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A psychedelic drug, combined with intense therapy, improves PTSD symptoms

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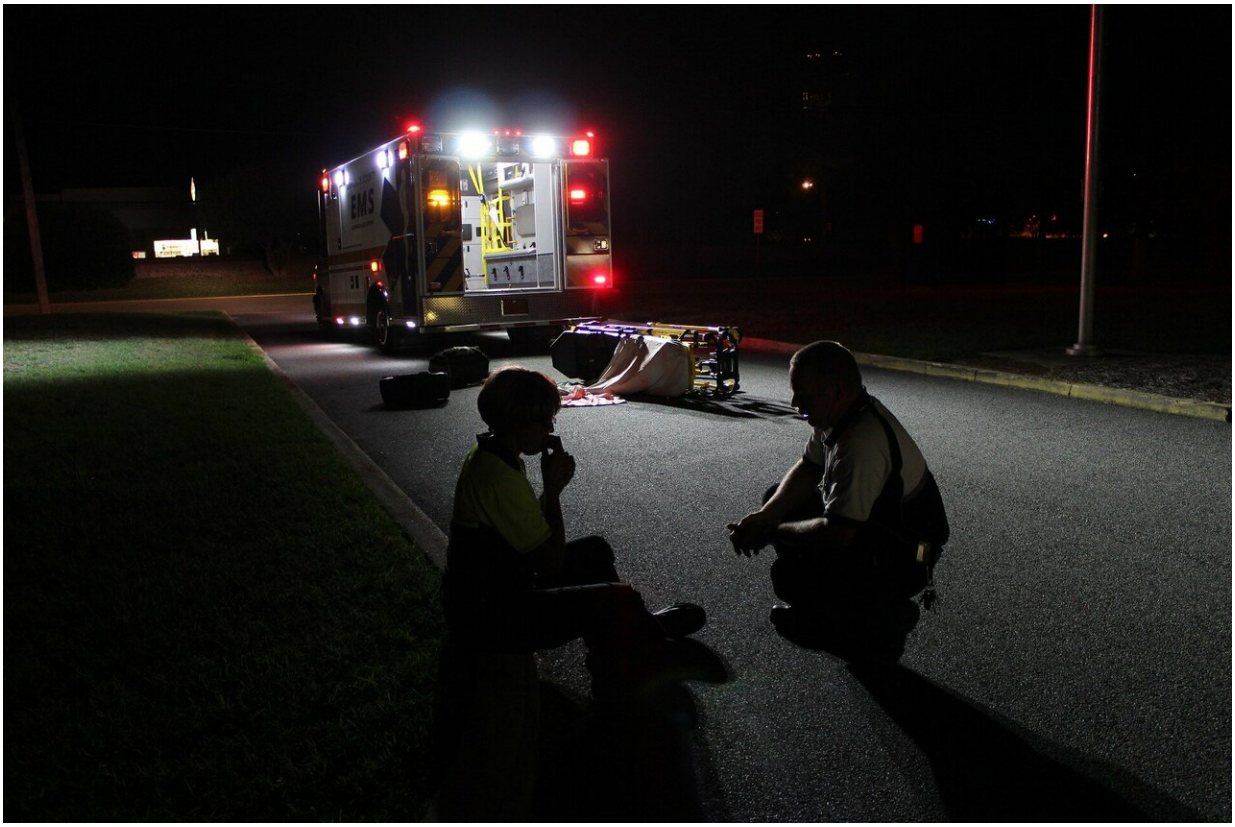

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Post-traumatic stress disorder (PTSD) affects millions of people each year, mostly survivors and witnesses of terrifying or shocking events, such as warfare, assaults or disasters. Because existing treatments don't

work for everyone, new therapies are urgently needed. Today, scientists report results and follow-up data from a phase 3 clinical trial of a psychedelic drug, 3,4-methylenedioxymethamphetamine (MDMA), known on the street as "ecstasy" or "molly," combined with psychotherapy for the treatment of PTSD. Their preliminary data suggest that the therapy works even in hard-to-treat patients, such as those with drug or alcohol use disorders.

The researchers will present their results today at the spring meeting of the American Chemical Society (ACS).

Recently, there's been a surge in interest and research on the use of psychedelic drugs, such as mescaline, psilocin and MDMA, for the treatment of psychiatric disorders. However, the idea that such compounds could enhance psychotherapy isn't new, says Jennifer Mitchell, Ph.D., the project's principal investigator, who is presenting the work at the meeting. Beginning in the 1970s, some psychiatrists used MDMA to enhance psychotherapy, despite a lack of formal clinical trials or U.S. Food and Drug Administration (FDA) approval.

"MDMA is really interesting because it's an empathogen," says Mitchell, who is at the University of California, San Francisco. "It causes the release of oxytocin in the brain, which creates feelings of trust and closeness that can really help in a therapeutic setting." In addition, animal studies indicate that MDMA can help "reconsolidate," or process, fear memories in an area of the brain called the amygdala. Notwithstanding the drug's small following in the psychiatric community, its rise in popularity as a street drug—followed by reports of overdoses and deaths—prompted the FDA to make MDMA illegal in the U.S. in 1985.

Mitchell and colleagues wondered if MDMA could increase the effectiveness of psychotherapy for the treatment of PTSD, a debilitating

condition characterized by amnesia, flashbacks and nightmares related to a traumatic event. People with PTSD have higher risks of depression, anxiety, substance use disorders and suicide. Selective serotonin reuptake inhibitors (SSRIs), the first-line therapeutics for the disorder, are effective in only about half of patients, Mitchell says. And many people with PTSD either fail to respond or quit going to psychotherapy sessions.

So, the team enrolled 90 people with severe PTSD in the first phase 3, randomized, double-blind, placebo-controlled study of MDMA-assisted therapy for treatment of this disorder. In prior phase 2 studies, researchers had determined the optimal oral dosage of MDMA, which consisted of a full dose, followed by a half dose an hour later. In the phase 3 trial, the participants attended an 8-hour therapy session after the half dose. This process was repeated twice, a month apart each time, in addition to weekly therapy.

Two months after the final session, about two thirds of people who received MDMA-assisted therapy no longer met the diagnostic criteria for PTSD, compared with one third of those who received placebo plus therapy. Side effects of MDMA, such as jaw clenching and nausea, were minimal, and there were no signs of addiction. "The effect size for MDMA-assisted therapy is better than that for the SSRIs that have been investigated, suggesting that MDMA is a far better therapeutic for PTSD," Mitchell says.

The team is currently enrolling participants for a second phase 3 trial, and if all goes well, they anticipate that MDMA-assisted therapy for PTSD could be approved by the FDA as early as 2023. The researchers also recently completed a study on whether MDMA-assisted therapy is equally effective in certain subgroups that are resistant to traditional PTSD treatment, such as those with drug or alcohol use disorders. "It definitely appears to be equally effective in people who are usually

considered treatment resistant, so we're very excited to think that MDMA-assisted therapy is going to be an effective therapeutic in that hard-to-reach population," Mitchell says.

To find out how long the treatment might last, the researchers are now analyzing long-term data from the phase 3 trial. "People in the phase 2 trial were better for years," Mitchell says. "They seemed to have a new perspective on life and engaged more. As their social skill set built up, they were happier over time." However, she notes that the people in the phase 3 trial had more severe PTSD symptoms, so their treatment might not be as durable.

Despite these promising results, Mitchell stresses that people with PTSD should not try to self-medicate with MDMA. "If MDMA is decriminalized, that doesn't mean it's safe," she says. "It can be a very powerful tool, but it needs to have the right dose in the right context with the right support system."

More information: Durable improvements in PTSD following MDMA-assisted therapy, ACS Spring 2022. acs.digitellinc.com/acs/live/22/page/677

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