lowest expression level. As a result, the decrease of BDNF, ERK and CREB in HFD+BCCAO, which are related to promote protein synthesis in neuronal dendrites, suggests interruption of a compensatory mechanism in BCCAO procedure. It is first finding that obesity exacerbates memory with damaged post-synaptic structure via disrupting BDNF-ERK-CREB compensatory mechanism. It is suggested that obesity should consider as an aggravating factor in vascular dementia and we should keep focusing on

weight control in patient.

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