Novel Concepts for Neurology and Medicine from the Interaction between Signalling Pathways Mediated by Ca^{2+} and cAMP: An Intriguing History

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attributed to adjust reflex of arterial pressure, but this conclusion remained not completely satisfactory. The year of 2013 would change this history forever! Through a creative experiment, we revealed that the solution for this so-called "calcium paradox" phenomenon was due to the increase of transmitter release from sympathetic neurons achieved by CCBs due to its handling on the interaction between Ca^{2+} and cAMP signalling pathways [9]. We demonstrated that contractions of the smooth muscle (vas deferens) were completely inhibited by L-type CCBs in high concentrations (>1 µmol/L), but puzzlingly increased in concentrations below 1 µmol/L, thus defined as sympathetic hyperactivity promoted by CCBs [4-6,9]. Our studies clearly established that the contradictory sympathetic hyperactivity is due to an augmentation of transmitter release from sympathetic neurons achieved by L-type CCBs due to its interfering on the interaction between Ca^{2+} and cAMP signalling pathways.

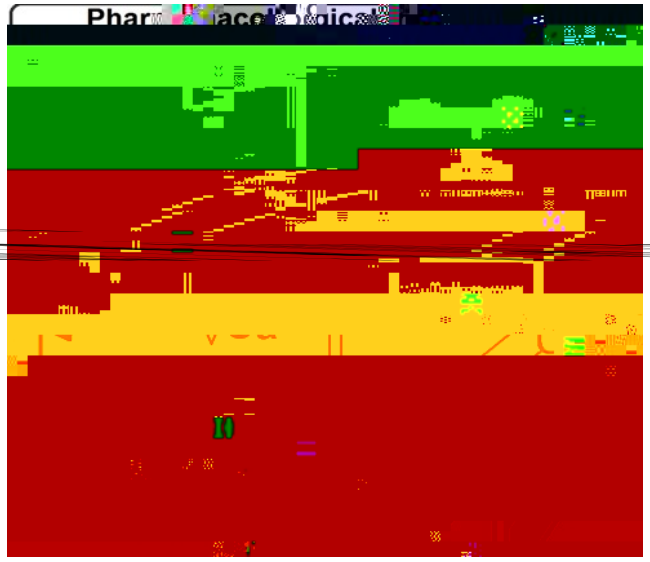

Figure 1: Transmitter release stimulation and reduction of neuronal death triggered by Ca^{2+} overload can be achieved due to pharmacological regulation of the interaction between Ca^{2+} and cAMP signalling pathways. In response to the decreasing of Ca^{2+} influx through L-type voltage-activated Ca^{2+} channels produced by CCBs, the adenylyl cyclase activity (and consequently cAMP) is increased. These CCBs-effects can be stimulated by cAMP-enhancer compounds (like PDEs inhibitors). PDEs: Phosphodiesterases, RyR: Ryanodine receptors, IP3R: IP3 receptors, SERCA: Sarcoendoplasmic reticulum Ca

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