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Effects of intermittent hypoxia on A-/E-FABP expression in human aortic endothelial cells

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Letter to the Editor

Obstructive sleep apnea (OSA) is a prevalent disorder affecting at least 9%–15% middle-aged adults, which is characterized by repetitive cycles of hypoxia followed by reoxygenation termed intermittent hypoxia (IH) [1]. Recently, there is growing epidemiologic and clinical data showing excess of cardiovascular morbidity and mortality in OSA subjects [2]. However, it remains unknown whether OSA contributes directly to atherogenesis or merely serves as a modifier of other effects.

Fatty acid-binding proteins (FABPs) are a group of molecules facilitating lipid transportation within cells. To date, at least nine subtypes have been described [3], each named after the tissue or organ that highly expresses the respective protein. They involved in the functions of transporting lipids, fats, and fatty acids across membranes, modulating metabolic pathways, and facilitating lipid transportation within cells. To date, at least nine subtypes have been described [3], each named after the tissue or organ that highly expresses the respective protein. They involved in the functions of transporting lipids, fats, and fatty acids across membranes, modulating metabolic pathways, and facilitating lipid transportation within cells.
significant difference could only be observed in E-FABP but not A-FABP. While the combination of TNF-α and IH caused a marginally higher elevation of A-/E-FABP mRNA levels compared to IH alone ($p = 0.056$ for A-FABP and $p = 0.055$ for E-FABP respectively), no significances were achieved at their protein levels (Fig. 1A–D).

There is accumulating evidence that OSA is associated with cardiovascular risks, especially atherosclerosis. However, due to high comorbid prevalence of other atherogenic risk factors, such as obesity, aging, hypertension, diabetes, and hyperlipidemia, it remains unclear whether OSA contributes directly to atherogenesis.

Atherosclerosis has been suggested to be an immunoinflammatory disease involving multiple pathways and a plethora of cell types. Endothelial cells and macrophages have been regarded as two active partners involved in the initiation and progression of atherosclerosis. Recently, two isoforms of FABP family, A- and E-FABP, have been detected to play a significant role in atherosclerosis, thereby giving rise to great interests and further exploration. Both circulating A- and E-FABP levels have been found to be independently associated with carotid atherosclerosis in clinical studies [5,6], and combined A- and E-FABP deficiency could provide synergistic protective effect on atherosclerosis in apoE−/− mice [4]. To date, the atheroprotective effect of A-FABP has been demonstrated to be predominantly related to its actions in macrophage [10]. To our knowledge, this is the first study to detect the co-expression of A- and E-FABP in cultured human aortic endothelial cells, which is the critical cellular component in the development of atherosclerosis. We also found that IH could elevate A- and E-FABP expression levels, and the presence of TNF-α might partially potentiate such effect. These data, together with previous clinical results showing elevated serum A-FABP levels in otherwise healthy men with severe OSA [7], imply that FABP may serve as a linkage between OSA and atherosclerosis. Further studies will be necessary to address the initial signaling events which occur in response to IH.

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References


Fig. 1. mRNA and protein expression levels after exposure to intermittent hypoxia (IH) and/or TNF-α in human aortic endothelial cells. IH alone significantly upregulated A-/E-FABP mRNA levels (A–B) as well as protein levels (C–D), TNF-α alone induced a trend of increase, while significant difference could only be observed in E-FABP but not in A-FABP. The combination of TNF-α with IH caused additive effect on elevation of A-/E-FABP mRNA levels with borderline significance (A–B), while no significant difference was observed in protein levels although there was a trend of further increase (C–D). Data were expressed as means ± SEM from at least 4 independent experiments in duplicate. *$p<0.05$ vs. control; **$p<0.01$ vs. control; ***$p<0.001$ vs. control; #0.05 $p<0.06$ vs. IH.


