

Cardiac over-expression of microRNA-1 induces impairment of cognition in mice

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Large cohort studies have revealed a close relationship between cognitive impairment and cardiovascular diseases, although the mechanism underlying this relationship remains incompletely understood. In this study, using a transgenic (Tg) mouse model of cardiac-specific over-expression of microRNA-1-2 (miR-1-2), we observed that microRNA-1 (miR-1) levels were increased not only in the heart but also in the hippocampus and blood, whereas its levels did not change in the skeletal muscle of Tg mice compared with age-matched wild type (WT) mice. Six-month-old Tg mice showed cognitive impairment compared with age-matched WT mice, as assessed using the Morris Water Maze test. The brain-derived neurotrophic factor (BDNF) level and cyclic AMP-responsive element-binding protein (CREB) phosphorylation were also significantly reduced in the hippocampi of the Tg mice, as evaluated by western blot. Further examination showed that BDNF proteins expression was down- or up-regulated by miR-1 over-expression or inhibition, respectively, and was unchanged by binding site mutations or miRNA-masks for the 3'UTR of *Bdnf*, indicating that this gene is a potential target of miR-1. Knockdown of miR-1 by hippocampal stereotaxic injection of an anti-miR-1 oligonucleotide fragment carried by a lentivirus vector (lenti-pre-AMO-miR-1) led to up-regulation of BDNF expression and prevented the reduction in cognitive performance in the Tg mice without affecting cardiac function. Our findings demonstrate that cardiac over-expression of miR-1 also induces behavioral abnormalities that may be associated, at least in part, with the down-regulation of BDNF expression in the hippocampus. This study definitely contributes to the understanding of the relationship between cardiovascular disease and cognitive impairment.

Biography

Jing Ai has completed her PhD from Department of Pharmacology, Harbin Medical University and Post-doctoral studies from College of Bioinformatics Science and Technology and Bio-pharmaceutical Key Laboratory of Heilongjiang Province, Harbin Medical University. She has published more than 40 papers in reputed journals and has been serving as an Editorial Board Member of PLoS One.

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