

Transformative Psychopharmacology: the Case of 5-Methoxy-N,N-Dimethyltryptamine

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Abstract

Since the 2nd part of last century neo-shamanic rituals using mind-altering extracts from plants or animals have become increasingly popular in Europe and the USA. The first rituals coming to the west were based on drinking a special Amazonian tea, Ayahuasca, based on 2 different plants, with active compounds belonging to the class of the beta-carbolines (harmala alkaloids) and tryptamines. The use of such compounds will be described from the perspective of the transformative psychopharmacology: that part of psychopharmacology studying the use of psychoactive compounds to achieve a new balance, a transformation or healing and sometimes even leading to a cure. Examples of curing are meanwhile well documented, for instance the positive influence on drug abuse and addiction, alcoholism. The importance of the healing aspects of these rituals however are often neglected or overlooked. For users, these are key however. As medicine becomes more and more personalized and postmodern, it will be relevant to understand why patients and healthy people decide to participate in healing rituals based on psycho-active compounds. We will present the pharmacology, the transformative psychopharmacology, the effects and adverse events of 5-methoxy-N, N-dimethyltryptamine (5-MeO-DMT) and its place in postmodern medicine.

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Introduction

Transformative psychopharmacology we can define as 'the use of certain psychoactive compounds to achieve a new balance, a transformation or healing and sometimes even cure.' Healing rituals are becoming increasingly popular in Europe and the USA, and previously we described some of these rituals based on Blue Lotus Extract or Kambo. [1-2] We also discussed the various transpersonal experiences of participants of such rituals. [3-4] Examples of curing, are the use of natural extracts from plants or animals such as iboga, Ayahuasca or Kambo for the treatment of drug addiction. Pure compounds such as mescaline, psilocybin, LSD and tryptamines are also used in the treatment of drug addiction and to assist during the withdrawal phase. For instance, a meta-analysis in 6 randomized controlled studies in a total of 536 patients demonstrated that a single dose of LSD in alcohol-dependent patients could significantly decreased alcohol misuse compared to control treatments [5] All these interventions, based on either extracts or on pure substances, have recently gained a place in a variety of modern rituals, mostly of neo-shamanic nature and based on the indigenous use of certain psychoactive extracts. The aim of these rituals is more related to healing in general than to curing, as we illustrated in the recent past by presenting the effects of the ritual use of Kambo, a secretion of a tropical frog containing many bioactive peptides. [2-4]

Kaspro and Scotton (1999) discussed the use of psychedelic drugs in a transpersonal context, and introduced the term 'transpersonal psychopharmacology', related to the use of psychoactive drugs to assist 'human growth beyond the ego' (6 p.12). the term 'transpersonal' however has been used in many different definitions, and its meaning is not always clear. It is therefore we feel it is better to use the term transformative psychopharmacology. Transformation in the context of healing can be induced by these compounds, in many different ways. For instance, Aldous Huxley referred to such compounds as mescaline as being not only valuable to widen once perception of the reality, but also to assist the dying. At our deathbed, many unsolved issues might emerge and disturb the process of 'letting go', for instance due to the induction

of anxiety, regret and depression. A cure cannot be offered in such a situation, but a healing can. Kaspro and Scotton (1999) suggest psychedelic drugs hold a promise as adjuncts to transpersonal therapy, and state that such compounds have been used by shamanic cultures for thousands of years to induce altered states of consciousness (ASC) important for transformation. [6] The use of serotonin analogues, including psilocybin and dimethyltryptamine (DMT) and its derivatives, are classical examples of compounds belonging to the transformative psychopharmacology, as intake leads to the dissolution of ego boundaries. (6p.20). We will here review the value of a special serotonergic tryptamine, 5-methoxy-N, N-dimethyltryptamine (5-MeO-DMT) in the context of modern neo-shamanic healing rituals and transformative psychopharmacology.

5-MeO-DMT: Brief Pharmacology

5-MeO-DMT is a methoxylated derivative of DMT, an indole alkaloid with psychoactive properties. In the same class we find other metabolites of tryptophan: N,N-dimethyltryptamine (DMT) and 5-hydroxy-DMT (bufotenine). In the 70s of last century it was already suggested by Shulgin that 5-MeO-DMT had quite potent psychological effects, effects quite different from other entheogens such as mescaline. [7] This could be further substantiated by the experimental work in an animal paradigm. [8] Furthermore the dose-effect curves clearly indicated a much stronger effect of a per weight dosis of 5-MeO-DMT compared to DMT (factor 8). [8]

DMT, 5-MeO-DMT, as well as psilocin have been reported to bind at two different serotonergic receptors probably leading to the main psycho-active effects: the 5-HT_{2A} and 5-HT_{2C} receptors. [9] The affinity on the 5-HT_{1a} receptor might have some additional anxiolytic and antidepressant effects. [10] The effects of its high affinity to the sigma-1 receptor are still unclear. [11]

5-MeO-DMT is natural compound and is present in a number of plants or animals, sometimes accompanied by DMT or its metabolite bufotenine. [12-13] The compound can be found in South American psychedelic snuff called Yopo, it is a minor part of the tea ayahuasca (DMT being the major part) and can be found in the secretion of the Colorado

River toad, *Bufo alvarius* in very high concentrations. [12-15] Already in the 60s it was presumed to be an endogenous compound in man, at that time it was suggested to be related to the pathogenesis of schizophrenia. [16] This hypothesis could not be proven in subsequent studies, and the role of endogenous produced 5-MeO-DMT in for instance the pineal gland is still somewhat in the dark, but probably needs to be rejected. While DMT and 5-MeO-DMT are both psychoactive, apparently only different in potency, the psycho-activity of bufotenine is still unclear. The transpersonal effects of DMT and 5-MeO-DMT are most probable comparable. A high dose DMT is expected to result in the same pharmacological and psycho-active effects than a somewhat lower dose of 5-MeO-DMT (around a factor 10 difference). Recently it was suggested that 5-MeO-DMT use may be also be therapeutically active in a wide variety of psychiatric disorders: anxiety, depression, substance use, and post-traumatic stress disorder. [17]

In Ayahuasca, and in a similar entheogenic brew Jurema, DMT stems from one specific plant (for instance in the case of Ayahuasca the *Psychotria viridis*) and is combined with a mono-amino-oxidase inhibitor such as the harmala alkaloids harmine, tetrahydroharmine and harmaline (available in *Banisteriopsis caapi*) to enhance its transformative effects by inhibiting the metabolism of DMT and 5-MeO-DMT. This changes the extreme rapid metabolism of the tryptamines and leads to a prolonged effect of hours. Furthermore, the combination of DMT with harmala alkaloids, as it natural occurs in most forms of Ayahuasca, or in artificial combinations of harmala alkaloids with 5-MeO-DMT leads to a pharmacodynamics interaction, the potentiation of its serotonergic effects. [18] The so called artificial spiking of ayahuasca teas with 5-MeO-DMT is not recommended as this may lead to serious adverse events. [19] While in Ayahuasca and its analogue brews the concentration of is only low concentrations of 5-MeO-DMT, much higher concentrations can be found in *Anadenanthera peregrina* (used as yopo or cohoba snuff) and in *Virola theiodora*. The history of human use of 5-MeO-DMT has been suggested to start in the late 8th Century. At that time, snuffing paraphernalia and snuff remnants from *Anadenanthera* containing DMT and bufotenin were

found at burial sites in Chile. [20] Very high concentrations of 5-MeO-DMT can be found in the skin secretion of the *Bufo alvarius* toad.

5-MeO-DMT: Inducing Transformative Experiences

The compound is clearly an example of the essence of transformative psychopharmacology, as it is well-known that this compound can be of great personally use, or even can lead to changing one's perspective off life. 5-MeO-DMT induces mystical experiences, which has been suggested by a number of users to possibly lead to long lasting beneficial effects. The general common transpersonal effect is described as experiencing 'an overwhelming sense of oneness with the universe, or a sense of being outside of time and space while seeming to experience the totality of both. The concept of the ego as a separate entity is typically lost'. [21] The latter is the major driver for transformative experiences. After taking the compound there is no way back into gaining control over the moment, and one is forced to let go of our grasping to the normal experienced reality. It is like creating a crash course into the essence of Advaita (Vedanta philosophy). In the Advaita one discovers during meditation that in the center of one's consciousness there is not such a thing as an 'ego', but rather an egoless awareness, referred to sometimes as 'the watcher'. The ego-dissolution induced by 5-MeO-DMT may also help to overcome the fear of death and bring about new inspiration for living in the now, without too much planning, fears and anxieties for the future, while letting loose of the past. In states of awareness free from the ego mystical insights may strike and act as a catalyst, transforming the person instantaneously. For instance, one such insight might be: 'God is to the universe what I am to my body', giving rise to the insight that I am a direct part on the divine, not even a part but an intrinsic aspect of it. Such insights are documented I many esoteric traditions, but experiencing it via a transpersonal state of awareness has a total different impact than reading about it in mystical texts.

Nowadays it is easy to find many testimonies of the internet, at Blogs and on YouTube, from people describing the transformative influences on their life after having taken a compound such as 5-MeO-DMT or related tryptamines. The power of transforming old

fears, anxieties, projections and observations, leading to a fresh start and a letting-go of old destructive social behavioral patterns, is clearly appreciated by many users. This all points to a deep wish for healing by participants of such healing rituals, and there should be more space and understanding for such healing aspects in modern medicine. Especially since within the philosophy of modern medicine it is often stipulated that although there is much attention for 'curing aspects' it is also the healing aspects which bring satisfaction to people. Even on a deathbed healing remains possible, 'reaching wholeness', while curing is a past station. We will present 3 experiences to highlight the essence of the transpersonal and transformative experiences:

Experience of Eternity: 'I lay on the bed and over the next three minutes felt it envelope everything that ever existed. I felt odd moments of resistance, then submission, then resistance, then submission, then total death into the eternal, no words to describe, not even consciousness or love or being, beyond all and everything, infinity.'

[<https://forums.5meodmt.org/index.php?PHPSEID=c774960be8570571cc498accf0062648&topic=50829.0>]

Ego-dissolving: 'Much of what I experienced today could never accurately be encapsulated in mere words. A great deal of the voyage was moving so quickly and with such overwhelming intensity, that I was sure that I was truly dying. I had to remind myself to breathe, often and with increasing urgency as the peak approached. Honestly, I have never been so quickly and thoroughly blown out of my socks before.... ever, nothing quite compares!!! In short matter of moments, my ego's self was suddenly shattered and so, dissolved all fixation of self into a translucency which defies any quantification.' And: 'Within seconds, my attention exploded from the normal/relative to the immensity of the absolute, from finite to infinite, from personal to supra-personal. Nothing I've experienced even compares with this Sacred Medicine. I seriously thought I might expire, given the pounding heartbeat and the rushing energy coursing throughout my system. I was devoured by the sheer power of the Omnipotent light, even as the ringing/roaring melodies of the universal frequency lifted my conscious-awareness

higher and higher, into the radiant bloom of the Unified Field of Being, pulling my enraptured attention into the deepest soul resonance.'

[<https://forums.5meodmt.org/index.php?PHPSEID=c774960be8570571cc498accf0062648&topic=50789.0>]

Let-go and surrender: 'Immediately, an intense overwhelming rush of energy flowed through my body forcing me to sit bolt upright. I was catapulted into a fractal landscape comprising of incredibly fast moving bands of bright light that I was surging through. The speed & intensity was overwhelming as 'I' collapsed into the experience, with no choice but to let go with each passing moment...trust, be open & let go, let go, let go. It felt as though an energy had re-awoken deep within and was now bursting out through every pore of my body, splitting 'me' into a billion tiny fragments. The narratives of 'me', as an identity, were being forced through the eye of an entheogenic needle until what remained was an embodiment of the energetic aspect of god consciousness within us all. Let go of the patterns, habits, stories that my ego has constructed, let go of fear, let go of all that isn't awareness of the divine beings that we are. And in that awareness of the need to let go, comes an awareness of the work that is needed, now. And: 'Wow - this was a deeply healing experience, which I feel so grateful for. The potential of this medicine is endless and I am keen to go deeper & open to further teachings'.

[<https://forums.5meodmt.org/index.php?PHPSEID=c774960be8570571cc498accf0062648&topic=50668.0>]

The last testimony was followed by the following statement of the user: 'I do think that working with these medicines can assist our process of 'spiritual evolution and growth, development, and healing processes'. I definitely feel like these amazing tools can open the doors to enhances states of consciousness where we have the opportunity to release the energy surrounding old traumas, and can be gifted a deeper understanding about the nature of reality, both of which involve spiritual growth and healing.'

Clearly all these impressions support the categorization of 5-MeO-DMT in the class of

transformative psychopharmacological compounds.

Use of 5-MeO-DMT: Effects, Adverse Events, Interactions and Contraindications and Precautions

The use can be via various routes of administration: vaporized, insufflated (snorted), parenterally given, sublingual and oral. A very quick onset of action can be expected after vaporization, with a short effect time, while orally use leads to erratic absorption and unpredictable onset and time-effects. Most users select a synthetic source and vaporization or smoking is the route of administration. [17]

In order to minimize negative effects, it is recommended for those who start taking this entheogen, to start with a low dose for the first time, 2 mg. [21]

There are a number of potential adverse events, all related to the pharmacological profile of the compound, and a number of solicited effects.

The adverse events are brief losses of consciousness. respiratory depression, tachycardia, sweating, hyperthermia, anxiety and panic attacks ('bad trips'), delusions, nausea, vomiting, memory loss, depersonalization, ataxia, excitation and delirium. In general, it is believed that 5-MeO-DMT has a safety/ risk profile similar to that of other tryptamines. [17] A recent epidemiological study showed that many users reported that 5-MeO-DMT use catalyzed transformative mystical experiences and improvements in symptoms related to anxiety, depression, substance use, and post-traumatic stress disorder. [17]

In addition to these 'cure' aspects, further solicited effects are within the transpersonal and transformative realm: mild visual and auditory hallucinogenic experiences, time distortion and ego-loss.

Interestingly recently (2018) it was demonstrated that 5-MeO-DMT may lead to very specific changes in brain structure and function: it enhanced cell proliferation, neuronal survivability, and induced morphological and functional changes in a part of the brain known as the Gyrus dentatus. [22] This part of the brain contributes to the formation of memories, and is known to form new neurons, for instance in response on aerobic exercises and during treatment with antidepressants. This thus indirectly suggests that

5-MeO-DMT might have an antidepressant and balancing effect. In addition to this it has effects on the functions of the cortico-thalamic pathways and can alter the proteome of central nervous tissue. [23-24]

As 5-MeO-DMT is a serotonergic drug, all classical precautions to avoid interactions leading to the serotonergic syndrome should be taken: no concomitant use of serotonergic drugs, such as the antidepressant serotonin-uptake inhibitors. [25-26] The combination with tryptophan is also contraindicated, as is the combination with antidepressants from the monoamine-oxidase inhibitor class (MOA-I). Furthermore, pharmacokinetic curves in mice showed non-linear kinetics, meaning that there is no clear 1 to 1 relation between dose and effect. [27] This implies careful dosing and taking increasing dosages only step by step in order not to provoke difficult to handle adverse events.

Contraindications are preexistent severe psychopathology, difficult to treat hypertension, cardiac instable conditions especially due to its sympathomimetic agonistic properties.

In general, it is recommended not to use 5-MeO-DMT alone, but either use it in a ritual context, supervised by an experienced guide, or to use it in the presence of someone who knows the effects and can guide the user in case of need (a so-called sitter). [21] One should preferably lay down while taking the compound.

Discussion

Hand in hand with the current tendency of patients increasingly searching and demanding more autonomy in their treatment of diseases, and in line with postmodern medicine, healthy people increasingly look for ways to expand their consciousness and look for transformative experiences. The most extreme example of this looking for healing outside of the current biomedical paradigm is the application of Kambo, a secretion of a tropical frog leading to pharmacological effects such as nausea, vomiting, tachycardia and facial edema. [2-4] Healthy people or patients suffering from chronic disorders use Kambo in neo-shamanic rituals to 'cleanse' and 'reboot' themselves. From a medical point of view the balance between risk and benefit clearly

would lead to judging Kambo use to be insane: healthy people intoxicating themselves briefly with a frog's poison. However, from a transpersonal perspective, many users of Kambo claim the effect was indeed one of a healing and transformative sorts. If we seriously embrace postmodern medicine, the choice of the individual for such treatments should be respected. Evaluation of the risk/benefit ratio should than be in the hands of the user, once the user understands all the ramifications of its use. So, rituals using a psychopharmacological compound such as 5-MeO-DMT, potentially leading to healing and transformation, should be accepted as a further step to empower people, who want to increase their human potential. Last but not least, there are indicators to suggest that the use of tryptamines such as 5-MeO-DMT might not only play a role in healing, but also in curing, for instance various forms of depression, post-traumatic stress disorders and substance abuse and dependency.

Conflict of Interest

none

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