On My Mind: Ketamine, psychedelics, and new frontiers in psychiatry.

A patient of mine lay on a gurney attached to heart, blood pressure, and oxygen monitors in the recovery room, or post-anesthesia care unit (PACU). He had suffered from severe depression that had been unresponsive to standard medication treatments for years. That day he had a smile on his face. His eyes were closed, and he was watching a magnificent display of colors. After months of unremitting sadness, he was feeling joy. "I can't believe that this is happening," he said. He was experiencing the effects of a low-dose infusion of ketamine, a psychedelic that heretofore has been used primarily as an anesthetic.

An intranasal formula of ketamine was recently approved for treatment of refractory depression, which is depression that has not responded to other, more commonly used treatments. Ketamine is the only legal psychedelic medication, and it is available in multiple formulations, including injection, intravenous drip, pill, a form that dissolves under the tongue, and even a salve. The medication itself has been around for decades. It is inexpensive and remarkably safe. The dose used in psychiatry is a fraction of the dose used in children and adults for pain relief and anesthesia.

There are now many clinics around the country where ketamine in its various forms is administered for depression, substance use disorders, anxiety disorders, PTSD, and existential angst. Psychedelics are being studied extensively, and appear to be a new frontier of psychopharmacology. There is an expectation that MDMA (ecstasy) and psilocybin (found in certain mushrooms), among others, will be FDA-approved in coming years. These medications appear to help people shift to new lenses on reality that leave them less preoccupied with neurotic concerns or overwhelming worries about things that are beyond their control. Psilocybin is being studied extensively for the relief from the emotional pain of terminal illness. Part-time Vineyarder Michael Pollan, author of the landmark book on psychedelics "How to Change Your Mind," describes a woman with terminal cancer who experienced paralyzing fear in the setting of ovarian cancer. She had never experienced psychedelics before. He reports, "She had an

experience with psilocybin that allowed her to enter her body imaginatively, and she saw this black mass under her rib cage, and she realized that was not her cancer. It was her fear. And she beheld this black mass, and she screamed at it. She said, Get the [expletive] out of my body. And it vanished." He later wrote that her fear had been markedly diminished, but months later, when a fact checker called the woman, she corrected him. Michael Pollan had misunderstood: Not reduced, she said; the anxiety was completely gone.

How amazing it would be if ketamine and other psychedelics not only reduced depression but actually eliminated it. So far, I have only seen people who have had diminished symptoms and who require repeated exposure to ketamine over time in order to maintain its benefits. Nonetheless, for some people it dramatically decreases psychic pain. And many clinicians do report full remissions. For people who are acutely suicidal, it can very quickly squelch the urge to end one's own life.

Most ketamine clinics administer ketamine in a serene environment, with people wearing eyeshades and listening to music. The experience, thought to be the result of the pharmacologic effect on certain glutamate receptors, results in relief of severe depression in 40 to 60 percent of patients. That is consistent with my experience with the people with whom I have tried this treatment. I have also found that it is much more effective if I am there offering a supportive presence, particularly during the early and later phases of the experience.

There seem to be two schools of thought around the efficacy of ketamine. One is that it is a medication that in itself is effective for treatment of depression. The context in which it is received, and whether or not the psychedelic or dissociative effects of ketamine are experienced, are not as important as the simple pharmacologic effect of the medication. Others insist that it is specifically the way that ketamine shifts the lens on reality, along with psychotherapy that is engaged in during the experience, that is transformative.

I have come to believe, particularly for my patients with whom I have long-term, deep relationships, that it is important for me, or another psychotherapist, to accompany them through this profound experience. There is an opportunity for a guide, a safe companion or psychotherapist, to enhance the experience and the results. Under the influence of ketamine, people easily experience parts of themselves as separate entities; a joyous playful child, a critical judge or teacher, or a voice that says that that they are failing at the psychedelic experience might appear. Engaging with these subpersonalities with the help of a trained therapist

can be useful. (See http://bit.ly/MVTMoreThanOne.) While there is a part of the journey that is usually apart from the therapist, explorations of goals before the experience and the processing of discoveries after the experience can, as Michael Pollan writes, "foster new perspectives on old problems."

A guru of the ketamine-assisted psychotherapy movement is Philip Wolfson, a psychiatrist who has been studying psychedelic medication for decades, and edited "The Ketamine Papers: Science, Therapy and Transformation." Inspired by a colleague who has also been using ketamine in his practice, I took a course led by Dr. Wolfson on ketamine-assisted psychotherapy. It was filled with essential information about the scientific background and medical use of ketamine.

After an exploration of the issues in a patient's life, setting goals, and engaging in an invocation, Dr. Wolfson generally starts by administering a quickly dissolving tablet left under the tongue for 10 to 15 minutes. If there is minimal or no response, the dose may be repeated. For the next hour or more, he plays enchanting and gentle meditation music that helps transport the recipient to what feels like another universe. Usually with a face mask to help distance this world, often with eyes open, there can be an experience of bright colors and glorious geometric patterns. Music might be experienced as light, or it might be experienced as very intense sound. Or the experience might be altogether different. For instance, some people have no visual experience. The sense of one's place in time and space usually changes, or is even lost. For almost all of the recipients whom I have seen, there is an immediate relief from the depression, dread, and anxiety that has crippled them for months or sometimes years. One person told me that it was the first time in her life that she had experienced the absence of anxiety. Another reported that it was the first time that there was complete comfort in being alone. There can be a sense of losing all connection to one's body. Many people experience an enormous feeling of love, often encompassing all of humanity and other life forms. Some people talk about losing their ego and sense of self, and only existing as pure energy. For many people there is a healing sense of feeling one with God, the universe, or the family of all living creatures.

For most people the experience is largely liberating and joyous. However, others may encounter dreadful fear, memories of traumas and lost loved ones, or a feeling of being dead. Some people feel that they are communing with ancestors, God, or demons.

Psychotherapy before and after the session can be transformative. The medication can help unveil sensations, good and bad, that are windows into one's soul and psyche. Even people who experience dread and loss usually feel that windows for growth and learning have been opened. Feeling that there is a safe, supportive person close by can be enormously comforting. For most people, the results of the experience can evolve over the course of days, weeks or even a lifetime. There is a wonderful "60 Minutes" piece that describes this: bit.ly/KetamineExperience.

The power of psychedelic medication such as ketamine is remarkable. However, I have also seen how dangerous psychedelics can be for people, particularly adolescents who use it recreationally in anxiety-provoking situations with unknown doses or content. It is often said that psychedelics can be used for three purposes: recreation, therapeutics, or spiritual awakening. In some ways they are all valid, but at best, purely recreational use is a lost opportunity, and at worst it can be terrifying. Perhaps all medications can have both good and adverse effects.

Nonetheless, when properly used, psychedelics seem to help rewire the brain. New connections are made that are absent in normal consciousness. I have previously written about areas of the brain coined the "default mode network." (See http://bit.ly/DefaultMode.) To a lesser or greater degree, in the absence of a purposeful task, we all fall into a default mode of worry, self-doubt, and angst about the past and the future. According to multiple research studies, psychedelic medications decrease activity in this area of the brain, often on a long-term basis. And for many or even most people, there is a complete turning off of these brain functions during the acute experience.

In studies of severe depression that has been unresponsive to usual treatment, ketamine is started with six treatments over two or three weeks. However, many people need boosters periodically afterward. While there is no doubt that ketamine can quickly change the brain and relieve depression, the big question is: How long does this effect last, and how can it be prolonged? Perhaps the new perspective on reality that ketamine offers is like learning a new language. For the woman that Michael Pollen described whose fear of dying disappeared after a single experience with psilocybin, the new perspective was instant and lasting. But perhaps for others who have long-term psychiatric symptoms, the language is only learned in a lasting way with repeated exposures over time and with the help of a psychotherapist or guide. What is clear is that there is a lot to be learned about the use of psychedelics to treat psychiatric symptoms. Nonetheless, it is an

exciting and hopeful time to be a mental health professional or patient as we embark on pathways into this new frontier.

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