Supplementation with tetrahydrobiopterin suppresses the development of hypertension in spontaneously hypertensive rats

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摘要

Abstract

It has been suggested that tetrahydrobiopterin (H4B), a cofactor of NO synthase, can reverse endothelial dysfunction caused by cardiovascular diseases, including atherosclerosis, coronary artery disease, and hypertension. Moreover, an impairment of H4B biosynthesis in spontaneously hypertensive rats (SHR) was observed. Thus, we hypothesized that the defect of the H4B synthesis system may play an important role in the development of hypertension in SHR. In the present study H4B (10 mg/kg per day IP) was used to treat SHR and Wistar-Kyoto rats (WKY) from the age of 5 through 16 weeks. Results demonstrated that chronic treatment with H4B significantly improved the impaired vascular responses to acetylcholine and suppressed the development of hypertension in SHR but did not affect WKY. The increase of inducible NO synthase expression, nitrotyrosine immunostaining, NO production, and superoxide anion formation in adult SHR were also significantly suppressed by chronic treatment with H4B. In contrast, H4B had no effect on WKY. In conclusion, this study demonstrated that H4B significantly attenuated the development of hypertension in SHR. The antihypertensive effect of H4B might be mediated through its direct antioxidant activity and/or decreasing oxygen free radical production from NO synthase, thereby reducing inducible NO synthase expression and peroxynitrite formation. Thus, the present study proposed that supplementation with H4B might be beneficial in preventing pathological conditions such as essential hypertension