CAN YOU FEEL IT?

On Psychedelic Microdosing

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> *"When it finally happens that psychedelic research—left sufficiently free to realize the potentials—is permitted, then that freedom must include an agreement that under no circumstances must it be monopolized by psychiatrists. Psychologists, philosophers, theologians, anthropologists, artists, scientists, engineers—those from the many different disciplines and fields—must be allowed to contribute to the body of knowledge that will be generated. Given the range and diversity of the psychedelic experience—and truly nothing human is alien to it—investigation must be multidisciplinary if it is not to be warped and stunted. And we must understand and agree that some of this work will be exploration, not subject to the kinds of constraints imposed if it were to be more narrowly defined."*
>
> -Robert Masters, *The Varieties of Psychedelic Experience* (2000 ed., p.vii)

At psychoactive doses, classical psychedelics increase introspection;[1] reduce social pain, enhance empathy;[2-3] promote social bonding/differentiating hormones;[4-5] increase sense of connectedness to self, others, and the world;[6] amplify emotions, intensify symbolic and analogical thought;[7-8] enrich indirect semantic associations;[9-10] relax rigid belief structures;[11] expand conscious experience, and broaden the repertoire of dynamic brain states;[12-14] enhance autobiographical recall;[15-17] increase sensitivity to context and set and setting;[18-20] scrub away assumptions, accelerate conditioning and de-conditioning;[21-22] reveal the structure and mechanics of thought and perception;[23-26] produce synesthesias;[27] increase meaningful thought content,[28] open us up to new experiences and increase appreciation for aesthetics;[29-31] enrich visual imagination;[32] improve forecasting of future life events;[33] and may even increase neuroplasticity,[34], and catalyze creative problem solving.[35] At higher doses they can be used to induce highly personally meaningful, mythical, mystical, insightful and transformative experiences.[32, 36-37] In a clinical setting they have been used to produce experiences which, when properly nurtured, lead to long-term relief from anxiety and depression, addictions and compulsions, and to a range of lasting positive outcomes including increases in wellbeing, pro-social behavior, re-evaluation of priorities, and renewed sense of optimism, which often last several months or more.[38-46]

This constitutes a small handful of the effects of psychedelics that have been revealed over the years by meticulous experimental and neuropsychological research from some of the most renowned research institutions in the world.

Sub-perceptual?

Microdoses have most often been claimed to be sub-perceptual doses that produce a detectable benefit. The best evidence for the utility of sub-perceptual microdoses so far seems to be that the effects of psilocybin remain subjectively undetectable in the average person as long as serotonin 2A receptor occupancy does not exceed 15-20%—a dose close to 1-1.5mg of psilocybin.[47-48] Now, does this 15-20% have physiological relevance? Could it reduce inflammation?[49] Functionally enhance dopamine signaling? Promote neuroplasticity?

Preliminary findings of self-report studies suggest that microdosing improves subjective sense of wisdom, mood, stress, creativity, energy, and focus and productivity.[50-52] One of these studies found microdosers came up with more clever, uncommon and remote potential uses for objects than non-microdosers on the Unusual Uses Task. One recent study [53] found that 1.5mg of psilocybin increased convergent and divergent thinking, but it was conducted openly at a psychedelic conference (in their words, a "natural setting"). But some participants in these studies reported that it sometimes made them uncomfortable, and found it impossible to focus or make decisions (a common side-effect of anxiety, which psychedelics tend to induce when not met with adequate emotional regulation). And the doses used by participants in these studies were not all sub-perceptual (i.e. below 1 to 1.5mg psilocybin or 7-10µg LSD).[76]

Still, none of these studies were placebo controlled, and the results are predictably dull in comparison to the full spectrum of psychedelic experience (which involves an alteration in consciousness)

Ongoing Research

The *Beckley/Imperial Psychedelic Research Programme* is set to investigate the effects of psychedelic microdosing on mood, creativity and cognition in a series of placebo-controlled trials. The first study in this series, The Naturalistic Self Blinding Microdose Study, led by Balázs Szigeti and David Erritzoe of Imperial College London, is due for publishing late 2019. Its use of an innovative QR code method for self-blinding has earned it David Nutt's applause as "the most sophisticated microdosing study yet." Still, there's one key problem: participants have to use their own LSD or psilocybin. And without having them all get their psychedelics tested at a service like Energy Control (EC), we don't know whether or not what they're microdosing with is real or accurately dosed.

In PsychedelicsToday's Jan 22 podcast episode, Szigeti and Erritzoe relentlessly stress the limitations and defend the design: to get approval to administer psychedelic microdoses in controlled experiments, they say, participants would have to come in to a lab two or

three times a week and be watched for most of the day in a somewhat unnatural laboratory setting; but people are *already* microdosing in their natural environments. That's good ecological validity. And a controlled lab experiment of this size would easily cost hundreds of thousands or even millions of dollars, whereas this study was mostly funded by the Beckley Foundation for a few thousand, and virtually everyone can participate. And 90% of "LSD" sent to EC these days is clean.

> "It's not because this is like, the best study imaginable you can do -- no. If we were to have infinite resources, we would come up with much better study designs. [...] It is basically costing very very little. But on the other hand it incorporates a placebo control and we are going to be able to have a very large sample size..."

Participants are required to report having prior experience with psychedelics. This, and going through the effort of setting up the self-experiment means participants are more likely to have positive expectations. Psychedelics also amplify sensitivity to the set and setting and increase suggestibility. Altogether, these are fertile conditions for placebo.[56] Interestingly though, Szigeti ad Erritzoe say that so far it doesn't seem like most participants can tell the difference between their microdose and the empty capsule. So we know they're measuring sub-perceptual doses, and this means the results on cognitive tests should give us an idea of whether sub-perceptual doses have any measurable effect on mood and cognition.

Moving Forward

As part of the same Beckley/Imperial Psychedelic Research Programme, Jan Ramaekers and Kim Kuypers at the University of Maastricht are investigating the effects of 5, 10 *and 20µg* of LSD on cognitive performance, emotional state, and resilience to pain and stress, using standardized measures of creativity, cognitive flexibility, mood and well-being, in a randomized and balanced cross-over design. They're also looking at basic physiological safety and blood markers of neuronal growth and neuroplasticity.

Finally, Amanda Fielding and the Beckley Foundation will begin a controlled experiment on the effects of microdosing, using the classic Chinese game GO–a timeless test of creative insight and intuitive pattern recognition. They will also examine neurological mechanisms at play using the latest brain imaging and evaluate the safety and tolerability of microdosing LSD. The use of sub-perceptual (5µg), threshold (10µg) and clearly psychoactive (20µg) doses of LSD in these studies should provide valuable information for finding the minimal effective dose.

Improvements in cognition at any dosage level would be impressive considering a body of research suggests that psychedelics dose dependently impair cognition, including attention, concentration, cognitive flexibility and behavioral control[57-59] and particularly psilocybin can cause drowsiness even at low doses. But the psychedelic state lends itself to unique testing problems. Low scores on cognitive measures may simply reflect the re-routing of attention to the increasingly rich emotional and often meaningful and awe-inducing internal world. At regular doses, paying attention to something like computerized cognitive tests may be mind-numbing in comparison to exploring the unique and impressive effects of the psychedelic on the lens of experience, even at very low doses. For many participants, the Cambridge cognitive test battery just isn't important or personally relevant; to some, it's entirely missing the point of the experience.

Some participants in prior psychedelic experiments have said, for instance, "the perception of the body is somewhat magnified and that can create challenges in focus or attention," or "I was actually having a little experiment of how much I could think of other things while doing the task." These kinds of reports are common. Motivations and expectations for participating in the study as well as the interpersonal chemistry of the subject and researcher further have an exaggerated effect. It should also be noted that impaired concentration diminishes while visualization increases with prior experience with hallucinogens.

Psychoactive

It is often claimed that a microdose is a sub-perceptual dose. Yet, as Szigeti and Erritzoe of the self-blinding microdosing study point out, the term microdose in pharmacological parlance is that of taking less than one hundredth of a normal dose, which is far less than the 5-25µg of LSD many are using. Recently, Fadiman also pointed out that his previous claims that Albert Hofmann "microdosed" until his death were inaccurate, and that he actually took low psychoactive doses of 20-50µg relatively infrequently. Torsten Passie states that Hofmann in fact took 30-90µg a handful of times a year. Passie explores many aspects of low-dose psychedelic research in intricate detail in *The Science of Microdosing Psychedelics*.

Low psychoactive doses are variously referred to as threshold doses, mini-doses, or museum doses, among a variety of others like '*lick*s, which I came up with some years ago.

Eric Osborne, M.Ed., uses the term 'mesodose' and adds,

> *"I occasionally feel like the courageous work done by the most adventurous psychonauts is being co-opted by individuals who haven't had the courage or discipline to consistently work with the medicine in its full potential. The trend seems to glorify those who, to paraphrase Terrence McKenna, 'take enough to say they're in the club but have no real skin in the game'. [...]*
>
> *Part of that respect is using them to their potential and not as a way to merely dip your toe in so that you can say you went swimming. Truly respecting the medicine, the plants, the importance and the impact is to authentically engage and apply them in a tangible manner. We owe them much more than that, for they have given us infinitely more."*

It is crucial to keep in mind that the lasting benefits of psychedelics have been found to correlate strongly with subjectively reported alterations in consciousness, including ego dissolution, visionary restructuralization, insight, and meaning, and importantly, relate to the lasting memory of the experience (consider that cannabis impairs memory consolidation!).[16, 32]

The analogy of Dreams

Psychedelics produce highly unusual, yet profoundly familiar experiences, inexorably distinguishing themselves from the effects of other drugs in "their capacity reliably to induce or compel states of altered perception, thought, and feeling that are not (or cannot be) experienced otherwise except in dreams or at times of religious exaltation."[60]

To take this further, REM (dream) sleep is key to psychological wellbeing,[61] yet it's so incapacitating we must lie down, lose muscle tonality and disconnect from the body. At the tremendous cost of requiring a safe, stable environment to do consistently, it confers outstanding benefit: REM sleep improves cognitive procedural learning (such as that required for strategizing and solving puzzles). REM dream content has been found to reflect a kind of metaphoric process of using memory traces to creatively construct scenes and scenarios for solving currently relevant complex procedural and social-emotional problems that require innovative solutions[62] (see: Does Dream Content Predict Cognitive Abilities?).

The necessity for a safe, stable environment bears strong resemblance to key elements of set and setting advice for the psychedelic state. And this is not a mere coincidence. Both the psychedelic state and REM state share key neurophysiological and phenomenological

features.[63] 1. vivid imaginary experiences and modular scene construction; 2. emotional memories and affects– heightened moods, often with fear memory retrieval. (i.e. imaginary exposure to fear-conditioned memory); 3. decrease logical and increased associative reasoning, similar to creative thinking. 4. depersonalization, loss of self and body boundaries, and nondual awareness. While the dream state typically involves disconnection from the body, and is constructed fully by long-term memory, psychedelics can tune this like a dial with increasing doses, with increments of intensity, complexity and vividness, all while maintaining a kind of sober wakefulness along with the ability to interact to a surprising extent with the outside world. Furthermore the content in both REM dreams and psychedelic states reflect elements of the content and emotions of daily life.

> "Dreaming may be our most creative conscious state, one in which the chaotic, spontaneous recombination of cognitive elements produces novel configurations of information: new ideas. While many or even most of these ideas may be nonsensical, if even a few of its fanciful products are truly useful, our dream time will not have been wasted."
>
> -Allan Hobson

REM sleep is fundamental to human flourishing and is widely prized around the world, and often attributed as the source of many revolutionary discoveries, including the benzene ring by Kekulé, acetylcholine by Loewi, insulin by Banting, the scientific method by Descartes, the periodic table by Mendeleev, the theory of natural selection by Wallace, and even Einstein's theory of relativity. Yet we wouldn't expect anyone inside of a dream to do well on a cognitive test; in fact, we'd be thrilled to get any score at all. With this kind of creative potential in the midst of total wakefulness, it may be no surprise that more than half the people that try psychedelics say it's one of the most significant and meaningful experiences of their lives.[42]

In practice

> "When LSD is used intentionally, it enables you to see all the tracks laid down and explore each one intensely. It also allows you to see the many parallel and redundant programs as well as the contradictory ones. It allows you to see the underlying unity of all opposites in the magic play of existence. This allows you to edit these programs and recreate superior programs which give you the insight to shake loose the restrictions and conflicts programmed into each one of us by our parents, our religions, our early education, and by society as a whole."
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> -Nick Sand, Mindstates (Berkley)

Maybe the best known and most impressive illustration of psychedelics as tools for creative problem solving is that of Harman et al (1966),[64] who administered clearly psychoactive doses of mescaline to “engineers, physicists, mathematicians, architects, a furniture designer, and a commercial artist,” for solving a complex problem they had invested themselves in for a long time without finding a satisfactory solution. During the experiment, many of them developed full or partial solutions that led to significant progress in their field or project. One architect, for instance, visualized at once in full detail a house constructed according to the specifications of his client. The majority of the real work, he said, involved putting it all on paper. [i]

Although the comparison to dreams serves to highlight some of the mechanisms at work in the psychedelic state, and though low-level visual alterations are integral to the experience, it is important to emphasize that the profound effects of psychedelics do not necessitate immersive hallucinations.

Some (including Amanda Fielding) believe the best use of microdoses and low doses might be for reconnecting to prior psychedelic insights and/or to sustain the lasting therapeutic effects of higher doses. In fact, research shows that with age and experience, the negative effects of psychedelics on concentration as well as anxiety appear to diminish, the benefits appear to magnify, and lower doses are needed to achieve the same effect.[x]

Warning

A great deal of caution to those experimenting with microdosing. A regimen specifically of one-day-on and one-day-off has been shown to lead to lasting symptoms of psychosis in rodents[65] and in some anecdotal reports. Also, chronic stimulation of the serotonin 2B receptor has been linked to heart valve disease.[66] David Nichols explains on the Heffter Research Institute’s website. Further, the serotonin system is involved in regulating energy metabolism,[67] social status (including resource access priority such as to food and mates),[68, 69] and psychedelics may lead to a challenging re-evaluation of priorities. Erica Avey talks about quitting her job in her article, *‘Microdosing Isn’t a Shortcut to Professional Success – But it might make you realize it’s time to move on‘*. Finally, psychedelics can amplify the expression of unconscious material, including psychological trauma, in thought and behavior. Altogether, their use may lead to unforeseen social and psychological consequences.

Footnotes:

[i.] Matthew Baggott recently revealed that Harman and Fadiman omit/ted the fact that participants were also given amphetamine at a certain point during the psychedelic problem solving experiment "as an energizer."[70] Amphetamine reduces drowsiness and would have served to help sustain attention during the loosened psychedelic state, and may explain why the experiment has not yet been successfully replicated: 1. It has been shown that serotonin 2A agonists (such as LSD) functionally enhance dopamine signaling in the primary motivation center in the brain (by increasing the affinity of dopamine ligands to D2 receptors, increasing G-protein coupling to the receptor complex, and elevating expression of D2 receptors in the cell). 2. Increased expression of serotonin 2A receptors has been found to increase behavioral response to potent dopamine agonists.[71] 3. More evidence suggests psychedelics[72] and serotonin receptors[73] modulate dopamine signalling, implicating dopamine in their therapeutic efficacy, particularly in cases regarding addiction, motivation and priority setting. 4. The D2 receptor appears to be key to the therapeutic effects of amphetamine on ADHD.[74] Incidentally, the modification of dopamine signalling by psychedelics, as well as the increasingly internally generated perceptual and thought content, and the shift of exteroception to interoception,[75] offer potential explanations for anecdotal reports including relief from ADHD symptoms.

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* see also [16]

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