Introduction:

What exactly is it that fascinates people about the psychedelic drugs? And how can we best define them?

1. Most psychiatrists will define psychedelics as those drugs that cause an acute confusional state. They bring about profound alterations in consciousness and may induce perceptual distortions as part of an organic psychosis.

2. Another definition for these substances may come from the cross-cultural dimension. In this context psychedelic drugs may be recognised as ceremonial religious tools, used by some non-Western cultures in order to communicate with the spiritual world.

3. For many lay people the psychedelic drugs are little more than illegal and dangerous drugs of abuse – addictive compounds, not to be distinguished from cocaine and heroin, which are only understood to be destructive - the cause of an individual, if not society’s, destruction.

4. But two final definitions for psychedelic drugs – and those that I would like the reader to have considered by the end of this article – is that the class of drugs defined as psychedelic, can be:

   a) Useful and safe medical treatments. Tools that as adjuncts to psychotherapy can be used to alleviate the symptoms and course of many mental illnesses, and
b) Vital research tools with which to better our understanding of the brain and the nature of consciousness.

Classifying psychedelic drugs: 1,2

The drugs that are often described as the ‘classical’ psychedelics include LSD-25 (Lysergic Diethylamide), Mescaline (3,4,5-trimethoxyphenylathylamine), Psilocybin (4-hydroxy-N,N-dimethyltryptamine) and DMT (dimethyltryptamine).

Another group of chemicals that share some properties of these drugs, but are not strictly speaking ‘psychedelic’ are the enactogens or empathogens – the best-known drug of this type is 3,4-Methylenedioxyamphetamine or MDMA (ecstasy). There are many other drugs in this group – mostly based around the structure of phenethylamine.

The group of chemicals belonging to the family of Dissociative Anaesthetics are also considered to have psychedelic effects at low, non-anaesthetic doses. These include synthetic compounds such as Ketamine and Phencyclidine.

Lastly, some researchers even class the psychological effects of cannabis (tetrahydrocannabinol) as psychedelic at very high doses.

Ancient uses of psychedelic drugs:

Psychedelic plants have been used by non-Western cultures as sacramental tools for thousands of years. They have shaped the course of many established religions and are still used throughout the world today as part of religious ceremonies for many cultures 3. Examples include the legendary ‘Soma’ that appears throughout the Sanskrit texts that form the Hindu religion, the active component of which was possibly the hallucinogenic Amanita Muscaria (the Fly Agaric mushroom). And in the Elyusinian Mystery Rites the ancient Greeks gave initiates a drink made from wheat most likely infected with the Ergot fungus - the active component of which is a close relative of the synthetic compound LSD.

Modern cross-cultural uses of psychedelic drugs:

‘The White man goes into his church house and talks about Jesus. The Indian goes into his tepee and talks to Jesus’

- Quanah Parker (1839 –1911)

Modern day usage of psychedelic plants by non-Western cultures include the Amazonian use of Ayahuasca, (a plant compound containing DMT), the North American Indian use of the Peyote cactus (containing mescaline) and the worldwide use of magic mushrooms (containing psilocybin). All these cultures
use these drugs as part of a religious ceremony lead by a Shaman – usually a respected elder of the tribe who held the role of both doctor and priest. He or she uses the plants – together with non-drug techniques to alter consciousness, such as drumming and chanting – to induce a dreamlike state and help the user communicate with the spiritual world. These ceremonies have a beneficial, cohesive effect on their communities, helping them to resist the mono-cultural invasion of the Western way of life; they are largely associated with lower levels of mental illness than those communities who are more heavily influenced by alcohol abuse – one of the trappings of Western culture.

It is not only humans that show a natural tendency towards altering their state of consciousness. Many animals, from insects to mammals, are attracted to hallucinogenic plants and fungi, above and beyond the normal quest for food. The reindeer of Siberia are frequently witnessed drinking the urine of those animals that have eaten the Amanita Muscaria mushroom - well known to the local Shamans to be excreted as an active compound.

The rediscovery of psychedelic drugs by the West:

The psychoactive effect of LSD was first discovered in the 1940s by Dr Albert Hofmann. The Swiss chemist accidentally absorbed the compound that he had synthesised as a potential medicine for the company Sandoz. After initial trials conducted by Hofmann and his colleagues, LSD was disseminated throughout the world by Sandoz to many psychiatrists. In the 1950s it was used in a number of applications. Initially thought to be useful as a psychotomimetic (for therapists to take themselves to help them understand the experience of psychosis) it was later found to be a helpful tool to assist in psychotherapy. The patient under the influence of LSD had the ability to recall distant, repressed memories and revisit past traumatic experiences with great clarity. Many patients, who had previously been disabled by unremitting neuroses, were able to benefit from this approach.

Exploring the nature of the psychedelic experience:

There are entire genres of art, literature and music dedicated to this subject. It is rumoured that Shakespeare enjoyed cannabis in his pipe and the chemical excursions into the inner worlds of Byron, De Quincy and William James are legendary.

From a medical point of view there is general agreement that these drugs act as potent psychotropic agents. The main psychedelic effects probably arise as a result of partial agonism of 5-HT(2A) receptors in the cerebral cortex. Other receptors are undoubtedly involved as well, particularly the noradrenergic receptors of the Locus Coreuleus. The LC is the nucleus that fires in response to the brain’s detection of a novel stimulus in the environment. It is thought that under the influence of LSD the LC fires continuously – thus everything is experienced a novel and exciting (and which may explain why hippies can stare wide-eyed for hours at otherwise banal objects).
What is clear is that LSD is an immensely potent drug. It can be centrally active at a dose of just 25 micrograms, and an average psychedelic dose of 100 micrograms allows for only 3,700,000 molecules alone to pass the BBB for a few minutes. Yet this powers an intense 12-hour psychological experience. This has lead some scholars to suggest the drug itself merely triggers a cascade of psychological processes that then continue without further psychopharmacological input. What is certain is that there is still a lot more we could learn about how these drugs work and that in turn, this further study can be immensely helpful in furthering our understanding of the normal workings of the brain and the nature of consciousness.

LSD has an intense and potent effect on perceptions, cognitions and emotions. The effects on perceptions are well documented. Despite the name hallucinogens, most people do not experience true hallucinations, but rather perceptual distortions or illusions. A common perceptual alteration is that of neurasthenia – when a stimulus from one perception is experienced in another sensory modality – such as hearing colours and seeing sounds.

Clinical applications for psychedelics in psychiatry:

Perhaps the most interesting effects of the psychedelic experience as far as psychiatrists are concerned are those that can be used to facilitate the psychotherapeutic experience. LSD, psilocybin and newer drugs like MDMA have the ability to improve the depth and speed of psychotherapy. They encourage an increased empathy and shared understanding between the patient and therapist. Under the influence of psychedelic drugs the patient is able to revisit and access otherwise repressed parts of their psyches. This can be particularly helpful in the recall of past painful memories that can then be worked through with the therapist in real, waking time. Another feature of the experience is the ‘cinematographic’ effects experienced when the eyes are closed or the user stares at a blank screen. The user can ‘see’ eidetic images before them. They may take the form as simple geometric shapes, but they may also present as complex figures involved in scenarios that have an intense personal meaning for the patient. These images often have a strong archetypal element and they all represent internal, individual material from the patient’s unconscious. In the therapeutic environment offered by a skilled psychedelic psychotherapist, they can be interpreted and explored to reveal to the patient otherwise inaccessible parts of their psyche. If Freud called dreaming ‘the royal road to the unconscious’ then this internal visual element of the psychedelic experience is more like a Technicolor super-highway to the unconscious.

During the early 1960s it became apparent that the quality and clinical effectiveness of an LSD user’s experience were extremely dependant upon the user’s constitutional (‘set’) and environmental factors (‘setting’). If these variables were carefully controlled and adhered to then the session could be very productive. If they were disregarded then the experience could be hellish. This is the same for both clinical and recreational use of psychedelic drugs.
Psychedelic drugs and the mystical experience:

Another aspect of the psychedelic experience that has come under particular scrutiny since the 1960s is the proposal that at high doses and deeper levels of intoxication the psychedelic experience is akin to a mystical or religious experience. During the 1960s, numerous studies explored this phenomenon.

One of the most famous projects was by the Harvard researcher Walter Pahnke. He conducted a double-blind placebo controlled trial on 20 theology students. He gave half of them psilocybin and half got a placebo. They then all attended a Good Friday Mass and were later asked to describe their experience. The results were blindly and independently assessed and rated according to the Stace criteria for a mystical experience. Rather unsurprisingly 9 out of the 10 experimental group believed they had experienced a genuine spiritual encounter, compared to just 1 of the control group. This experiment has since been repeated many times, and recently the cohort who took part in the Good Friday experiment was followed up. Decades later all psilocybin subjects participating in the long-term follow-up, but none of the controls, still considered their original experience to have had genuinely mystical elements and to have made a uniquely valuable contribution to their spiritual lives.

Nevertheless, much debate rages as to whether or not these experiences really can be called religious or spiritual experiences. Our western, Christian-based religions usually preach that an intoxicated state could not possibly allow access to God. An outspoken critic of the 1960s psychedelic community was the Oxford professor S.C. Zaehner. He gave the infamous quote ‘whatever else this is it is not a spiritual experience. God cannot be found in a bottle’. But of course to the Bwiti tribes in West Africa who use the Iboga tree as a sacrament, or North American Indians who unashamedly use the peyote cactus as part of their religious ceremonies, there are no doubts that this is a bone fide mechanism of worship.

Who are we in the West to say our form of worship is the right one? Many of these ‘archaic’ tribes of the ‘developing’ world are far older and more stable than the relatively recent Christian culture. And as for God not being found in bottle, it depends on whether one believes God actually gave us the bottle in the form of psychedelic plants – as the mushroom-munching Mazatec tribes of Mexico do. They display a strange mixture of Christian and pre-Christian religious symbolism, as ancient Indian ceremonial rites of worship lie side by side with the adopted Christian ceremony. The Mazatecs preach that the sacred mushrooms grew out of the earth where Christ’s tears fell as he hung on the cross.

From a neuro-scientific point of view perhaps the most interesting aspect of this debate is not whether these psychedelic experiences actually are spiritual (whatever that means) but rather that they feel spiritual – and therefore what does this tell us about the workings of the brain? How can an organic substance make us at least believe we are talking to God? And what was the
role of these psychedelic plants in the development of religions, or indeed in the very emergence of human consciousness? Some researchers have suggested that it is early humankind’s accidental ingestion of psychedelic plants the most likely explains the relatively rapid advance from spiritually benign primates to sentient, spirit-worshipping humans 16.

It is known for certain that psychedelic drugs played a part in the beginnings of some, if not most, modern religions. Of the 1200 Sanskrit texts that make up the Hindu Rig Vedas some 100 are dedicated to the mythical ‘Soma’. And in ancient Greece, the 2000 year-old practice of worshipping the Goddess Demeter through ingestion of a drink made from Paspali grass, inadvertently impregnated with Ergot, allowed the initiates to see and communicate with the Goddess herself.

Christianity itself is not immune from the possible psychedelic influences. Some scholars have suggested that the ‘apple’ consumed by Adam and Eve that allowed them to ‘open their eyes and see the world as it truly appears’ was in fact the Stopharia Cubensis mushroom, which still grows today in abundance at the base of trees in the parts of Palestine thought to be the site of the Garden of Eden 16.

**The early success and decline of LSD:**

As the 1950s progressed, psychiatrists on both sides of the Atlantic discovered the product being given away by Sandoz. Britain has a rich history of successful LSD-assisted psychotherapy from this time. Dr Ronald Sandison at Powick Hospital, Gloucestershire, pioneered the use of ‘psycholytic’ (mind-loosening) psychotherapy when he combined low doses of LSD with on-going psychodynamic psychotherapy and found the drug useful in helping patients to access deeper, repressed parts of their psyches 17. Between 1950 and 1965 LSD was used with good success and with safety by psychiatrists throughout the world. Some 40,000 patients were treated with LSD and over 1000 papers were written on the subject. The results were overwhelmingly beneficial – even though often the drug was being used on only the most resistant and chronic patients 18. The number of adverse incidents was low and doctors were developing an increasingly sophisticated method for achieving the most comfortable and productive psychedelic sessions. Their methods were often informed by Eastern tradition – with elements of meditation, chanted verses and a relaxing, facilitative environment 19.

‘I was seeing what Adam has seen on the morning of his creation – the miracle, moment by moment of naked existence.’

- Aldous Huxley

But LSD leaked from the scientific community. Popularised by writers such as Aldous Huxley, the drug spread firstly to the intellectual and artistic community and then to the wider public. The popularisation of LSD in the United States owes a lot to the dissemination by clinical mavericks such as the American psychologist Timothy Leary, who preached about the benefits of widespread use. Dr Leary initially started his career as a clinical psychologist at Harvard
University, conducting experimental psychedelic research on prison inmates and university students. After leaving the institution in 1963 he went on to promote a more liberal use of the then still-legal drug, and became a well-known figurehead of the developing drug culture. Ironically, another major contributor to the spread of LSD to the general public is the United States government. Through their project MK-Ultra, they hoped to develop LSD as a truth drug for the military. The drug was given clandestinely to unsuspecting members of the public, who were then observed by the researchers, in a series of experiments that went far beyond any unethical practices attributed to the medical profession from this period.

By the mid-1960s, LSD had been taken by over a million people in the USA. It was then that increasing reports of the dangers of these drugs emerged. When used recreationally, without undue care paid to set and setting, some users had negative experiences. In 1966 LSD was made illegal in the USA and the rest of the world soon followed. It was demonised by governments and was even frequently blamed for the left-wing eruption, opposition to the Vietnam War and the general widespread social changes occurring globally.

The result of this action was that whilst recreational use spiralled out of control, the majority of the medical research ground to a halt. Despite the medical profession’s promising results of the safe use of LSD, the government grants were cut and the research stopped. Faced with increasing media scare stories associated with the non-clinical use of LSD, doctors were forced to distance themselves from research with psychedelics.

Since the end of the 1960s the entire subject of psychedelics in medicine has fallen out of the standard training for doctors. It is as if the pioneering work started in the 1950s and 60s had never happened.

**MDMA-assisted psychotherapy:**

When LSD was made illegal, some therapists, particularly those who had been disheartened to see what they considered to be promising research grinding to a halt, turned to another compound, MDMA – the active component that was later to become the street drug ‘ecstasy’. MDMA shares LSD’s capacity for increasing empathy and encouraging improved recall and exploration of painful memories, but it lacks the often distracting distortions in time and perception that LSD users experience. With an effect lasting 2 to 5 hours rather than 8 to 12 hours duration, the drug is more manageable clinically than LSD. It proved again to be useful as a tool to assist the psychotherapeutic process.

Since MDMA was made illegal in 1985, therapists were again forced to distance themselves from using it with their clients but, like LSD before it, there has nevertheless been an enormous growth in its recreational use.

Like all treatments in medicine, these drugs must be examined according to the risk benefit ratio. It is especially important to apply this principle when researchers are receiving criticism based upon flawed methodology and a
challenge coloured by emotionally laden socio-political counter arguments. The debate about the neurotoxicity of MDMA has been affected by all these issues. Despite early scares about the severe neurotoxicity of MDMA after just a single dose, this is not borne out by more recent research. And in the absence of researchers being able to conduct prospective cohort studies on human subjects, those who often quote the exaggerated neurotoxicity of MDMA are restricted to conducting uncontrolled, biased studies on groups of ‘ecstasy’ users – for whom polydrug use, concomitant alcohol use and any other naturalistic environmental influence can both complicate and distort results.  

In contrast, the Phase One studies of the new psychedelic trials mentioned below, have demonstrated that when MDMA is used in infrequent and moderate doses in a controlled environment, the drug adequately satisfies the risk benefit argument, and to disregard it’s therapeutic potential entirely would be unwise. Recent publications are also increasingly questioning the current prohibitive scheduling of MDMA and are seeking a more balanced approach that will better reflect the actual risks and open the way for more constructive and freer research.

The new renaissance for psychedelic psychotherapy:

After a hiatus of almost 40 years, there are now several new psychedelic drug research projects underway. At the Charleston Medical University of South Carolina, USA, the psychiatrist Dr Mithoefer is currently running a double-blind trial comparing MDMA-assisted psychotherapy with a placebo in the treatment of Post Traumatic Stress Disorder. The treatment consists of a combination of drug-assisted and non-drug psychotherapy sessions – with strict baseline, outcome and follow-up evaluations using standard psychiatric rating scales. Dr Mithoefer hypothesises that the MDMA group will show a significant and lasting reduction in symptoms beyond the placebo effect. He also hypothesises that there will be no evidence of neuropsychological or neurocognitive deficit. Similar projects are planned for Switzerland and Israel.

Another double-blind placebo-controlled trial is being run by the Professor of Psychiatry at University College Los Angeles, Dr Charles Grob. He is hypothesising that the drug psilocybin can treat the pain and anxiety associated with end-stage cancer. He proposes that the psilocybin group will experience a greater reduction in pain, reduced use of anxiolytic medication and an improved quality of life over the placebo subjects. In this context the nature of the transcendental effect of the psychedelic experience can be a useful tool to help a patient to address existential issues associated with death and dying.

Following an Internet support group, a cohort of cluster headache sufferers pooled their anecdotal experiences that LSD and psilocybin was highly effective at reducing the symptoms of this rare and disabling condition. Not only during the experience itself, but also for months afterwards users report a great reduction in symptoms. This data is being followed up and there are plans underway to conduct a placebo controlled RCT at Harvard University.
testing LSD and psilocybin on human patients for the treatment of cluster headaches.

These projects are all still on going, but so far results are looking very promising. The details for these studies can be found at the websites for the Multidisciplinary Association for Psychedelic Studies and the Heffter Research Institute.

The ethical considerations associated with this kind of research are immense. These projects have taken decades in the planning, and authorities are rightly cautious about research involving drugs that have been abused in the past. However, if we can look beyond the preconceptions based on our limited knowledge of these compounds we may be able to devise safe and effective treatments for psychiatry. The profession has changed a lot in the 50 years since these compounds were first re-discovered and used on patients. Modern day studies are subject to strict and rigorous ethical conditions that are essential to ensure patients are fully informed and consenting to these treatments.

**Psychedelics as tools for neuroscience research:**

> ‘Psychedelics, used responsibly and with proper caution, would be for psychiatry what the microscope is for biology and medicine or the telescope is for astronomy’ Professor Stan Grof

What is the nature of consciousness? What is the relationship between mental states and brain states? How can the different levels of consciousness be accessed, and how do these levels relate to the physiology and chemistry of the brain?

The field of consciousness research could make great use of psychedelic drugs. After all, they are organic compounds with known structure and well-understood pharmacokinetics and pharmacodynamics that have profound psychological effects on the user. They induce marked and predictable mental states; they can induce specific emotions and allow repressed feelings and distant memories to be recalled with a greater clarity. What does their action tell us about the mechanisms of the normal brain? Does it suggest there are similar endogenous chemicals in our brains? Can spontaneous states of Enlightenment and Peak Experience be related to a natural release of psychedelic compounds?

The neuroscience community could use psychedelics as a lens – a concentrating agent with which to probe the dark caverns of the mind. These drugs could inform us about the Psi-Phenomenon, parapsychology, ESP and the Near Death Experience, all areas of 'pseudoscience' that have been on the fringe of mainstream psychology research for so long because the observed phenomena do not fit neatly with the current knowledge about the brain. And more accepted, but still poorly understood areas of brain science such as the conscious seat of perceptions, the nature and purpose of
dreaming and the neurophysiological changes occurring during the meditative state could all benefit from the new perspective offered by psychedelic drugs used as research tools.

Human consciousness research with psychedelics is beginning to get underway again since the prohibitions of the last 40 years. New projects are planned worldwide to examine the functional MRI, PET and MEG scans of human subjects under the influence of LSD. But like the clinical projects described earlier, because of the legal scheduling of these drugs, any such project proposals are met with such stringent and often insurmountable objections that they never get off the ground. The result is that the progress of human neuroscientific research is put back years. When once psychedelics can be properly accessed by research scientists, we may look back at the era of pre-psychedelic research as blind stabbing in the dark for clues, before we realised we could illuminate the subject with the light offered by these compounds.

Conclusion:

In this paper, I have at times allowed myself to stray from my usual objective, scientific boundaries into a colourful and fantastic realm populated with possibilities and pipedreams. I do not intend this approach to put off the more hard-nosed and sceptical readers but merely for this to reflect the level of excitement and hope I hold for these fascinating substances. Like any scientist with enthusiasm for a new angle, I must endeavour to remain objective and focused. The psychedelic drugs are not a panacea - they do not offer a magic wand with which to cure all the ills of society. That was exactly that sort of attitude that contributed to the downfall of the last psychedelic revolution. After all, it was not only the pop-stars and poets of the 1960s that were preaching mass recreational use of these drugs; it was also some of the clinicians too!

We need to be sceptical, and we are right to be cautious, for these drugs certainly can be dangerous. They can cause great harm, destroy lives and wreck communities, but they may also be of tremendous benefit to huge populations of patients who are suffering. Before we can know for sure how they might be developed in order to assist the medical profession, we need to submit these substances to the rigorous test of modern scientific trials. The case reports of the 50s and 60s, though numerous and promising in their results, are by today’s research standards little better than crude anecdotal studies. They lack control groups and they lack proper follow-up.

Yet because of their vast number, they certainly represent enough of a reason to at least look again at this subject. There is a growing interest coming from both the medical profession and the general public. Psychiatrists, disillusioned by the costly, ineffective and drug-company-lead policies whereby patients are maintained indefinitely on SSRIs, are increasingly looking ‘outside the box’ towards new and creative solutions for their patients.
A lot of water has flowed under the bridge since the ‘Turn On Tune In and Drop Out’ day of the 1960s. If clinicians can remain dispassionate and stay true to principle of evidenced based medicine, then we may be able to reconsider the therapeutic possibilities of psychedelic drugs. If we can do this, then there is a real chance that these fascinating chemicals could play a positive role in the future of psychiatry and neuroscience. That much we owe to the population of patients with unremitting, resistant psychological illnesses that may benefit from this novel and brave approach.

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