Nicotine-derived compounds as therapeutic tools against post-traumatic stress disorder

Barreto G.E.

Yarkov A.

Ávila-Rodriguez M.

Aliev G.

Echeverria V.

Post-traumatic stress disorder (PTSD) is an anxiety disorder that develops after experiencing trauma. Actual therapies do not help majority of patients with PTSD. Moreover, extinguished fear memories usually reappear in the individuals when exposed to trauma cues. New drugs to reduce the impact of conditioned cues in eliciting abnormal fear responses are urgently required. Cotinine, the main metabolite of nicotine, decreased anxiety and depressive-like behavior, and enhanced fear extinction in mouse models of PTSD. Cotinine, considered a positive modulator of the ?7 nicotinic acetylcholine receptor (?7nAChR), enhances fear extinction in rodents in a manner dependent on the activity of the nAChRs. Cotinine stimulates signaling pathways downstream of ?7nAChR including the protein kinase B (Akt)/glycogen synthase kinase 3? (GSK3?) pathway and the extracellular signal-regulated kinases (ERKs). The stimulation of these factors promotes synaptic plasticity and the extinction of fear. In this review, we discuss the hypothesis that cotinine relieves PTSD symptoms and facilitates fear memory extinction by promoting brain plasticity through the positive modulation of presynaptic nAChRs and its effectors in the brain.

Anxiety

Depressive-like behavior

Fear extinction

Tobacco

Trauma

cotinine

nicotine derivative

cotinine

nicotine

anxiety

Article

depression

fear

human

nerve cell plasticity

nonhuman

posttraumatic stress disorder

priority journal

smoking

tobacco

analogs and derivatives

animal

brain

drug development

drug effects

metabolism

pathophysiology

procedures

psychology

reinforcement

Stress Disorders, Post-Traumatic

Animals

Brain

Cotinine

Drug Discovery

Extinction, Psychological

Fear

Humans

Nicotine

Smoking

Stress Disorders, Post-Traumatic