Cognitive impairment in adiponectin-knockout mice

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Introduction: Alzheimer's disease (AD) is the most common cause of dementia in the elderly. AD is characterised by amyloid-beta (Aβ)–mediated neurotoxicity and neuronal insulin resistance. Adiponectin, an adipokine with insulin-sensitising and anti-inflammatory actions, bears potential as novel therapy for AD. We aimed to study the cognitive function of adiponectin-knockout (APN-KO) mice.

Methods: APN-KO and wild type (WT) mice of 9 and 18 months old had cognitive functions assessed by Morrison water maze test and open field test. Mice were sacrificed with 1 week after cognitive functions tests and forebrain cortex was studied immunohistologically for Aβ (using 2C8 and 7A1a antibodies) and microglial activation (by Iba1 immunoreactivity). Frontal cortex homogenate was analysed for insulin receptor substrate-1 phosphorylated at serine 616 (IRS-1pS^{616}, marker of insulin resistance) by western blot.

Results: APN-KO mice of 9 months old had increased anxiety (shorter distance moved, slower velocity, less time of movement, less time in centre, more time in margin and less exploration; $P < 0.05$) but indifferent in spatial memory compared to WT mice of the same age. APN-KO mice of 18 months old had increased anxiety (shorter distance moved, slower velocity, less time of movement, less time in centre, more time in margin and less exploration; $P < 0.05$) and impaired spatial memory (longer hidden platform latency; $P < 0.01$) compared to WT mice of the same age. Histologically, APN-KO mice had increased immunoreactivity for Aβ ($P < 0.0001$) and Aβ oligomers ($P < 0.0001$) and increased microglial activation ($P < 0.05$) than WT mice. Western blot revealed that frontal cortex homogenate of APN-KO mice had higher level of IRS-1pS^{616} than that of WT mice of the same age ($P < 0.05$).

Conclusion: APN-KO mice of 9 and 18 months old had impaired cognitive functions associated with increased cerebral Aβ deposition and neuronal insulin resistance compared to WT mice of the same age.

The relationship between glucose metabolism, metabolic syndrome, and bone-specific alkaline phosphatase: a structural equation modelling approach

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Introduction: Serum alkaline phosphatase plays a role in vascular calcification. It is found in various tissues, whereas bone-specific alkaline phosphatase (BAP) more specifically reflects mineral metabolism. The relationship of serum alkaline phosphatase (total and bone-specific) with diabetes and metabolic syndrome, which are two major risk factors of vascular calcification, is largely unknown. We aimed to investigate the relationships between glucose metabolism, components of metabolic syndrome (MetS), and alkaline phosphatase.

Methods: Data on 3773 non-diabetic participants of the National Health and Nutrition Examination Survey 1999–2004 were examined. Serum BAP and total alkaline phosphatase were measured as outcomes. Linear regression was used to assess the association of glucose metabolism and metabolic syndrome with serum alkaline phosphatase levels.

Results: In multivariable linear regression, HOMA2-IR ($\beta = 0.068$), HOMA2-B ($\beta = 0.081$), insulin ($\beta = 0.065$), mean arterial pressure ($\beta = 0.15$), and high density lipoprotein (HDL)–cholesterol ($\beta = 0.209$) were positively associated with BAP, whereas HOMA2-IS ($\beta = -0.065$) was negatively associated with BAP. On the other hand, only mean arterial pressure and HDL-cholesterol were significantly associated with total alkaline phosphatase. Moreover, structural equation model revealed that hypertension, low HDL, and insulin resistance had significant direct effects on serum BAP levels, whereas obesity and inflammation might have indirect effects on serum BAP levels. The overall model showed very good fit to the data (comparative fit index = 0.995, root mean square error of approximation = 0.037, and standardised root mean square residual = 0.006).

Conclusion: Glucose metabolism and MetS are significantly related to serum BAP levels. How BAP mediates vascular calcification in diabetes and MetS warrants further studies.