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Michael Lyvers
Bond University, michael_lyvers@bond.edu.au

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The Neurochemistry of Psychedelic Experiences

Psychedelics constitute a class of psychoactive drugs with unique effects on consciousness. Psychedelic means "mind-manifesting" and refers to the ability of these drugs to illuminate normally hidden aspects of mind or psyche. Native American shamans consumed psychedelic plants such as the peyote cactus (contains mescaline), psilocybe "magic" mushrooms (contains psilocybin), or the brew called ayahuasca (contains DMT and harmaline) in order to communicate with God or the spirit realm.

The most potent psychedelic is the semi-synthetic ergot derivative lysergic acid diethylamide (LSD), which has detectable effects at microscopic doses. This drug's powerful psychedelic effect was discovered by the Swiss chemist Albert Hoffman in 1943. While handling vials containing the chemical, he accidentally absorbed some of it through his skin, and later experienced a strange state of consciousness. Suspecting that LSD was the cause, Hoffman decided to test the drug on himself, starting with what he thought would be a small and probably ineffective dose - only ¼ of a milligram. However, for LSD this isa rather large dose. Hoffman's ensuing "trip" was overwhelmingly intense and he assumed he was either dying or going insane (Hoffman, 1981). Hoffman recovered and a period of scientific research on LSD began.

Researchers first thought LSD induced a "model psychosis" that might shed light on the nature of schizophrenia. However, as the psychedelic experience or "trip" does not resemble endogenous psychoses, this interpretation was later discarded. In the 1950s the therapeutic potential of LSD was investigated under the assumption that LSD was a key that could unlock the secrets of the unconscious mind. Thousands of people in the U.S., including the actor Cary Grant, underwent "psycholytic" ("mind-loosening") therapy under LSD during the 1950s and early 1960s (Grinspoon & Bakalar, 1979). Other work investigated the religious aspect of high-dose psychedelic experiences. In a 1961 experiment known as the "Miracle of Marsh Chapel," Boston Divinity Students were given psilocybin or placebo in a double-blind design; most subjects in the psilocybin group (and none in the placebo group) reported profound religious experiences with lasting beneficial consequences (Doblin, 1991). Scientific and clinical work with psychedelics was interrupted when the drugs were outlawed in the U.S. in 1965 as a response to their growing non-medical use, but in recent years, renewed scientific interest in consciousness has led to a small revival of psychedelic drug research.

Unlike most drugs, psychedelics do not produce reliable, consistent effects across users, or even in the same user at different times. The most positive accounts describe mystical revelations such as gaining direct knowledge of God or an all- encompassing cosmic unity. More commonly reported is a kaleidoscopic display of intensely colorful visions, ranging from continuously unfolding abstract designs to fully formed images of animals, plants, landscapes or more bizarre scenes. However, taking a psychedelic also entails the risk that the user may spiral down into the black hole of a "bad trip," an overwhelming state of terror and psychic anguish that can be followed by lasting PTSD-type symptoms such as flashbacks. "Bad trips" are the main hazard of psychedelic drug use, as the possibility of a lethal overdose is vanishingly small.

Psychedelic drugs are not addictive. Even enthusiastic proponents of psychedelics take them infrequently due to the intensity of the "trip." Animal research indicates that *Homo sapiens* is the only species that will voluntarily take a psychedelic drug again after having experienced the effects. Although laboratory animals such as rats or monkeys will readily self-admininister

most other drugs abused by humans, including cocaine, heroin, amphetamine, nicotine and alcohol, they find psychedelic drugs highly aversive (Yokel, 1987).

The question of how these agents produce their striking alterations of consciousness has long fascinated brain researchers. The first clue was that LSD, psilocybin, DMT, and many other psychedelics bear a close structural similarity to the neurotransmitter serotonin. Research in the 1970s showed that LSD temporarily suppresses the firing of serotonin-releasing neurons of the raphe nuclei (Rechs & Rosecrans, 1982), a part of the brainstem reticular activating system. These neurons send axons into widespread regions of the cerebral cortex and limbic system, where they release serotonin when active. Because the raphe nuclei also go silent during REM sleep, the notion that the psychedelic state represents "dreaming while awake" became the standard account. However, subsequent research contradicted this interpretation by showing that LSD and other psychedelics act postsynapticallyas agonists at 5-HT2 receptors (Jacobs, 1987), the most common serotonin receptors in the brain. The silencing of the raphe nuclei was due to LSD's agonist action at presynaptic autoreceptors (inhibitory 5-HT1) on the serotonin-releasing cells. Autoreceptors serve a negative feedback function such that the neurotransmitter (in this case serotonin) inhibits its own release when extracellular levels are too high. LSD thus acts like serotonin both presynaptically and postsynaptically, inhibiting serotonin release via inhibitory 5-HT1 autoreceptors while simultaneously activating excitatory postsynaptic 5-HT2 receptors; only the latter action is relevant to the psychedelic state (Feldman, Meyer & Quenzer, 1997). This interpretation was bolstered by the finding that serotonin antagonists can block psychedelic effects. Recent PET scans of volunteers under the influence of psilocybin showed hyperactivity of the frontal and occipital lobes, especially in the right hemisphere, presumably reflecting strong activation of excitatory 5-HT2 receptors in the cortex (Vollenweider et al., 1997). But how and why these brain changes translate into psychedelic experiences are questions as difficult as the mind-body problem itself.

Research on the brain actions of psychedelic drugs has potential implications for theories of consciousness and the brain correlates of mystical experiences. People who claim to have had a mystical experience under the influence of a psychedelic give reports that are often similar to the accounts of non-drug using religious mystics from the major religious traditions (Pahnke & Richards, 1966). Themes such as the unity of all sentient beings, oneness with God and the universe, and the illusory nature of human existence have been reported by figures as diverse as Buddha, the Christian mystic Meister Eckhart, and psychologist turned sixties LSD guru Timothy Leary. The psychedelic experience thus represents a unique intersection between mind, matter, science and mysticism thatstill defies explanation.

Michael Lyvers
Associate Professor of Psychology
Bond University
Gold Coast Qld 4229 AUSTRALIA
e-mail: mlyvers@staff.bond.edu.au

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