**The reversal of atrial fibrillation after depression via the chronic stimulation of sigma-1 receptor and the associated roles of myocardial inflammation and gap junctions**

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**Introduction**: Sigma-1 receptor, known as a putative chaperone protein, regulates ion channels as well as ER stress response and plays a protective role in cardiogenic disease. The present study assessed whether sigma-1 receptor (S1R) stimulation could alleviate atrial fibrillation (AF) after depression by regulating myocardial inflammation and gap junctions.

**Methods**: One hundred male rats were randomly divided into four treatment groups for four weeks: saline [control (CTL)], saline + intragastric administration of SA4503 agonist of the S1R, [control + SA4503 (CTS)], chronic unpredictable mild stress (CUMS) to produce major depression disorder (MDD), and CUMS + intragastric administration of SA4503 [MDD + SA4503 (MDS)]. After four weeks, depression-like behaviors including sucrose preference, body weight, and immobility time were measured to evaluate the success of model preparation. Microelectrode array (MEA) technology was used for extracellular electrophysiological recordings.

**Result**: The results showed that the total activation time (TAT) significantly increased and the excitation propagation was markedly disordered in the MDD group compared to the CTL group ($P < 0.01$ for both groups). The rats in the MDD group also displayed a higher frequency of AF incidence, heavier fibrosis, greater expression of inflammatory factors (TGF-$\alpha$ and IL-6), and lower expression of gap junction proteins (CX40 and CX43) compared to those in the CTL group ($P < 0.01$ for all groups). Furthermore, chronic S1R stimulation partially alleviated the above indices in the MDS group ($P < 0.01$ for all groups).

**Conclusion**: The results indicates that myocardial inflammation and gap junctions may be key contributors to AF after depression. By increasing atrial conduction velocity, recovering excitation propagation disorder, and reducing myocardial inflammation, S1R stimulation has the potential for treatment of AF.