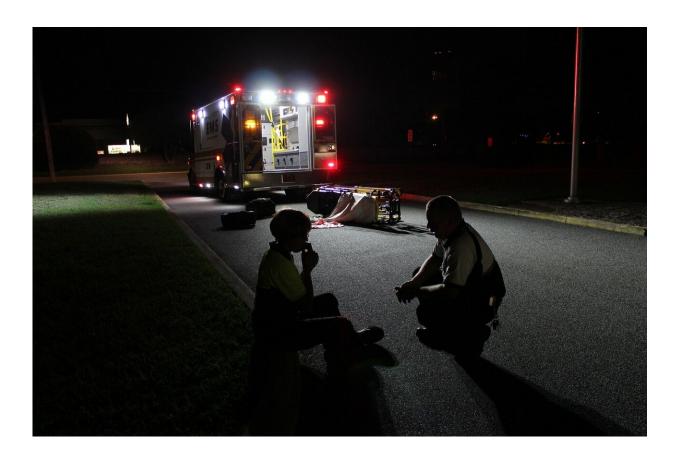


New anticholinergic drug keeps PTSD flashbacks and nightmares away

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Post-traumatic stress disorder (PTSD) is prevalent in today's society. Medical researchers have been seeking solutions to combat this condition and its manifestations. Unfortunately, the neurological



mechanisms of PTSD aren't clear.

A group of Japanese researchers from the Sogo PTSD Institute, Medical Corporation Sogokai, Japan, led by Dr. Masanobu Sogo, appear to have made a breakthrough in PTSD treatment. They have identified a drug called trihexyphenidyl that can significantly reduce the flashbacks and nightmares experienced by patients with PTSD, according to a study published in *Brain and Behavior*.

Trihexyphenidyl is a central anticholinergic drug used to manage disorders like Parkinsonism and alleviate several <u>side-effects</u> induced by drugs acting on the central nervous system (CNS). It acts by blocking the activity of a neurotransmitter, acetylcholine, in the CNS. Interestingly, it has been available for therapeutic use for around 66 years.

In 2009, the researchers encountered a patient who had suffered severe PTSD-related flashbacks and nightmares for nine years, was diagnosed with bacterial diarrhea at another hospital, and administered a drip infusion containing antibiotics and scopolamine butyl bromide (SB), which is a peripheral anticholinergic that doesn't cross the blood-brain barrier (BBB, penetration rate 0.01%). Twenty minutes after the infusion, the patient's flashbacks completely disappeared.

Since SB is a "peripheral" anticholinergic agent, it shouldn't be able to cross the BBB, but it is probable that the patient's brain was in a state of severe excitement due to PTSD. There are eight acetylcholine basalganglia in the brain, of which the largest, the Meynert nucleus, is closely associated with BBB permeability. The researchers hypothesized that due to abnormal excitement of the Meynert basal ganglia, SB enters the brain and activates anticholinergic action to suppress abnormal acetylcholine secretion of acetylcholine-memory-related circuits centered on the Meynert basal ganglia, eliminating the flashbacks.



From this <u>clinical experience</u>, they hypothesized that PTSD is generated through an acetylcholine-memory-related-circuit centered on Meynert. Based on this, Dr. Sogo and his team considered the use of a central anticholinergic agent: trihexyphenidyl.

The researchers went on to devise an exploratory study to determine whether trihexyphenidyl was effective against similar symptoms in other patients with PTSD. They administered trihexyphenidyl in 34 patients with PTSD who had previously received psychiatric treatment for several years without therapeutic benefits, and determined its effect through interviews.

A significant 88% of the analyzed patients reported mild to no PTSD-related nightmares. Similarly, 79% of the analyzed patients reported similar responses for PTSD-related flashbacks. Notably, the researchers found that trihexyphenidyl has efficacy and a rapid onset (one to two days) in the treatment of PTSD-related nightmares and flashbacks.

Dr. Sogo says, "To the best of our knowledge, this is the first pharmacological report describing the novel use of trihexyphenidyl for PTSD-related nightmares, which doesn't respond to conventional psychiatric treatment." Further studies are needed to prove the mechanism of PTSD; repurposing trihexyphenidyl to treat PTSD would be a promising turn of events, since the drug is inexpensive, and has no adverse effects.

More information: Katsumasa Sogo et al, Centrally acting anticholinergic drug trihexyphenidyl is highly effective in reducing nightmares associated with post-traumatic stress disorder, *Brain and Behavior* (2021). DOI: 10.1002/brb3.2147



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