A novel mutation in SCN1B associated with Brugada Syndrome

Wang Linlin

Introduction: Brugada syndrome (BrS) is a highly arrhythmogenic cardiac disorder characterized by ventricular fibrillation. Here, we identified and characterized a novel SCN1B mutation, A197V, associated with BrS. We aimed to identify and characterize a novel SCN1B mutation, A197V, associated with BrS.

Methods: Whole-exome sequencing was employed to explore the potential causative genes in 8 unrelated clinically diagnosed BrS patients. A novel A197V variant was detected in exon 4 of SCN1B in a 46-year-old patient, who was admitted due to syncope. Wild type (WT) and mutant (A197V) genes were co-expressed with SCN5A in human embryonic kidney cells (HEK293 cells) and studied using whole-cell patch clamp and immunodetection techniques.

Result: Coexpression of 5A/WT+1B/A197V resulted in a marked decrease in current density compared to 5A/WT+1B/WT. The activation velocity was decelerated by A197V mutation. No significant changes were observed in recovery from inactivation parameters. Cell surface protein analyses confirmed that Nav1.5 channel membrane distribution was affected by A197V mutation.

Conclusion: The current study is the first to report mutation in SCN1B/ A197V, serving as a substrate responsible for BrS.