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Guanfacine normalizes the overexpression of presynaptic α-2A adrenoceptor signaling and ameliorates neuropathic pain in a chronic animal model of type 1 diabetes.

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Background: Diabetes is associated with several complications, including neuropathic pain, which is difficult to manage with currently available drugs. Descending noradrenergic neurons possess antinociceptive activity; however, their involvement in diabetic neuropathic pain remains to be explored.

Methods: To infer the regulatory role of this system, we examined as a function of diabetes, the expression and localization of alpha-2A adrenoceptors (α2-AR) in the dorsal root ganglia and key regions of the central nervous system, including pons and lumbar segment of the spinal cord using qRT-PCR, Western blotting, and immunofluorescence-based techniques.

Results: The data revealed that presynaptic synaptosomal-associated protein-25 labeled α2-AR in the central and peripheral nervous system of streptozotocin diabetic rats was upregulated both at the mRNA and protein levels. Interestingly, the levels of postsynaptic density protein-95 labeled postsynaptic neuronal α2-AR remained unaltered as a function of diabetes. These biochemical abnormalities in the noradrenergic system of diabetic animals were associated with increased pain sensitivity as typified by the presence of thermal hyperalgesia and cold/mechanical allodynia. The pain-related behaviors were assessed using Hargreaves apparatus, cold-plate and dynamic plantar aesthesiometer. Chronically administered guanfacine, a selective α2-AR agonist, to diabetic animals downregulated the upregulation of neuronal presynaptic α2-AR and ameliorated the hyperalgesia and the cold/mechanical allodynia in these animals.

Conclusion: Together, these findings demonstrate that guanfacine may function as a potent analgesic and highlight α2-AR, a key component of the descending neuronal autoinhibitory pathway, as a potential therapeutic target in the treatment of diabetic neuropathic pain.

Biography

Ms Neha Munawar is presently pursuing PhD in Pharmacology and Toxicology on Excellence scholarship under the supervision of Prof. Milad Bitar and Prof. Willias Masocha in the Faculty of Medicine at Kuwait University. She completed her Bachelor's degree in Pharmacy and Master's degree in Pharmacology and Toxicology from Kuwait University. She has been awarded by Her Heighness Sheikha Dana Nasser Sabah Al-Ahmed Al-Sabah for her outstanding performance in Bachelor's in Pharmacy program. She has research expertise in neuropharmacology, especially neuropathic pain.