DRUG-FREE MICRODOSING PERSONAL GUIDE

neuroVIZR®

The Change Maker

"IT'S THE LITTLE THINGS THAT COUNT."

Garnet Dupuis

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IT'S THE LITTLE THINGS THAT COUNT
A DEEP & EVOLVING DIVE INTO MICRODOSING

INTRODUCTION.

In culture, there are trends and fads. Trends are waves of social evolution and change that grow and permeate communities. They often have lasting cultural impact. Fads are splashes that dramatically crash onto shore and quickly disappear into the mist.

Is "microdosing" a trend or a fad?

There's evidence suggesting that "microdosing" is a trend. Let's delve deeper and see if you agree.

CURRENT CONCEPT.

This is the description from the Microdose Institute (https://microdosinginstitute.com/). It reflects the most common understanding and attitude among the active psychedelic community as well as, at least in part, what most persons in the general population may understand from social media and friendly conversation.

"*Microdosing is best described as the practice of regularly consuming a very small amount of a psychedelic substance, usually 5–10% of a regular dose, with the intention of improving one's quality of life.*

Microdosing does not cause classic psychedelic effects such as visual disturbances; instead, microdosers experience more subtle, "sub-hallucinogenic" effects from the practice. Microdosing is a practice that yields the best results when done over an extended period of time following a dosing scheme or protocol. The exact effects and results of this practice depend greatly on the person, the substance, the dosage, and many other personal factors such as their intention, expectations, and mindset."

There is good evidence that psychedelic compounds have played a significant role in developing human civilization. Archeological evidence and anthropological analysis all give credibility to the idea that psychedelic compounds in human use have been around a very long time. They seem to have been often restricted to special persons with the community and also limited to special groups at ceremonial gatherings. There is evidence derived from current indigenous cultures to support these ideas. The emerging impression is that the compounds were used at higher doses to induce stimulating

and sometimes dramatic altered states. Broad popular "recreational" use is much harder to assess and is less likely. It is also not clear that practices representing "microdosing" have a real place along this historical timeline.

The mid-20th century represents an inflection point in the awareness in popular modern society of psychedelic compounds. Anthropological interactions with indigenous cultures began to create new levels of curious interest in psychedelic plants. Around the same time, Albert Hofmann, a Swiss pharmacological researcher, accidentally synthesized LSD in 1938 from the ergot fungus and experienced the ever-first LSD trip. LSD was first utilized in psychotherapy and scientific study in the 1950s, mostly to treat anxiety, depression, addiction, and psychosomatic diseases.

LSD was the subject of intensive (psycho) pharmacological study, which resulted in almost 10,000 scholarly papers. In the years that followed, medical experts, scientists, and even the U.S. government expressed an interest in the novel chemical. The CIA's infamous MK ULTRA program looked at the use of LSD for "mind control". (https://microdosinginstitute.com/)
To stay on target regarding "microdosing", it is time to introduce James Fadiman. Fadiman is often credited as being the Father of Microdosing.

James Fadiman *is an American writer known for his research on microdosing psychedelics. Fadiman received a Bachelor of Arts degree from Harvard University in 1960 and a Master's degree and a doctorate (both in psychology) from Stanford University, the PhD in 1965. While in Paris in 1961, his friend and former Harvard undergraduate adviser, Ram Dass (then known as Richard Alpert), introduced him to psilocybin. In the early sixties Fadiman was also part of the team in the psychedelics in problem-solving experiment at the International Foundation for Advanced Study, which was abruptly halted in 1966. Fadiman's 2011 book The Psychedelic Explorer's Guide discussed the use of psychedelics in sub perceptual doses and unknowingly helped to drive the modern microdosing movement.* (https://www.esalen.org/faculty/james-fadiman)

"*In 1966, a team of scientists under the leadership of Dr. James Fadiman studied the influence of psychedelic agents on participants' creative problem-solving skills. In the "Psychedelic agents in the creative problem-solving" experiment, they tested 27 people working in creative professions such*

as engineers, architects, scientists, and designers. They gave them 200 milligrams of mescaline sulfate (This is comparable to 100 micrograms of LSD, so hardly a microdose) and had them work on a work assignment or problem. The results were positive, leading many participants to come up with technologically advanced project proposals, products, and solutions that have been mostly accepted by their clients.

Participants reported various forms of increased performance:

- Less burden of inhibitions and fears
- The ability to see a problem in the right context
- Increased idea generation
- Better ability to visualize and use fantasy
- Better concentration
- Increased empathy for external processes and issues
- Increased empathy for people
- Access to unconscious information
- Increased motivation to complete a project
- Visualizing solutions

Shortly after this experiment, the FDA banned all scientific research on psychedelics. The influence of psychedelics on our creativity and problem-solving ability could not be investigated further for decades that followed." (https://microdosinginstitute.com/)

It is apparent that the current concept of "microdosing" is inseparably linked to the chemical nature of psychedelic compounds. The definition above, supplied by the Microdose Institute, states "*The exact effects and results of this practice depend greatly on the person, the substance, the dosage and many other personal factors such as their intention, their expectations and mindset." As you can see, there are a lot of factors and variables involved with the process of "microdosing*".

Is it possible that there exists some unrecognized unifying principle that allows for a more cohesive understanding of "microdosing"? Spoiler alert – the answer is YES, and it is hidden in the actual neurology of our brain.

It is now time to also introduce both the Grandfather and Great Grandfather of "microdosing".

An Unexpected Lineage.

These two Canadians may or may not be familiar to you, especially in the context of "microdosing. Meet Hans Selye, the Great Grandfather and Donald Hebb, the Grandfather.

We will start with **Hans Selye** (1907 – 1982) – **The Great Grandfather of Microdosing**

Hans Selye & Stress:

To start with Selye is known more commonly as the Father of Stress Research. Here, he is also recognized as a key link in the evolution of the neurological foundation of "microdosing". (Hang in there, we will make this clear down below.) Selye's relentless work ethic was evident in his publications, which numbered more than 1,600 scientific articles and about 40 books. He was a nominee for the Nobel Prize in 1949, won many accolades, and published his best-known book, *The Stress of Life*, in 1956.

So, what does "stress" have to do with "microdosing"? Now is the time to put on your "thinking cap" for a little while.

Today, the concept of stress and the word itself have a strongly negative connotation. In 1939, Selye introduced his landmark theory of stress. Selye saw "stress" in more complex ways and was very inventive in his exploration. He is most famous for what is known as the General Adaptation Syndrome (GAS) but we will not focus on that major insigh.

Rather we will look at a few of his more fundamental understandings.

These are the factors that link Selye/stress/neurology to "microdosing".

Selye #1 – Stress in and of itself is neither good or bad – its nature depends on a number of related factors.

Selye #2 – Some type of "agent" acts to introduce challenge into the system – if the degree of challenge (aka "stress") is sufficient to match and slightly exceed the minimal level of

excitation, it will result in an arousal of the adaptive response in the system.

Selye #3 – The stressor "agent" perturbs the "status quo" of the system – the "agent" acts to disrupt or de-stabilize the system and provoke an adaptive response.

Selye #4 – The stress "agent" is not the main factor but instead it is the degree or amount of challenge that is at the core of its action.

Selye #5 – Depending on the context, the challenge may be either a "eustress" (positive) or a "distress" (negative).

Selye #6 – As much as "distress" is definitely a negative, "eustress" is not only positive...it is critical for growth, learning, adaptation and even survival itself.

Selye #7 - Eustress occurs when the gap between what one has and what one wants is slightly pushed, but not overwhelmed. The goal is not too far out of reach but is still slightly more than one can handle. This fosters challenge and motivation since the goal is in sight. The function of challenge is to motivate a person toward improvement and a goal. (https://en.wikipedia.org/wiki/Eustress)

Now we have the insightful elements collected from Selye that allow us to clarify the first step in linking "microdosing" to our innate neurology.

1. An adaptive response in our system is triggered fundamentally by the degree of stress and not the type of the stressing agent.

2. A small degree (low level/micro) of any stressing agent is capable of eliciting a positive eustress response.

3. The eustress response will drive the system towards positive new growth and adaptive change.

4. Any stressor "agent" that can be calibrated into lower (or higher) degrees of challenge can act to induce a "eustress" response.

5. It is well known that psychedelic compounds at higher levels act to significantly disrupt or de-stabilize common neurological activities in our brain – it can be assumed that the same compounds are capable of very gentle de-stabilizing "eustress" actions at much lower, "micro" levels.

6. It is noted that the current approach to Conventional Compound Microdosing utilizes a range of different types of compounds some of which are not even considered classic psychedelics.

7. Following the principle, any stressor "agent" (and not the type) that can be calibrated to low levels of "dose" can also trigger the same neurological adaptive responses.

Next, we have **Donald Hebb** (1904 – 1985) – **The Grandfather of Microdosing**

Donald Hebb & Neuroplasticity:

Donald Hebb was a Canadian psychologist who was influential in the area of neuropsychology, where he sought to understand how the function of neurons contributed to psychological processes such as learning. He is best known for his theory of Hebbian learning, which he introduced in his classic 1949 work The Organization of Behavior. He has been described as the father of neuropsychology and neural networks. (https://en.wikipedia.org/wiki/Donald_O._Hebb)

Hebbian Learning is now called "neuroplasticity". Neuroplasticity is the concept that states that the adult human brain is capable of positive neurological growth, change and new adaptive learning. Adult brain neuroplasticity occurs predominantly in the hippocampus area of the brain which is responsible for learning, long term memory formation and memory retrieval. https://www.news-medical.net/health/Hippocampus-Functions)

The basis of the theory is when our brains learn something new, neurons are activated and connected with other neurons, forming a neural network. These connections start off weak, but each time the stimulus is repeated, the connections grow stronger and stronger, and the action becomes

more intuitive. (https://thedecisionlab.com/reference-guide/neuroscience/hebbian-learning)

Above, we asked what does Selye and "stress" have to do with "microdosing"? It is fair to ask the same basic question now. What does Hebb and "neuroplasticity" have to do with "microdosing"?

These are the factors that link Hebb/neuroplasticity/neurology to "microdosing".

Hebb #1 – the adult brain can change in positive ways if it is induced to change with effective stimulation.

Hebb #2 - to get the neurology to change you must "fire it to wire it" (which goes very nicely with "use it or lose it).

Hebb #3 – in neuroplasticity, "the brain changes what matters" – which means you have to "get the attention" of the brain by inducing a disruptive or de-stabilizing challenge (aka a "stressor").

Hebb #4 – the challenge must not be too great and all at one time – the challenge must act at a low level and create just "marginal demand". (Here you may recall from above Selye #7 – "Eustress occurs when the gap between what one has and what one wants is slightly pushed, but not overwhelmed.")

Hebb #5 - a "eustressor" is a gentle but effective trigger for neuroplastic adaptation and positive change – other than the low level of stimulation, the amount of regular repetition and reinforcement is mandatory for actual integration – the "firing" must repeat for the "wiring" to stabilize.

Hebb #6 – Repeating the low-level stressor at regular periods will slowly move the "short-term state change" (which relies on the stimulus to be present) towards "long-term trait change" (which is now habituated and does not require the stimulus to be present) – this is the State to Trait principle of new neurological learning.

Now we have gathered from Hebb understandings about "neuroplasticity" that allow us to even further clarify the realistic linking of "microdosing" to our innate neurology.

1. Actual neuronal connections and growth can change towards positive new learning and behaviors – this is a natural and innate capacity of our adult human brain.

2. Repeated low-level, "marginal demand" "eustress agents" are capable of gently and reliably triggering positive neuroplastic change.

3. The types of "eustressor agents" include psychedelic compounds while also including a wide range of other agents that are capable of triggering the "marginal demand" aspect of neuroplastic change.

4. With repeated "doses" of the "eustress agent" as stimulation combined with reinforcement, the process will lead to progressive integration of the new positive neuroplastic change – State to Trait transformation.

Putting It All Together:

Like we say in the title of this paper...It's the Little Things that Count.

Our adult brain is still capable of positive change. Just nudge it along with a eustress agent of any kind at low-levels of marginal demand and repeat it often enough that the brain accepts it as a State to Trait integration.

A "eustress agent" must be able to gently perturb the "status quo" of our brain without triggering an outright defensive reaction (a "distress" instead of a "eustress").

To better understand the brain, remember that our brain is physical. So much of what you have learned about our physical body also applies to your brain...because our brain is physical!

Think about your experience in doing stretching exercise for your muscles. A little bit every day and you will get progressively more flexible. If you aggressively attempt to lengthen the muscle all at once, it will tear. Major OUCH. The same is true of strengthening your muscles. A little bit of "marginal demand" on a regular basis will result in stronger muscles.

Try to heavy lift all at once...and again the result is injury.

So, perhaps think of making your brain stronger yet more flexible in small regular steps.

Consider microdosing.

Exploring the Fadiman Protocol as an Example:

When looking at "microdosing" from a neurological brain point of view instead of solely focusing in the psychedelic compound as the stimulating agent, we have new fascinating information emerge. Here the classic Fadiman Protocol serves as a great template.

Essentially, the human organism organizes itself around core principles. Harmonic relationships are one such principle.

Delving briefly into the essence of neuroplastic evolution: Neuro-Stimulation begins as an «input reaction» in the first two hours. Neuro-Modulation, the «reaction response,» occurs from hours 2 to 8. Neuro-Relaxation, the «response relief», takes place from hours 8 to 24, and Neuro-Differentiation, the «relief result», develops between hours 24 and 48.

We'll explore the Fadiman Protocol in more detail later in this guide.

What is Drug-Free Microdosing:

Considering all the information above, it is definitely realistic to consider Microdosing in a different and expanded neurological light. Microdosing appears to an approach of gently and progressively inducing positive neuroplastic changes in our brain. The keys appear to be low-level eustress agents that are capable of safely inducing triggers of change in the brain. With repetition and eventual integration, the State to Trait evolution will occur.

Exploring Microdosing (whether Conventional Compound or Drug-Free) from the neurological perspective instead of the chemical opens the doors to many critical insights -- "Microdosing – it's all about your brain regardless how you get there".

One dynamic approach to Drug-Free Microdosing is the regular application of well-crafted Light and Sound stimulation as a series of progressive "eustress agents". The stimulation acts in a manner similar (if not perhaps as the same) as a low-level psychedelic compound.

The concept of Drug-Free Microdosing is not meant as a replacement for Conventional Compound Microdosing but rather as an optional alternative or even companion – there is no intention of discrediting the psychedelics as a means of Microdosing – if anything, these insights into the dynamics of Microdosing can be viewed as a support to the credibility of the use of sub-perceptual psychedelics when viewed neurologically as effective "eustressors" (positive stimulation) triggering beneficial neuroplastic changes in the brain.

"MICRODOSING – IT'S ALL ABOUT YOUR BRAIN REGARDLESS HOW YOU GET THERE".

Paul Stamets.

DRUG-FREE MICRODOSING - GENERAL INFORMATION.

BASIC PREMISE OF DRUG-FREE MICRODOSING:

1. Our human brain is neuroplastic which means it is capable of positive new synaptic patterns and even new nerve growth when properly stimulated.

2. Such neuroplastic changes lead to adaptation, behavior modification, new learning and growth.

3. Our human brain has a very broad range of innate natural, normal and even healthy states of consciousness including what may be referred to as non-ordinary, altered and psychedelic.

4. There is no single non-ordinary, altered, psychedelic state – this concept covers a wide spectrum of states that vary from our more common waking state.

5. The non-ordinary, altered, psychedelic states are all innate capacities of our brain which can be excited into conscious experience – such states are native to our brain and not foreign.

6. Simply because a state is uncommon does not make it abnormal.

7. There are numerous agents that are capable of stimulating non-ordinary, altered and psychedelic states.

8. The agents can be bio-chemical (eg. serotonergic psychedelic compounds), bio-physical (eg. light/sound), psychological (e.g., hypnosis) and methodological (eg. meditation).

9. At higher levels of stimulation, the non-ordinary, altered, psychedelic states are dramatically evident at a conscious level– at lower levels of stimulation, these states are not obviously evident.

10. Whether at higher or lower levels of stimulation, there is still a neuroplastic effect that enables positive change. (1, 2, 3)

11. Conventional Microdosing uses a variety of low-level bio-chemical compounds as agents to stimulate the neuroplastic activity in the brain.

12. Drug-Free Microdosing uses low-level bio-physical agents to stimulate positive neuroplastic change in the human brain.

13. Drug-Free Microdosing using bio-physical agents can optionally be combined with bio-chemical compounds used in Conventional Microdosing in a process called "stacking".

NOTE: *"In humans, neuroplasticity can be reflected by the presence of Brain Derived Neurotrophic Factor (BDNF) in blood plasma. BDNF is a protein that is in part responsible for regulating the processes of cell birth, cell growth and cell death in the brain. Brain-derived neurotrophic factor (BDNF), is a protein found in the brain and the periphery. BDNF acts on certain neurons of the central nervous system and the peripheral nervous system, helping to support survival of existing neurons, and encouraging growth and differentiation of new neurons and synapses. Given the interest in BDNF as a key player in several neurodegenerative and neuropsychiatric disorders and preclinical data showing psychedelics induced neuroplasticity even at low doses of psychedelics, our Beckley/Maastricht dose-finding microdosing study included, among other measures, that of changes in BDNF plasma levels following low doses of LSD (5, 10, and 20 µg) and a placebo, in healthy volunteers. The findings demonstrated an increase in BDNF blood plasma levels starting 4h after LSD administration. 6h after administration, the plasma level of BDNF was proportionate to the dose of LSD administered." (https://www.beckleyfoundation.org/2020/09/09/low-doses-of-lsd-acutely-increase-bdnf-blood-plasma-levels-in-healthy-volunteers/)*

BECAUSE A STATE IS UNCOMMON DOES NOT MAKE IT ABNORMAL.

Garnet Dupuis

WHY SHOULD ANYONE MICRODOSE?

1. The question is simple enough on the surface however the answer may not be equally as simple. The issue is that there remains no single, clearly recognized definition and method of microdosing. This fact complicates any answer as well as interfering attempts to perform consistent research. (8)

2. One thing for sure is that microdosing is getting a LOT of attention – as of August 2022, on Netflix, Fantastic Fungi and How to Change Your Mind are some of the streaming service's most popular documentaries - over on TikTok, the hashtag #mushies has amassed 27.9 million views while #microdoselife has racked up 20.9 million - on top of this, Google searches for "how to microdose mushrooms" are up on average too compared to last year, and searches asking "are microdosing magic mushrooms legal" skyrocketed at the tail end of 2021. (17)

3. Some studies (9) indicate a very real and significant benefit from microdosing, whereas others are much less convincing and show little to no benefit. One recent study (10) used a naturalistic, observational design to study 953 psilocybin microdosers compared with 180 non-dosing participants for 30 days, and found «small to medium-sized improvements in mood and mental health that were generally consistent across gender, age, and presence of mental health concerns.

4. The fact that our human brain is capable of positive neuroplastic growth is inspiring – full dose psychedelic compounds do show evidence of inducing neuroplastic activity (12) - the research is still young exploring microdosing and neuroplastic activity however early results point towards probable confirmation that microdosing has a neuroplastic effect as well.

5. "Given the increased interest in using low doses of psychedelics for psychiatric indications and the importance of neuroplasticity in the therapeutic response, this placebo-controlled within-subject study investigated the effect of single low doses of LSD (5, 10, and 20 µg) on circulating BDNF levels in healthy volunteers. Blood samples were collected every 2 h over 6 h, and BDNF levels were determined afterward in blood plasma using ELISA. The findings

demonstrated an increase in BDNF blood plasma levels at 4 h (5 μg) and 6 h (5 and 20 μg) compared to that for the placebo". (11)

6. Brain-derived neurotrophic factor (BDNF) plays an important role in neuronal survival and growth, serves as a neurotransmitter modulator, and participates in neuronal plasticity, which is essential for learning and memory. (13)

7. Persons generally microdose for different reasons:

- *to decrease uncomfortable or negative states such as depression and anxiety and
- *to increase attractive and positive states such as improved mood, focus and creativity.

8. "The most common reasons given for taking up microdosing were clinical in nature, especially for mood disorders. Addiction treatment, suicidality, trauma, chronic pain, and intrusive thoughts were all also reported as reasons for microdosing. Four participants explicitly noted that they microdosed psychedelics as a substitute for conventional medicine." (18)

9. "The next most commonly reported reasons for microdosing were for productivity and to facilitate novel or creative thought. Schoolwork was explicitly noted by two participants. Participants also reported using microdosing to effect more permanent changes in their perspectives than single bursts of novelty, seeking to improve their ability to take other perspectives, change their personalities, or grow as people." (18)

10. Others used microdosing to improve their social aptitude or gain a deeper "insight into life". (18)

11. Some persons consider microdosing as a positive influence on simultaneous psychotherapy and psychological counselling. (14)

12. Microdosers were generally similar to non-microdosing controls with regard to demographics. However, they were more likely to report a history of mental health concerns - among individuals reporting mental health concerns, microdosers exhibited lower levels of depression, anxiety, and stress across gender - health and wellness-related motives

were the most prominent motives across microdosers in general, and were more prominent among females and among individuals who reported mental health concerns. (15)

13. Mommies who microdose for anxiety and depression are among the fastest growing groups of followers in the psychedelic movement, according to industry observers and academics studying psilocybin. (16)

CHALLENGES IN CONVENTIONAL MICRODOSING:

1. In a 2019 study, (4) both the Benefits and Challenges of Conventional Microdosing were evaluated.

2. In the category of Challenges, the highest-ranking item (29.5%) was the "illegal" status of the psychoactive compounds typically used in Conventional Microdosing techniques - the second highest Challenge (18%) was Physiological Discomfort.

3. As a comparison, the highest-ranking Benefits were Improved Mood (26.6%), Improved Focus (14.8%) and Creativity (12.9%).

4. It is noteworthy that the "illegality" Challenge (29.5%) ranked higher than the "Improved Mood" Benefit (26.6%).

5. A second study from 2020, (5) determined:

*the three most common challenges of microdosing will be concerns about illegality, physiological discomfort and impaired focus.

*the majority of participants who micro-

dose will not have tested the substance they used to microdose.

*participants who report an approach-intention will report significantly more benefits than participants who report an avoidance-intention.

6. Another more recent study from 2021 (6) found the most frequently cited reasons for quitting (Conventional) microdosing were the risks associated with taking an illegal substance (24.28%) and the difficulty of obtaining psychedelic compounds (22.63%).

7. "From anecdotal experience, a medium-strength dose of psilocybin is 2 to 3 grams of dried mushrooms, and a microdose is typically around 0.3 grams. One obstacle is that the potency of mushrooms can vary greatly, as they are not regulated outside of clinical trials; so, this isn't an exact science. Likewise, LSD is an invisible, tasteless, odorless substance that usually comes either in liquid form or embedded into a piece of paper to be slipped under the tongue» (8)

8. Given its current illegality and lack of regulation, there is no good way to know what dosage you are taking unless you have an extraordinarily reliable supplier. LSD is an extremely powerful and long-acting drug, and you don't want to take more of it than intended. Further, psychedelics such as psilocybin and LSD can produce physiological tolerance, which might suggest that, even if microdosing does help, there could be diminishing returns if one stays at the same dosage." (8)

9. "Psilocybin is a compound produced by almost 200 species of fungi (mushrooms), and the mushrooms must come from a trusted source. It is very easy to poison oneself with the wrong type of mushroom, as there are many types of mushrooms in nature that can look quite similar to each other, but some are poisonous and can harm your liver, causing severe illness or even death." (8)

10. Because low, "micro", sub-perceptual doses are key to the process, another Challenge in Conventional Microdosing is the lack of obvious positive, attractive subjective experience – consequently, the user must rely primarily on trust, belief and/or intention as the motivator that maintains

continued compliance to the prolonged schedule and commitment.

11. One of the key motivators in compliance is the subjective "reward" that is inherent to higher dosing of a psychoactive compound – this real-time subjective experiential reward is lacking in Conventional Microdosing which leads many users into actually increasing the sub-perceptual micro-dose to more of a feel-good, "meso-dose" of the compound.

12. Fundamentally, Conventional Microdosing relies significantly on a combination of belief and delayed gratification.

13. There is an inferred medical concern related to Conventional Microdosing of serotonergic psychedelic compounds that focuses on the valves in our heart. There is a pathology known as valvular heart disease (VHD) as associated with a class of medications with strong serotonin 2B receptor (5HT-2B) binding affinity – because LSD and psilocin also bind to the 5HT-2B receptor, there presents an indirect concern that the low dose compounds taken repeatedly over a period of weeks to months may create an increased risk of VHD. (7)

14. "In an epidemiologic case-control study of 29 MDMA users who averaged 3.6 tablets per week for 6.1 years, 28% had VHD confirmed by echocardiography versus none in the gender- and age-matched controls. This evidence demonstrates that chronically dosing another "psychedelic" with 5HT2B affinity, even when only taking a few doses per week, has also been associated with VHD. Though derived from an epidemiologic study rather than a randomized controlled trial (RCT), this is a troubling statistic, since the psychedelics LSD and psilocybin used for microdosing have even stronger binding affinity for 5HT2B receptor than MDMA and its active metabolite MDA (+LSD Ki = 30 nM, psilocin Ki= 3.6 nM; MDMA Ki = 500 nM, MDA Ki = 100 nM), in addition to their "psychedelic" 5HT2A receptor effects." (7)

CALL IT ADAPTATION. CALL IT NEW LEARNING. CALL IT NEUROPLASTIC CHANGE.

Garnet Dupuis

ALTERNATIVE THEORY FOR MICRODOSING
IS MICRODOSING A SPECIAL FORM OF BRAIN PRIMING?

INTRODUCTION.

The concept of psychedelic Microdosing is moving in waves throughout society and offers strong promise in many areas from depression to creativity and performance.

Science is rapidly pursuing quality research to fortify the numerous positive anecdotal reports that move from friend to friend and often into social media.

So, a question could be...is Microdosing an entirely new process or does it have any history that could support the claims?

Let's talk about the principle known as Brain Priming.

Fundamentally, the brain is always trying to make sense out of nonsense – finding signal in the noise. Brain Priming works to optimize the search for new signals amidst that noise.

Call it adaptation. Call it new learning. Call it neuroplastic change.

It is possible to increase the "learning" efficiency of the brain by preparing it with sets of sensitizing signals that allow for better message recognition and integration.

Brain Priming is the influence a previous experience has on our likelihood of responding in a particular way later on.

BASICS OF BRAIN PRIMING.

Scientifically, Brain Priming was first investigated in the field of behavior-based psychology in the 1950's and then later semantically in the 1970's. It became apparent that semantically (meaning "involving words") when a person was shown a word from a certain topic, the person would then be able to more quickly recognize another different word that was also from the same topic.

For example, if first shown the word "doctor", the person would then more easily recognize the word "nurse" within a group of unrelated words.

In general terms, there are two types of "brain priming":

1. Psychological Priming
2. Physiological Priming.

Certain methods can integrate the two forms in sequenced or overlapping processes.

Priming represents an example of what is often referred to as implicit memory – a nonconscious influence of past experience on current performance or behavior.

Priming is often assessed with experimental tasks that do not require conscious recollection of particular previous experiences.

Brain Priming presents a range of creative design possibilities. In designs, two approaches can be considered.

The first is more direct and is known as "modal-specific". This means the priming action is directly related to the following main action.

The second design approach is called "cross-modal". In cross-modal, the priming action is not directly related to the main action and acts indirectly to facilitate the subsequent main action.

An example of "modal-specific" Brain Priming could be Movement Priming in which the person gently rehearses the motions they will use in the subsequent main action. Picture a basketball player, softly rehearsing his free-throw attempt

at the foul line before they take the actual shot.

An example of "cross-modal" Brain Priming could be "semantic" in which the person mentally repeats positive words or phrases associated with calmness or confidence before engaging in the subsequent main physical action.

Priming is often the result of a three-step process:

1. First, a person is exposed to a priming stimulus, which could be any of the six types (described below).

2. Second, the priming increases accessibility in the aspect of the brain that is related to the priming message. This increases the likelihood of better encoding the main signaling which will follow.

3. Finally, the newly activated representations result in an increased integration of the main signal messaging.

There are two apparent neural mechanisms for priming: gating and homeostatic plasticity.

1. Simultaneous Effect:

Gating occurs by disinhibition of intracortical inhibitory circuits. It is a neurochemical action involving calcium. Gating is instantaneous and happens simultaneously with the activity.

2. Delayed Effect:

Homeostatic plasticity is the ability of neurons to increase excitability after a period of low synaptic activity is related to changes in postsynaptic glutamate receptors. The time scale of homeostatic plasticity, takes place over a longer period of time when compared to gating. The state of the neurons is modulated prior to training in order to induce synaptic plasticity.

So, the **Simultaneous Effect** of gating is involved with the priming effects that are simultaneous with the main action while the **Delayed Effect** of homeostatic plasticity priming effects modulate the neurology before the main action.

With this in mind, it becomes easier to appreciate the variations in Brain Priming methodologies.

Following this understanding, it is easier to appreciate the method of microdosing as related to the **Delayed Effect** of homeostatic plasticity.

Technically, when considering physiological Brain Priming, the term "cortical neuroplasticity" is common especially in rehabilitation techniques. Priming prior to traditional therapeutic interventions, such as manual and exercise therapy, are capable of improved clinical outcomes.

We all want our brain to be healthy and function well. Knowing confidently that even our adult brain can still keep learning and changing through neuroplastic adaptation opens up a long list of action strategies.

Prepping that adaptation with various forms of Brain Priming makes a lot of sense. Much of childhood adaptive learning comes from natural imitation and mimicry. Adult adaptive learning can benefit from the same, no doubt.

The brain priming paradigms that are supported by the greatest amount of evidence are:

1. Psychological/Semantic – based (eg. verbal language/body language)
2. Energetic Stimulation – based (eg. electromagnetic);
3. Mental/Motor Imagery – based (eg. visualization/mental rehearsal);
4. ***Sensory – based (eg. light/sound activations – Drug-Free Microdosing.)***
5. Movement – based (eg. rehearsal pre-task no-load movements);
6. ***Pharmacological – based (eg. Conventional Microdosing using psychoactive compounds).***

Considering the list above, it is easy to recognize that the methods and techniques considered to be Brain Priming are increasingly dynamic and expansive. The unifying principles also appear to fit nicely into the features of neuroplastic brain change. In neuroplasticity methods, the logical "state to trait" condition is foundational. Another way of expressing it is initial "activation" followed by "installation".

WHAT NEUROPLASTICITY TEACHES US ABOUT BRAIN PRIMING.

The "plastic" capacity of the brain opens the door to techniques that more efficiently advantage this ability of change.

A Brain Priming action is intended to make the initial short term "state" or "activation" stimulation more effective.

One could say that a Brain Priming activity better potentiates the effects of any neuroplastic "activation" process.

We also know that the neuroplastic "trait/installation" change aspect requires regular reinforcements of "Fire Together to Wire Together" principles.

So, it doesn't take much to begin to see that the neuroplastic brain capacity for change integrates with the potentiating features of Brain Priming which also nicely overlap with the regular and repetitive characteristics of "pharmacological" Microdosing methodologies.

MICRODOSING.

Back to Microdosing – basically, the idea of Microdosing is to use a low-dose, sub-clinical psychedelic compound to potentiate a psycho-neurological shift or change. Originally, the process was enabled by either LSD or psilocybin.

Currently, many other compounds are involved experimentally which supports the concept of a potentiating "psycho-active agent" rather than a chemical limitation specifically to either LSD or psilocybin.

The potentiating "psycho-active agent" may in fact extend even beyond biochemical psychedelic compounds into biophysical potentiating "psycho-active agents" as exampled by the NeuroVizr® Light/Sound approach know as **Drug-Free Microdosing.**

In conventional Brain Priming, pharmacological agents are among the oldest and most common adjuvants for inducing priming effects. Based on successful animal studies, five groups of pharmacological agents have been proposed to enhance motor recovery after neurological injury: amphetamines, dopaminergic agents (DA), norepinephrines (NE), cholinergic agents (ACh), and selective serotonin re-uptake inhibitors (SSRI).

Focusing specifically on the last item (selective serotonin re-uptake inhibitors - SSRI) and aligning them for comparison with the well-known serotonin dynamics associated with certain psychedelics seems like an obvious first step consideration.

Generally thinking, once accepting that pharmacological agents (listed above) can act as effective Brain Priming potentiating "psycho-active agents", it is but a very small step to consider the probability that psychedelic compounds, in proper sub-perceptual doses, can also act to support the integration of subsequent stimulation and information.

BACK TO BRAIN PRIMING:

In conventional physiology, it is recognized that the vast majority of self-regulation and adaptive functions occur at either subconscious or unconscious levels of awareness.

This perspective integrates nicely with the fundamental appreciation that various Brain Priming techniques can act efficiently at unconscious levels (aka "implicit memory").

Conscious attention and/or awareness may or may not be required for a Brain Priming process to yield an effect.

Remember that the principle of Brain Priming (as stated above) is the influence a previous experience has on our likelihood of responding in a particular way later on.

Here is (simplified) an example of psychological semantic Brain Priming:

1. Two homogenous groups of people were separated into Group A and group B;

2. Each group was given a list of words with letters scrambled;

3. The (seeming) simple task was to unscramble the letters to discover the original words:

4. Unknowing to the groups, Group A was given a list of negative words (eg. hate, war, fight, etc) and Group B was given a list of positive words (eg. love, compassion, friend, etc);

5. The directions given were to unscramble the words and then go into an adjoining room and report your results to the study director who was waiting at a desk in the adjoining room;

6. BUT...also unknowing to the groups was the fact that the experiment also involved having another unrelated person standing at the desk of the study director and being engaged with the study director in such a way as to obstruct the group person attempting to make their report – the actual experiment was designed to measure the amount of time the reporting would wait (aka be patient and tolerate) before interjecting into the obstructing conversation;

7. You guessed it...the Group B (with positive words) waited about 8 minutes before interjecting themselves while the Group A (with negative words) waited about 3 minutes;

8. Result – unconscious semantic Brain Priming with positive words enforced subsequent patience and tolerance while Brain Priming with negative words enforced subsequent impatience and lack of tolerance.

IS MICRODOSING A SPECIAL FORM OF BRAIN PRIMING?

There is a good argument for saying YES, Microdosing is a special form of Brain Priming. And, if so, this perspective can certainly give a strong push to validate Microdosing based on reasonable and acceptable psychophysiological precedents in accepted science.

Categorically, as a special form of Brain Priming, Microdosing (Conventional or Drug-Free) would be a bio-chemical compound and/or bio-physical stimulation, cross-modal approach relying principally on sustained long term homeostatic plasticity dynamics for induced neuroplastic change.

That's a mouthful!

THE FOUNDATIONAL PHYSIOLOGY OF MICRODOSING PROTOCOLS.

BASIC CONCEPT.

Microdosing involves some type of structuring concept typically called a "protocol". This would be true regardless of whether a person is considering Conventional Microdosing using psychoactive compounds or Drug-Free Microdosing using Light/Sound or even some combination of the two (Conventional & Drug-Free).

As a general reference regarding Conventional Microdosing, The Third Wave project created by Paul Austin is a respected source of tons of information. See "the thirdwave.co" online. Their information is expanding beyond microdosing for those interests in related topics. Another excellent and well-developed source for information regarding microdosing is the Microdose Institute online at https://microdosinginstitute.com.

For a fun and more personal exploration of microdosing, Janet L. Chang has posted (some time ago - 2017) *"The Curious Beginner's Guide to Microdosing Psychedelics for Work, Relationships and Happiness". See "https://betterhumans.pub/the-curious-beginners-guide-to-microdosing-for-work-relationships-and-happiness-7ceff261e9fb".*

It still holds up well for honesty and a great example of an earlier perspective when there was very little guidance or real experience.

There is no single "best effect & proven" Microdosing protocol. In many cases, there is still a certain amount of personal experimentation involved in figuring out what works best for you. This experimentation is made more elusive when one is not quite sure what to look for as evidence that it is "working" or not. It is very likely that variations on basic protocol structures all work "well-enough" to provide the incentive to stay committed to the process. Then there is the issue of which agent to use – LSD, mushrooms or any number of new proposed chemical compounds including MDMA and cannabis...or whether to go "drug-free" and use some other bio-physical agent such as light/sound processes.

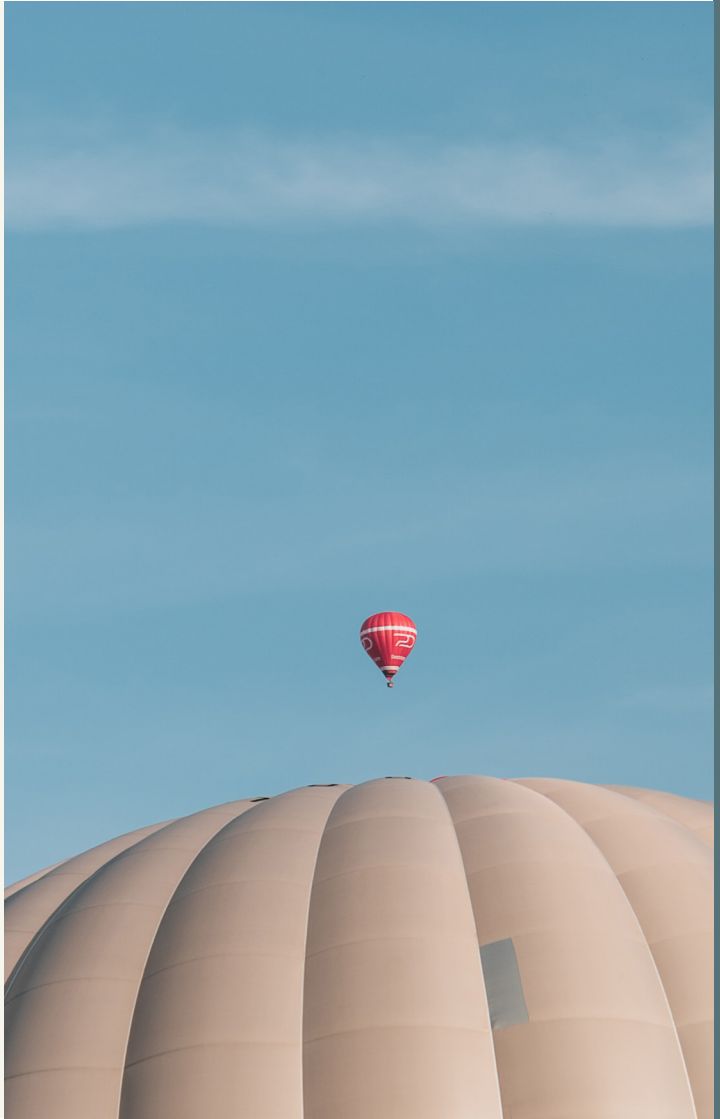
One thing for sure is that the best choice is one that you will actually do with a reasonable amount of commitment and discipline over the typical time required for benefit and outcome.

ABOUT NEUROPLASTICITY.

"It is hypothesized that neurobiological changes, specifically enhanced neuroplasticity, underlie psychedelics' therapeutic effects. Evidence from preclinical studies shows that psychedelics acutely stimulate structural neuroplasticity processes at a molecular and (sub)cellular level after a single dose. Repeated administration of psychedelics is shown to stimulate neurogenesis acutely and molecular plasticity, sub-acutely." (21)

There is evidence that low-dose levels of serotonergic hallucinogens such as LSD and psilocybin do produce degrees of neuroplastic excitation in the brain. Brain Derived Neurotrophic Factor (BDNF) values which are indicative of neuroplastic activity have been detected in the blood following low-doses of the compounds (1, 2, 3).

Neuroplasticity in the human brain is increasingly well studied and related understandings could have a direct impact on the designs and rationale of microdosing protocols.



Neuroplastic Processes follow predictable structural dynamics. In one popular approach, neuroplasticity is regarded in four inter-related and overlapping stages. The four are:

TAKES PLACE IN "MOMENTS"

Preexisting under-functioning synaptic connections that already exist are aroused into higher levels of efficient function.

TAKES PLACE OVER DAYS TO WEEKS

New and different synaptic pathways are created to accommodate new demands.

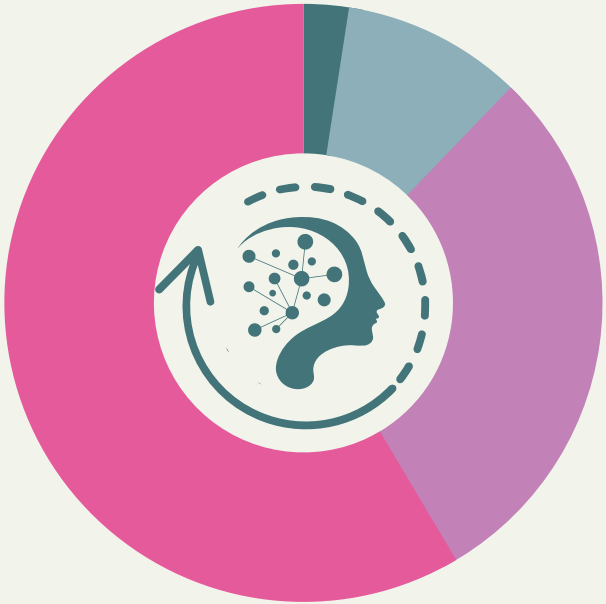
TAKES PLACE OVER MONTHS

New and different physical nerves (neurons) are created to allow the new synaptic connections and patterns.

TAKES PLACE OVER YEARS

The new physical neurons and their evolving signal connections and pathways are integrated into all of the global systemic metabolic, adaptation and self-regulatory aspects of the organism as a whole. (19)

For an even deeper look at neuroplastic dynamics that is more directly applicable to the "microdosing" concept and its protocol structures - There are four basic stages or steps that happen as the Brain as a Whole responds to Neuroplastic Change:



Now let's break these down to better understand.

Neuro-Stimulation (0-2 hours): Known as the «Input reaction». Similar to feeding a hungry brain with essential information, addressing its appetite for learning and problem-solving.

Neuro-Modulation (2-8 hours): Termed the «Reaction response». As it takes effect, Brain Networks see enhanced function, diminishing super-sensitivities arising from a lack of certain Adaptive responses.

Neuro-Relaxation (8-24 hours): Described as the «Relief response». Post Neuro-Modulation, it re-adjusts arousal levels and alleviates super-sensitivities, emphasizing the brain's «Rest & Restore» phase during deep sleep.

Neuro-Differentiation (24-48 hours): Referred to as the «Relief result». Represents the lasting stage where sustained learning integrates into Stable State brain function, setting the stage for the recovery of lost abilities.

To go even further into the specific science and from a somewhat different perspective, we can look at the neuroplastic dynamics in targeted steps.

At a molecular level, neuroplastic changes occur via signaling pathways, that is, cascades of intracellular proteins transmitting signals from receptors to the DNA. (21, 22)

At a cellular level, changes can be structural or functional. Neuronal plasticity consists of neurogenesis, the generation of neurons, and occurs in distinctive phases. (21, 23) Dendritic plasticity includes changes in the number or the complexity of dendritic spines, where a high number of spines and complex dendritic branches reflect more synaptic strength (21, 24, 25).

At the synapse, the strength of synapses is related to learning and memory formation. Synaptic plasticity is regulated by various factors, with the protein BDNF as the primary regulator; BDNF is expressed highly throughout the central nervous system, particularly in the hippocampus. (21, 26)

NEUROPLASTICITY VS. NEUROELASTICITY.

The term and concept of "neuroplasticity" is well known as the ability of the adult brain to undergo positive synaptic and neuronal changes over time. The much less known concept of "neuroelasticity" is usually described as "reversible neuroplasticity" which means that once a neurological state has evolved into a long-lasting trait, that condition will possibly revert back to its old condition unless it is reasonably reinforced. It is another application of the "use it or lose it" process.

Here, we are using the term "neuroelastic" in a new and unique way.

Before we have a deeper look at this new use of the term "neuroelastic", lets examine the basic meanings of "elastic" as compared to "plastic". Both words come from the Greek. "Plastic" means as the shape is deformed or changed, it will stay in this new shape configuration (hence the term "plastic surgery" – does not mean the material compound of plastic is used but rather that the new surgical shape will persist after the surgery). "Elastic" means as the shape is deformed or changed, when the force of change is removed, the shape

will return to its original form (think of an elastic band which snaps back after being stretched).

So, what is the new and unique meaning here for "neuroelastic"?

Our adult human brain is not a static organ. It must be constantly active and responsive to adaptation demands. We now know that our brain remains very active even during sleep as it traverses in and out of many conditions and states. Our sleeping dreams are famously dynamic and, in some senses, hallucinogenic. Our prolonged waking state is a complex mixture of conditional cognition ranging from intense concentration to lofty day dreams, all saturated with a variety of emotional "feelings", pleasures and pains. The transitional hypnagogic (waking to sleep) and hypnopompic (sleeping to wake) states are an alluring mix of creative information and vivid imagery.

Then we also have the dramatic and expansive "altered states", "mystical states" and "non-ordinary states" of consciousness that can be experienced from a profound list of triggering "agents".

All of this means that our brain is innately designed and capable to shift into all of these various "states" or conditions. And, our brain can move fluidly back out of these states in the constant dance of adaptive activity. ***This is, here, the new assigned meaning of "neuroelastic" – the ability of our brain to enter a certain state as an adaptive response and then, like an "elastic band" return back to its previous state or even another additional state as required.***

This "neuroelastic" quality is clearly evident even in our basic circadian cycle as well as in "macro" movements related to special forms of stimulation. These "special forms of stimulation" are none other than the "**psycho-active agents**" explored here in this guide.

In this sense, the innate "neuroelastic" capacity of our brain is a very positive feature of natural, healthy brain activity. When our brain gets "stuck" in a state and is not able to adjust in and out of that condition, we have problems with unprocessed experience and even the expression of pathological conditions. The "neuroelastic" capacity of our brain is then being inhibited or restricted.

So, here we have two definitions of "neuroelastic":

*The conventional and seldom discussed meaning of "reversible neuroplasticity" in which an established neuroplastic change is not reinforced and the brain slowly evolves back to an original behavior (use it or lose it) – this is a slow incremental process;

*The new meaning in which our brain is capable of moving fluidly in and out of adaptive responses and states that are positive for certain periods of time – this fluid behavior can be fast and is dependent on the need for state change in the moment.

NON-PSYCHEDELIC COMPOUND INDUCED NEUROPLASTICITY:

The premise underlying Drug-Free Microsdosing is that the human brain has a range of innate natural and normal states of consciousness which includes what is typically referred to as "non-ordinary" or psychedelic. Furthermore, the premise declares that these uncommon "non-ordinary" states can be stimulated into expression with many "psycho-active agents" that are not conventional serotonergic hallucinogens (aka "psychedelics"). These agents may be bio-chemical compounds (such as a classic hallucinogen), bio-physical sensory or energetic stimulations (such as uniquely crafted light/sound) or cognitive methodologies and/or techniques (such as meditation)..

A "**psycho-active agent**" is any stimulation process, including bio-chemical, bio-physical, psychological and methodological techniques, that "*affect mental processes eg. perception, consciousness, cognition or moods and emotions.*" Not only does this approach expand the mind altering "agency" possibilities but it also removes the implied "negative bias" that occurs with the use of the term "drug" which is only slightly softened by making some of the "agents" "substances".

The typical "not-so-hidden" message is that any "psycho-active" activity is bad even if the motivation is one of relief, healing, exploration, new learning and self-discovery. This is an odd bias considering the massive medical and social acceptance of pharmaceutical drugs many of which are specifically designed to affect psycho-emotional states..

CAREFUL WITH NAMES:

It is quite obvious that psychedelic compounds are "psycho-active agents". It must also be said that although all psychedelic compounds are "psycho-active agents", not all "psycho-active agents" are psychedelic compounds. (BTW, notice we have abandoned both "drug" and "substance" terms in favor of "compound" for a little social neutrality.)

Keep in mind the criteria for qualifying as a "Psycho-Active Agent" is that it "*affects mental processes eg. perception, consciousness, cognition or moods and emotions.*"

The term "psychedelic" is currently used very loosely and even inaccurately. Surprisingly, perhaps the best example would be in the developing professional medical treatment approach known as Psychedelic Assisted Therapy (PAT). In PAT, compounds such as ketamine and MDMA are being explored which are not classic "psychedelics" in molecular structure or neurological process which raises a red flag.

The term psychedelic, from the Greek for "**mind-manifesting**", was coined by Humphry Osmond, a British psychiatrist working in Canada in the 1957. "To fathom hell or soar angelic / Just take a pinch of psychedelic," he wrote in a letter to the writer Aldous Huxley.

For example, *"the antidepressant effects of ayahuasca may also be produced by its non-psychedelic β-alkaloids harmine, tetrahydroharmine, and harmaline present in the ayahuasca brew. Findings from in vitro and in vivo studies show that these compounds stimulate neurogenesis, BDNF, and have antidepressant effects. Neuroplastic changes induced by ayahuasca may result from DMT, β-alkaloids, or an interaction between these compounds, something that should be taken into consideration when interpreting findings from biological studies using ayahuasca." (21, 27, 28, 29, 30, 31)*

"T*he dissociative ketamine is another substance whose antidepressant effects are suggested to result from enhanced BDNF and synaptic plasticity*". (38) Ketamine is not a serotonergic hallucinogen ("psychedelic") yet it demonstrates positive BDNF and neuroplasticity.

Another very significant but largely unexplored factor is that of gender. Does being female or male make a difference in the actions and results?

"T*he second significant finding concerns sex-differences in response to psychedelics, which were shown in a preclinical study where male, but not female rats showed increased anxiety behavior directly after prolonged ayahuasca administration. T<u>his could be related to sex-specific changes in neuroplasticity.</u> The female sex hormone estrogen exhibits antidepressant effects through stimulation of BDNF and synaptic plasticity, in a manner that is distinct for males and females. In that line, female rats showed greater sensitivity to the antidepressant effects of ketamine than male rats, and effects were abolished in rats whose ovaries had been removed and restored when estrogen and progesterone were supplemented. The antidepressive effects of ketamine and psychedelics are both suggested to result from changes in neuroplasticity, and these findings indicate a potential role for gonadal hormones in the sex-specific response to these substances. Neurobiological research in animal models is biased toward males.*" (21, 32, 33, 34, 35, 36, 37)

WHATEVER THE STATE OF YOUR BRAIN TODAY, IT CAN BE BETTER TOMORROW.

Garnet Dupuis

IS A PSYCHO-ACTIVE AGENT DYNAMIC INVOLVED IN THE NEUROPLASTIC PROCESS?

There are numerous studies that recognize that classic psychedelic compounds are directly involved in neuroplastic brain changes. "Clinical studies suggest the therapeutic potential of psychedelics, including ayahuasca, DMT, psilocybin, and LSD, in stress-related disorders. These substances induce cognitive, antidepressant, anxiolytic, and antiaddictive effects suggested to arise from biological changes similar to conventional antidepressants or the rapid-acting substance ketamine. The proposed route is by inducing brain neuroplasticity. (Front Psychiatry. 2021; 12: 724606. Psychedelics and Neuroplasticity: A Systematic Review Unraveling the Biological Underpinnings of Psychedelics, Cato M. H. de Vos, Natasha L. Mason, and Kim P. C. Kuypers)

The question then is whether other non-psychedelic compound "psycho-active agents" are also capable of inducing brain neuroplasticity.

"Neuroplastic mechanisms are triggered by various natural or artificial stimuli, which may arise in the internal or external environment, and they may differ quantitatively or qualitatively. Manifestations of plasticity have probably the same basis, irrespective of the cause which triggered them or the brain region where they were accomplished." (Physiol Res. 1999;48(2):87-97. Theoretical aspects of neuroplasticity, S Trojan , J Pokorný)

Learning experiences and environments that offer plenty of opportunities for focused attention, novelty, and challenge have been shown to stimulate positive changes in the brain. Packaging "focal attention" with unusual and surprising qualities increases the probability of neuroplastic change. Adding some modest or reasonable level of challenge creates again another level of benefit.

Sensory Enrichment is a subset of the larger concept of Environmental Enrichment which has demonstrated significant positive neuroplastic growth for many decades of experimental research.

DRUG-FREE MULTI-SENSORY NEUROPLASTICITY:

Drug-Free Microdosing is a process based on "multi-sensory integration" which promotes functional neuroplastic changes over time. Technically, this approach is considered "cross-modal" because the form of stimulation (multi-sensory light/sound) and the expression of the outcome (cognitive, mood and behavior) are in separate but related domains. For another perspective on "cross modal", see above in the **«Is Microdosing a Special Form of Brain Priming?**" section.

"*The human ability to perceive and understand the surrounding world relies essentially on multi-sensory integration, as incoming information from multiple senses is unified in order to form a coherent percept, or segregated in order to dissociate distinct events.*" (41)

"*Multisensory integration refers to the process by which a combination of stimuli from different senses (i.e. "cross-modal" stimulus) produce a neural response product that differs significantly from that evoked by the individual component stimuli, indicating a fusion of information.*" (40)

The Role of Sensory Enrichment.

Diving deeper into experiential techniques, Sensory Enrichment emerges as a crucial subset of the overarching Environmental Enrichment concept. Historically backed by decades of research, this approach emphasizes:

*Merging two distinct senses, such as touch with smell or light with sound.
*Crafting an experience that's novel and unexpec ted.
*Ensuring a distraction-free environment that per mits undivided attention
*Guaranteeing participant's free will and consent.
*Making the experience intrinsically enjoyable.

In essence, Sensory Enrichment operates as a psycho-active agent. The unique blending of multi-sensory signals not only facilitates delightful «altered states» but also fosters long-term, beneficial neuroplastic growth.

Targeted Neuroplastic Techniques.

Parallel to Sensory Enrichment are the targeted neuroplastic methods, which pivot on a set structure comprising:

*Focal Attention: Attention without «tension».
*Marginal Demand: Slightly pushing past one's comfort zone.
*Open-minded Willingness: A genuine belief or rea diness, not coerced.
*Enjoyment: The essential 'secret sauce' amplifying the method's efficacy.

DRUG-FREE MICRODOSING DYNAMICS

There are different types of change as we can see from the neuroplastic information stated before. Essentially, in the simplest view, the changes can be short term or long term. Short term is typically labeled "state change" and long term is "trait change". Semantically, it reflects the difference between the original Greek terms of "elastic" and "plastic". "Elastic" would be comparable to "state change" in that it is a more temporary shift that will likely return to its original ordered condition once the provocative influence is withdrawn. "Plastic" would be like "trait change" that tends to persist once the shaping influence ceases.

This dual dynamic is much discussed in psychedelic forums as it applies to whether a person can maintain and integrate into their life insights experienced when "tripping" or whether the insights simply disappear as in a dream. Elastic or plastic?

The concept of change implies a movement from one ordered state and into another new and different ordered state. Microdosing expects that brain/mind change is possible and this expectation is in alignment with modern neuroplastic principles.

Destabilization & Chaos:

Psychedelic compounds reliably induce an interruption of normal neural organization, disrupt certain key neural networks and permit an unfiltered flood of unpredictable sensory stimulation throughout the brain. In effect, they successfully reduce Order and introduce Chaos for a sustained period of time ranging from 2 to 12 hours. **It is suggested that we recognize the serotonergic psychedelic substance as a temporary "destabilizer" of ordered processes.**

In full "macro" dose applications, the destabilization is profound with evident modifications in consciousness. In "micro" dose applications which are sub-perceptual, the expectation is that the "glue" of Order and Habit is just slightly softened permitting neural-energetics to proceed along their habitual courses with a mildly increased degree of liberty and choice not typical of their metabolic set points.

The proposal here is that there are other available neural "destabilizers" which can reliably trigger "microdose" levels of adaptive regulation – specifically, in this case, uniquely crafted Light/Sound Drug-Free Microdose Experiences.

Tempered Instability:

The Ordered state of efficient Adaptive Learning, has strong integrity that resists breakdown. The Predictive nature of habitual brain functions makes it very difficult to rearrange neural responses while the patterns remain cohesive. Fortunately, like all CAS (Complex Adaptive Systems), the brain is always dancing at the edge of Chaos and this drift into Chaos can be induced and sustained within reasonable limits. It is when the "filters" weaken and "noise" is allowed to increase that the doorways to new adaptive learning open up.

This is the basis of neuroplastic change and rests at the heart of compositional designs and is especially prominent in **the Drug-Free Microdosing Collection.**

Using special Light/ Sound signal structures, it is possible to induce and temporarily sustain an unstable condition in the brain. In positive processes, it is critical that the degree

and length of the destabilization be controlled to match the neuroplastic capacity of the individual. This is the basis of the term "Tempered Instability" as it respects the relation of the neuroplastic demand with the common neuroplastic capacity of the human brain.

In the composition, Tempered Instability is used judiciously to first "soften the glue" of Order and trigger a positive degree of Attention without pushing it too far into Vigilance or, worse, Threat. Later in the composition, one or more periods of Tempered Instability are typically reintroduced as "message challenges" or "induced conflict" with the purpose of reinforcing the cardinal new information.

At a foundational level, once the initial Tempered Instability is introduced and the Attention (Attention is the key trigger in any neuroplastic action) has been aroused, the composition immediately introduces the Primary Attractor which carries the signals aligned with the main theme or "vector" of the composition.

After injecting the Primary Attractors, the Secondary Attractors are introduced which complement the Primary Attractors. The Secondary Attractors help create a messaging "context" for the Primary Attractors.

Tempered Instability & Drug-Free Microdosing Sessions:

Tempered Instability is a fundamental dynamic of a "microdosing" process using low dose, sub-perceptual *destabilization* generated by the psychedelic substance. Adequate degrees of *destabilization* can also be achieved using properly crafted light/sound stimulation techniques.

The degree of Tempered Instability in psychedelic microdosing is managed by the amount of the substance that is ingested combined with the frequency at which the dose is administered. In a Drug-Free Microdosing composition, the degree of Tempered Instability can be managed more precisely by modifying the light/sound signal characteristics along a number of technical parameters. As in the use of substances, the frequency of the dose is also an important factor (39)

DRUG-FREE MICRODOSING PROTOCOLS.

BASIC CONCEPT.

The Drug-Free Microdosing app has two basic and interrelated sections:

*The Drug-Free Microdosing Themes;
*The Drug-Free Microdosing Protocols.

When using the Drug-Free Microdosing app, you first choose the Theme and then you select the Protocol that will structure the process.

THE DRUG-FREE MICRODOSING THEMES.

The "Theme" supplies the specific frequencies and design elements that facilitate certain neurological and psychological "probability states". Each "Theme" offers unique and distinct sessions.

In Conventional compound Microdosing, the "theme" is primarily driven by a personal, intention-based psychological state. Conversely, in Drug-Free Microdosing, while the same psychological intention-driven state is generated through selecting the "Theme", what sets it apart (and this is crucial) is the inclusion of additional frequencies and intricate design structures of Light/Sound sessions. These sessions serve as a potent and effective neurological driver for the experiences.

This added Light/Sound-driven neurological stimulation mimics the adaptive neuroplastic stimulation achieved in Conventional Microdosing through the use of low-level biochemical compounds.

«THE IDEA BEHIND MICRODOSING IS NOT TO PERCEIVE IMMEDIATE CHANGES BUT TO NOTICE SHIFTS IN WELL-BEING OVER TIME.»

Dr James Fadiman

THE THREE STAGES OF EACH THEME.

Each Theme has three "stages" or variations tailored to the primary purpose of the Theme. These stages are rooted in the classical protocol structure devised by Dr. James Fadiman.

Dr. Fadiman was an early pioneer who acknowledged the benefits of high-dose psychedelics and their induced experiences, provided they were taken safely and in the right environment.

In 1966, he released a study titled 'Psychedelics in the problem-solving experiment,' which explored the positive effects of LSD on creativity.

This study remains a touchstone in hallucinogenic drug research. However, not long after its publication, the FDA banned all psychedelic research. (42)

Albert Hofmann, the creator of LSD, was known to microdose and reaped significant benefits from it.

Robert Forte, a researcher in the field of psychedelics, informed Fadiman about Hofmann's microdosing habit. This led Fadiman to write «The Psychedelic Explorer's Guide: Safe, Therapeutic, and Sacred Journeys» in 2011.

An entire chapter in this book is dedicated to microdosing. Here, Fadiman underscores his support for the «set & setting» approach for high-dose psychedelic experiences but posits that microdosing doesn't require such a setting.

He suggests that one can safely integrate microdosing into their daily routine. This groundbreaking publication attracted a diverse group, including creatives, software developers, and influential Silicon Valley entrepreneurs. (42)

The classic Fadiman Protocol :

This Protocol is based on a three "stage" and three-day concept.
This protocol repeats in a regular three-day cycle.

Dose Day

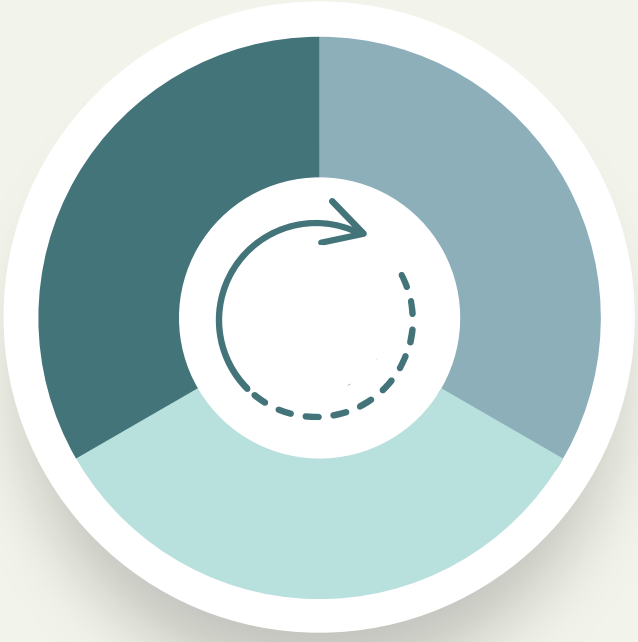
In Conventional Microdosing, when you take the compound.

Transition Day

In Conventional Microdosing, when you let the compound continue its effects.

Normal Day

In Conventional Microdosing, when you let the effect diminish.



The Drug-Free Microdosing Protocol :

In the Drug-Free Microdosing app, we have the same structure as a basic design feature.

Dose Day

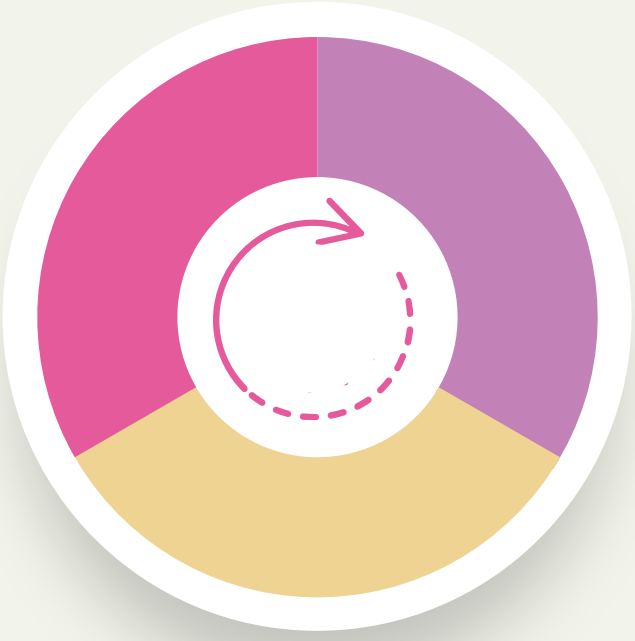
The Dose Day session has the highest level of neuroplastic demand and acts to trigger or activate the neuroplastic adaptive process.

Transition Day

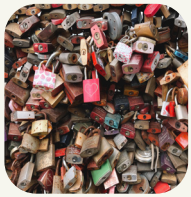
The Transition Day follows the same design structure but decrease the level of neuroplastic demand – this helps reinforce the neuroplastic adaptive process

Normal Day

The Normal Day also follows the same design structure but with a minimal amount of neuroplastic demand – this helps to integrate the neuroplastic adaptive process.



«THEMES» AVAILABLE IN THE DRUG-FREE MICRODOSING APP



Blockage : When things get blocked intellectually, psychologically, or emotionally, consider melting the barrier with gradual neuroplastic change rather than pushing forcefully.

Burn Out : When you go too far past the line for too long, the body/mind shuts down whether you like it or not. Turning to a safe port for healing becomes the only choice.

Calm : Anxiety can sit in your gut and lungs, diminishing focus and contentment. Rediscovering a relieving calm brightens your day and soothes your nights.

Creativity : Seeing with a fresh mind reveals unexpected new perspectives. The joy of creation bolsters the heart, and being open relieves pressure to force outcomes.

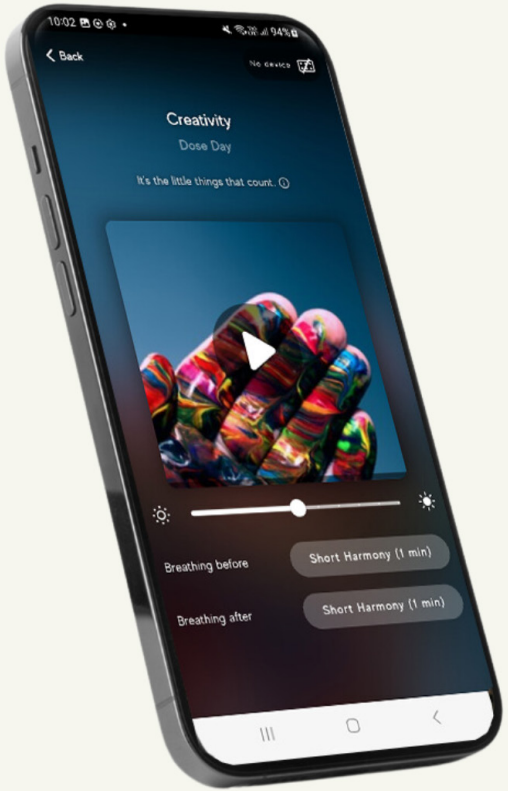
Dependency : Dependency stretches from negative habits to destructive addictions. Shifting to an expansive view steers tough decisions towards new goals and intentions.

Focus : The ability to generate attention without tension is a critical key in accomplishing any task. Focus without applying force results in sustained concentration without added effort.

Intuition : Amazing as intellect is, knowing without thinking exists. Intuition brings a deeper understanding, gentle yet dependable insights to the mind.

Motivation : Motivation is the spark that lights the fire. Tasks become reachable, gravity lighter with wind in your sails, propelling you along the path.

Uplift : A shadow may cast over your mind and heart. Depression steals air, burdens heart. Rising energy lifts mood, restores the bounce to your step.



THE FOUR PROTOCOL CHOICES IN THE DRUG-FREE MICRODOSING APP:

Along with the classic Fadiman Protocol described above, there three other established protocols to choose from to manage your Theme sessions. It is your open decision as to which protocol you choose to work to use.

For simplicity, the Fixed Weekly Protocol is set as the "default" protocol. It is the default protocol because it is the easiest to follow especially for beginners.

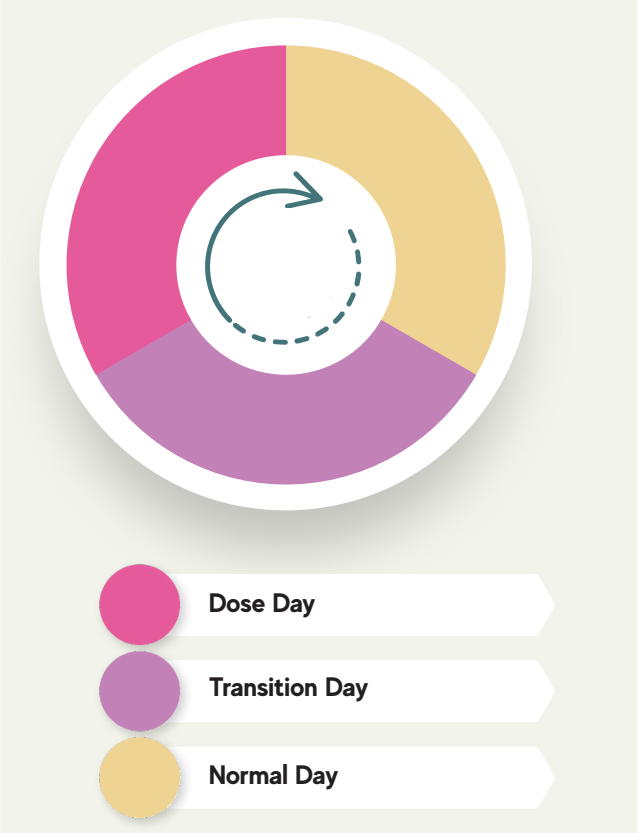
You will notice that not every protocol uses the complete three "stage" process.

Fadiman Protocol :

Cycle: Repeat this cycle continuously for 4 to 8 weeks.

Rest Period: After completing the cycle, rest without microdosing for 2 to 4 weeks.

Note: This protocol has withstood the test of time and remains a favorite among many microdosers.



Stamets Stacking Protocol:

Cycle: Continue the microdosing regimen for 4 weeks.

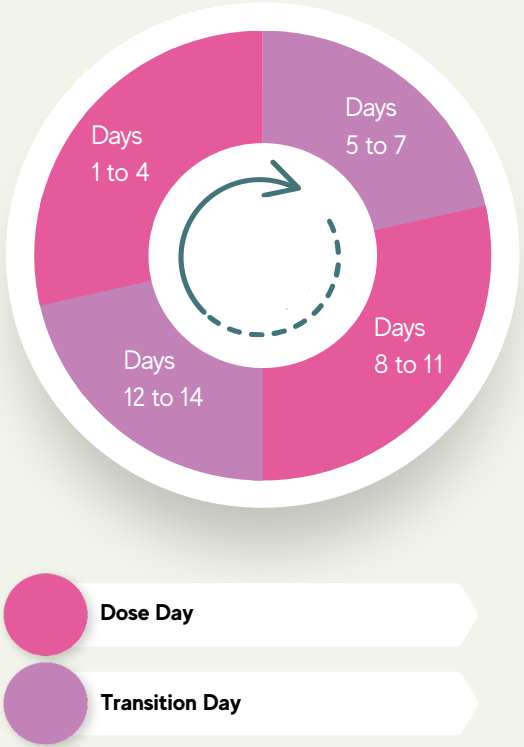
Rest Period: After completing the cycle, take a 2 to 4-week break from microdosing.

Notes:

*Due to Paul Stamets' esteemed reputation, his "Stacking" protocol has attracted significant attention. The very idea of "stacking" is intrinsically appealing. This concept is explored further in the context of the Drug-Free Microdosing app under the section "Stacking the Drug-Free Microdosing Approach".

*This protocol is characterized by its assertive stimulation, attributed to the frequent doses in short intervals and the addition of other compounds in the "stack".

*A distinctive feature of this schedule is the presence of only Dose Day and Transition Day, with no Normal Day in its framework.



Microdose Institute Protocol:

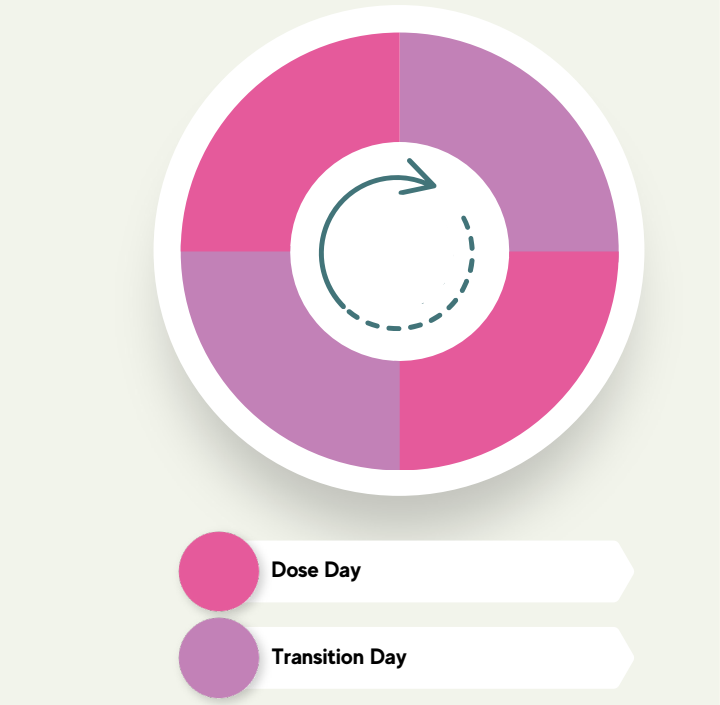
Cycle: Continue the microdosing regimen for 4 weeks to 8 weeks.

Rest Period: After completing the cycle, take a 2 to 4-week break from microdosing.

Notes:

*This approach is somewhere between Fadiman and Stamets – it is more concentrated than the Fadiman Protocol but not as demanding or complicated as the Stamets Protocol – for some users, this is a good compromise concept.

*You will notice, as in the Stamets Stacking Protocol, that this schedule has only Dose Day and Transition Day but no Normal Day in the structure.



Fixed Weekly Protocol:

*Choose two days of the week that are convenient for you

*Ensure there's a reasonable gap between these two days, for instance, Sunday and then Wednesday.

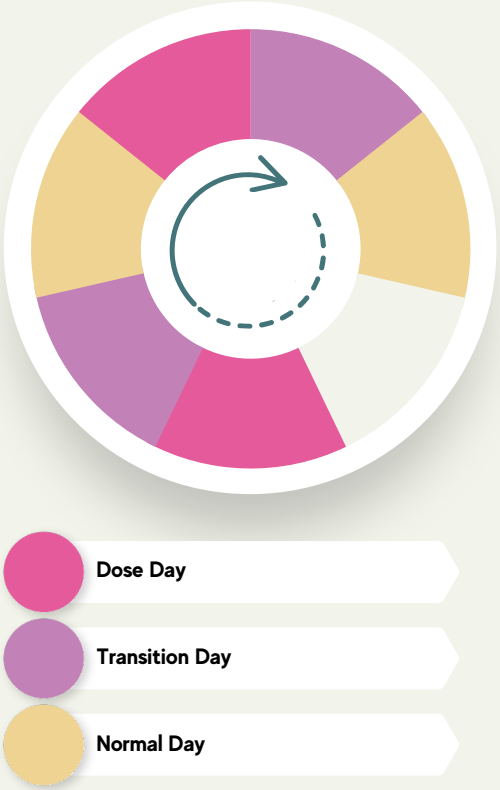
*Designate these chosen days as your regular Dose Days.

*Treat the days in between as yourTransition and /or Normal Days.

Cycle: Continue the microdosing regimen for a duration of 4 to 8 weeks.

Rest Period: After completing the cycle, take a break from microdosing for 2 to 4 weeks.

Notes: This approach can be lightheartedly termed as "Microdosing for Dummies" because of its simple structure. Its user-friendliness ensures high compliance and ease of remembrance. The structure of a seven-day week ensures that users naturally get a "day off", simplifying the process further.

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DRUG-FREE MICRODOSING - KEY QUESTIONS ANSWERED.

What is Microdosing?

Microdosing, a term derived from the roots «micro-» (from Ancient Greek «μικρός» meaning «small») and «dose» (referring to a specified quantity of a substance), literally means «small dosing.» It is the practice of consuming sub-threshold quantities of a substance to achieve specific benefits without the pronounced effects that a full dose might induce. While the concept applies to various compounds, it has garnered significant attention in relation to psychoactive substances like psychedelics.

What is Drug-Free Microdosing?

Conventional Compound Microdosing uses small amounts of psychedelic compounds to trigger gentle levels of positive, adaptive neuroplastic change in the brain. Drug-Free Microdosing acts to achieve the same positive results but uses uniquely crafted Light and Sound as the trigger and guide for this same neuroplastic change in the brain.

What are the main differences between Drug-Free Microdosing and Conventional Compound Microdosing?

1. The first is perhaps obvious. Drug-Free Microdosing does not require the use of a psychedelic compound for attractive benefits. Some users do choose to "stack" Drug-Free Microdosing with a micro dose of a psychedelic compound with the perspective that they enhance each other.

2. Drug-Free Microdosing offers 9 different "themes" that help drive and support the gentle brain changes. This is a huge advantage when compared to Conventional Compound Microdosing which relies almost entirely on mental intention as the driver of neurological change.

3. Drug-Free Microdosing has four popular protocols built into the software of the App that give you daily guidance in the process.

4. Drug-Free Microdosing does not rely on compounds that are illegal in most societies while also not risking unknown sources or questionable quality of compounds.

5. The luxurious Drug-Free Microdosing session experiences are richly satisfying while providing regular motivation and high levels of compliance.

6. Conventional Compound Microdosing uses a compound on the "Dose Day" and has no additional "reinforcement" or "integration" on the other Transition Day or Normal Day. Drug-Free Microdosing uses attractive dynamic light/sound experiences for each Dose, Transition and Normal Days.

Can you combine Drug-Free Microdosing with Conventional Compound Microdosing?

Yes, if that is your choice. This combination is a form of "stacking". "Stacking" is an approach to microdosing in which more than one form of neuroplastic stimulation is used simultaneously. "Stacking" has a broad potential and is at its early stage of exploration and discovery.

Is there scientific support for Drug-Free Microdosing?

Yes, and you might be surprised that it has existed for quite a while. The support comes from two related areas:

1. the Neuroplastic Capacity of our brain to change in positive ways when given the proper stimulation

2. Brain Priming which is the science of helping our brain change and perform more efficiently.

What is Neuroplastic Capacity?

The most exciting and meaningful recent scientific discovery is that our adult brain can still change in positive ways.
Given effective stimulation and support, we can not only make new connections, we can even grow new nerves in our brain despite the aging process. So, you can teach an old dog new tricks.

What is Brain Priming?

There are ways to help prepare our brain better when it comes to change and new learning. The ways can be bio-chemical (like a small dose of a psychedelic compound) or bio-physical

(like crafted Light & Sound). Basically, Brain Priming has two steps: introduce the stimulation that gets our brain ready to act commence the new activity. We call this one-two process Brain Prime / Brain Time.

Are there protocols to follow when we do Drug-Free Microdosing?

Yes, the protocols are actually the same protocols used in Conventional Compound Microdosing. These protocols reflect the neurological dynamics that are common in general neuroplastic changes in our brain. We follow the dynamics of our brain because that's where the changes happen.

What are the protocols used in Drug-Free Microdosing?

There are four protocols, all of which are derived from the general and evolving Microdosing principles:

1. Fadiman Protocol which is the first perhaps the best known

2. Stamets Stacking Protocol which is more complex and assertive;

3. Microdose Institute Protocol which roughly in between the two above;

4. Two Day Fixed Protocol which is, respectfully, Microdosing for Dummies.

How long do I have to use Microdose to get results?

The protocols all permit some range of time and commitment. In general, the advice is to microdose regularly following the protocol for 4 to 8 weeks followed by 2 to 4 weeks of rest with no microdosing.

Why has the Fixed Weekly Protocol been chosen as the default for the app?

The Fixed Weekly Protocol is the simplest approach to microdosing because the start of the dosing cycle always occurs on the same two fixed days of the week. It's ad-

vised to select two separate days in the week, preferably not consecutive days, like Wednesday and Sunday, for better compliance and effectiveness. Remembering these two days helps in ensuring adherence to the protocol. While there's no solid agreement on which Protocol is best in terms of results, everyone can agree that consistently following a Protocol is more important than any theory alone.

If I start with the Fixed Weekly Protocol, is it OK to switch to another protocol such as Fadiman or Stamets?

Yes, you can switch but use common sense when you switch. Jumping from one protocol repeatedly will not yield the best results.It is understandable that you may want to explore the different protocols and if so, do your best to give any one protocol a chance. For sure, each protocol has its own unique characteristics. Practicality and ease of use is itself a powerful factor

Is Drug-Free Microdosing safe?

Yes, it is safe based on 50 years of industry experience in the use of eyes-closed flickering light and pulsed sound. The exception is persons with seizure disorders who should avoid any flicker or pulsed signal device. Drug-Free Microdosing is completely under your control. You can adjust the general level of brightness and volume according to your liking. You can turn in "on" and "off" any time and for any reason.

Is Drug-Free Microdosing legal?

Yes, Drug-Free Microdosing is legal since it does not involve the use of any illegal substances. The technology used in Drug-Free Microdosing primarily relies on flickering lights and pulsed sound which are considered safe and non-invasive.

Is there a specific time to do the session?

Choose a time that is convenient for your daily schedule. It is better to do the session at approximately the same time every day but it is not mandatory.

What if I miss a session?

If you miss a session one day, simply jump back into the protocol the next day as if you had not missed the session. Can I do other sessions from the NeuroVizr® App while on Drug-Free Microdosing?

n general, try to achieve the most while doing the least. There is no actual "rule" as to what can or cannot be combined. Perhaps comparing it to body exercise would help. If you are working on regular stretching for flexibility, including some simple cardio could be fine but simultaneously doing strength training with flexibility can get very complicated.

Doing other NeuroVizr® sessions from the other Collections will be most compatible if the purpose or "theme" of these sessions align more or less with the Theme you have chosen in the Drug-Free Microdosing Collection.

What is the difference with the other NeuroVizr® collections & protocols?

There is a significant difference in the core design principles used in these other Collections The Drug-Free Microdosing sessions combine the light/sound signaling that drive the Theme of the session with the special type of light/sound signaling that acts at different levels of neuroplastic demand. The neuroplastic demand factor relates to the level of the stressing challenge that is at the heart of the microdosing effects.

Are there certain things we can do to support Drug-Free Microdosing?

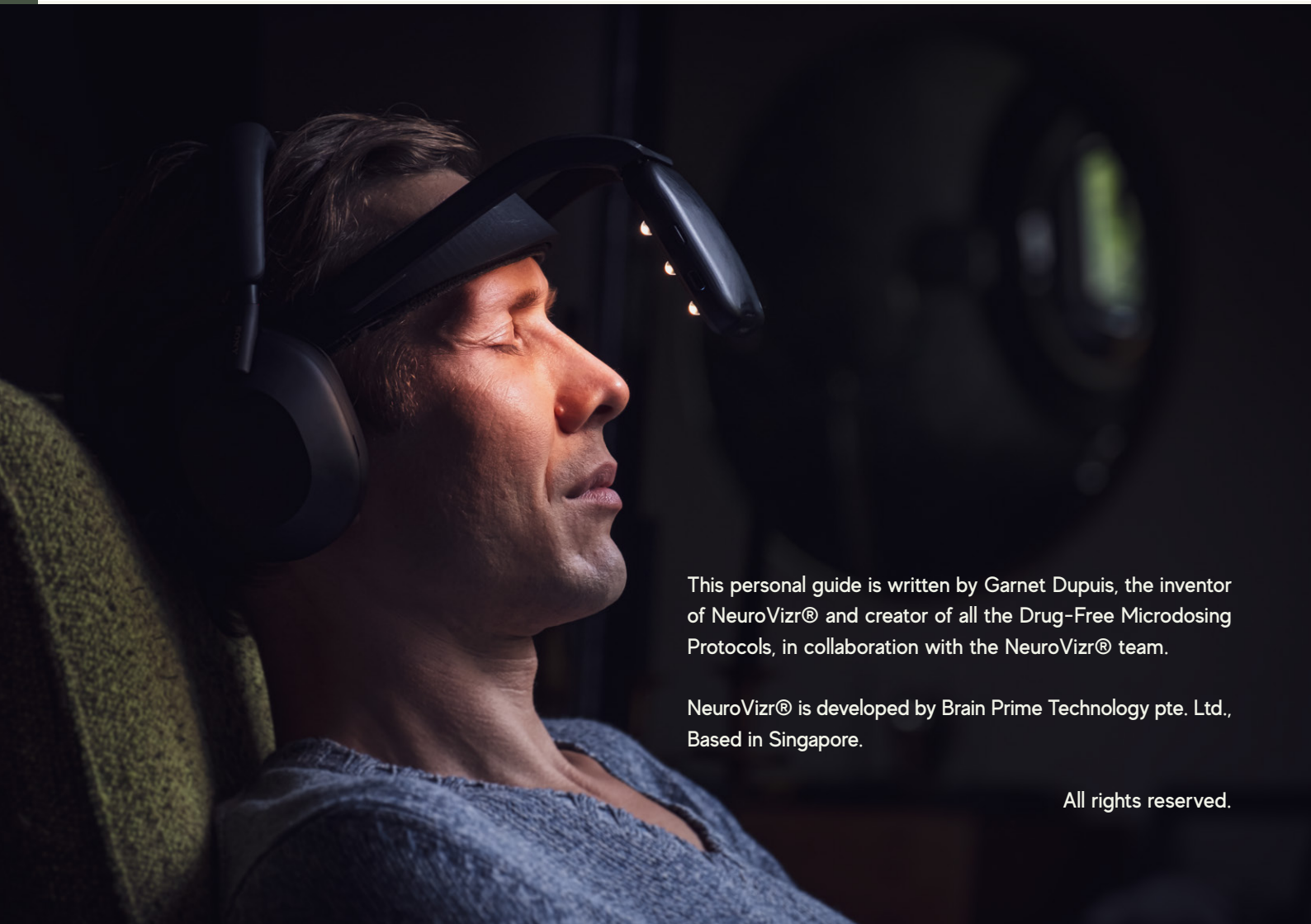
Remain mindful of the specific Theme you have chosen. Positive intention supported by credible psychological techniques such as repeating affirmations or even keeping a journal can help to reinforce the neuroplastic processes of change that are characteristic of microdosing whether it is Conventional Compound Microdosing or Drug-Free Microdosing.

Do Set & Setting have a role in Drug-Free Microdosing?

As compared to full dose psychedelics, "set & setting" have a much smaller role in microdosing. Remaining aware of your general psycho-emotional state can help you identify disruptive influences. Life-style in general including proper sleep habits, nutrition and exercise will certainly contribute to Drug-Free Microdosing experience.

SIMPLE THINGS DONE WELL,
WORK WELL.

Garnet Dupuis



This personal guide is written by Garnet Dupuis, the inventor of NeuroVizr® and creator of all the Drug-Free Microdosing Protocols, in collaboration with the NeuroVizr® team.

NeuroVizr® is developed by Brain Prime Technology pte. Ltd., Based in Singapore.

REFERENCES

1. Serotonergic Psychedelics: Experimental Approaches for Assessing Mechanisms of Action, Clinton E. Canal, Handb Exp Pharmacol. 2018; 252: 227–260.,doi: 10.1007/164_2018_107
2. Martin DA, Nichols CD. The effects of hallucinogens on gene expression. Curr Top Behav Neurosci. 2017 doi: 10.1007/7854_2017_479.
3. Low Doses of LSD Acutely Increase BDNF Blood Plasma Levels in Healthy Volunteers, Nadia R. P. W. Hutten, Natasha L. Mason, Patrick C. Dolder, Eef L. Theunissen, Friederike Holze, Matthias E. Liechti, Nimmy Varghese, Anne Eckert, Amanda Feilding, Johannes G. Ramaekers, Kim P. C. Kuypers, ACS Pharmacol. Transl. Sci. 2021, 4, 2, 461–466, Publication Date:August 31, 2020, https://doi.org/10.1021/acsptsci.0c00099
4. Psychedelic microdosing benefits and challenges: an empirical codebook, Thomas Anderson, Rotem Petranker, Adam Christopher, Daniel Rosenbaum, Cory Weissman, Le-Anh Dinh-Williams, Katrina Hui & Emma Hapke , Harm Reduction Journal volume 16, Article number: 43 (2019)
5. Microdosing psychedelics: Subjective benefits and challenges, substance testing behavior, and the relevance of intention, Rotem Petranker, Thomas Anderson, Adam R Winstock, Journal of Psychopharmacology, Volume 36, Issue 1 October 2020.
6. Psychedelic Microdosing: Prevalence and Subjective Effects, Lindsay P. Cameron, BSc, Angela Nazarian, MA, and David E. Olson, PhD, J Psychoactive Drugs. 2020 Apr Jun; 52(2): 113–122.
7. https://blog.petrieflom.law.harvard.edu/2022/04/13/safety-first-potential-heart-health-risks-of-microdosing/; April 13, 2022 The Petrie-Flom Center Staff A Macro View of Microdosing, Pharmaceuticals, Public Health, Scientific Evidence
8. https://www.health.harvard.edu/blog/the-popularity-of-microdosing-of-psychedelics-what-does-the-science-say-202209192819
9. A systematic study of microdosing psychedelics, Vince Polito, PLoS One. 2019; 14(2): e0211023.Published online 2019 Feb 6. doi: 10.1371/journal.pone.0211023
10. Psilocybin microdosers demonstrate greater observed improvements in mood and mental health at one month relative to non-microdosing controls, Joseph M. Rootman, Maggie Kiraga, Pamela Kryskow, Kalin Harvey, Paul Stamets, Eesmyal Santos-Brault, Kim P. C. Kuypers & Zach Walsh , Scientific Reports volume 12, Article number: 11091 (2022)
11. Low Doses of LSD Acutely Increase BDNF Blood Plasma Levels in Healthy Volunteers, Nadia R. P. W. Hutten, Natasha L. Mason, Patrick C. Dolder, Eef L. Theunissen, Friederike Holze, Matthias E. Liechti, Nimmy Varghese, Anne Eckert, Amanda Feilding, Johannes G. Ramaekers, Kim P. C. Kuypers, Department of Neuropsychology & Psychopharmacology, Faculty of Psychology & Neuroscience, Maastricht University, Maastricht 6200 MD, The Netherlands, ACS Pharmacol. Transl. Sci. 2021, 4, 2, 461–466, Publication Date:August 31, 2020
12. Towards an understanding of psychedelic-induced neuroplasticity, Abigail E. Calder & Gregor Hasler, Neuropsychopharmacology volume 48, pages104–112 (2023)
13. Brain-derived neurotrophic factor and its clinical implications, Siresha Bathina and Undurti N. Das, Arch Med Sci. 2015 Dec 10; 11(6): 1164–1178.Published online 2015 Dec 11.
14. https://www.washingtonpost.com/wellness/2023/02/08/microdosing-mushrooms-anxiety-depression-moms/
15. Rootman, J.M., Kryskow, P., Harvey, K. et al. Adults who microdose psychedelics report health related motivations and lower levels of anxiety and depression compared to non-microdosers. Sci Rep 11, 22479 (2021). https://doi.org/10.1038/s41598-021-01811-4
16. https://www.cpr.org/2022/08/16/moms-microdosing-mushrooms/
17. https://www.dazeddigital.com/life-culture/article/56672/1/start-microdosing-mushrooms-a-guide-psilocybin-psychedelics
18. Microdosing as a response to the meaning crisis: a qualitative analysis, Rotem Petranker, Juensung Kim, Thomas Anderson, Preprint, Univer-

sity of Toronto, Canada.
19. The "First Language" and Neuroplasticity, March 2018 – Garnet Dupuis – amended July 30, 2021.
20. The Super-Dynamics of Neuroplasticity - Garnet Dupuis - Amended August 13, 2021
21. de Vos CMH, Mason NL and Kuypers KPC (2021) Psychedelics and Neuroplasticity: A Systematic Review Unraveling the Biological Underpinnings of Psychedelics. Front. Psychiatry 12:724606. doi: 10.3389/fpsyt.2021.724606
22. Gulyaeva NV. Molecular mechanisms of neuroplasticity: an expanding universe. Biochemistry. (2017) 82:237–42. doi: 10.1134/S0006297917030014 22. Pathania M, Yan LD, Bordey A. A symphony of signals conducts early and late stages of adult neurogenesis. Neuropharmacology. (2010) 58:865– 76. doi: 10.1016/j.neuropharm.2010.01.010
23. Pathania M, Yan LD, Bordey A. A symphony of signals conducts early and late stages of adult neurogenesis. Neuropharmacology. (2010) 58:865– 76. doi: 10.1016/j.neuropharm.2010.01.010
24. Ribak CE, Shapiro LA. Dendritic development of newly generated neurons in the adult brain. Brain Res Rev. (2007) 55:390–4. doi: 10.1016/j.brainresrev.2006.12.005
25. Runge K, Cardoso C, de Chevigny A. Dendritic spine plasticity: function and mechanisms. Front Synaptic Neurosci. (2020) 12:36. doi: 10.3389/fnsyn.2020.00036
26. Leal G, Afonso PM, Salazar IL, Duarte CB. Regulation of hippocampal synaptic plasticity by BDNF. Brain Res. (2015) 1621:82–101. doi: 10.1016/j.brainres.2014.10.019
27. Osorio F, de L, Sanches RF, Macedo LR, dos Santos RG, Maia-de-Oliveira JP, et al. Antidepressant effects of a single dose of ayahuasca in patients with recurrent depression: a preliminary report. Rev Brasil Psiquiatria. (2015) 37:13–20. doi: 10.1590/1516-4446-2014-1496
28. Farzin D, Mansouri N. Antidepressant-like effect of harmane and other β-carbolines in the mouse forced swim test. Euro Neuropsychopharmacol. (2006) 16:324–8. doi: 10.1016/j.euroneuro.2005.08.005
29. Fortunato JJ, Réus GZ, Kirsch TR, Stringari RB, Fries GR, Kapczinski F, et al. Chronic administration of harmine elicits antidepressant-like effects and increases BDNF levels in rat hippocampus. J. Neural Transm. (2010) 117:1131–7. doi: 10.1007/s00702-010-0451-2 72.
30. Fortunato JJ, Réus GZ, Kirsch TR, Stringari RB, Stertz L, Kapczinski F, et al. Acute harmine administration induces antidepressive-like effects and increases BDNF levels in the rat hippocampus. Progress Neuro-Psychopharmacol Biol Psychiatry. (2009) 33:1425–30. doi: 10.1016/j.pnpbp.2009.07.021 73.
31. Morales-García JA, De La Fuente Revenga M, Alonso-Gil S, RodríguezFranco MI, Feilding A, Perez-Castillo A, et al. The alkaloids of Banisteriopsis caapi, the plant source of the Amazonian hallucinogen Ayahuasca, stimulate adult neurogenesis in vitro. Sci Rep. (2017) 7:5309. doi: 10.1038/s41598-017-05407-9
32. Colaço CS, Alves SS, Nolli LM, Pinheiro WO, de Oliveira DGR, Santos BWL, et al. Toxicity of ayahuasca after 28 days daily exposure and effects on monoamines and brain-derived neurotrophic factor (BDNF) in brain of Wistar rats. Metab Brain Dis. (2020) 35:739– 51. doi: 10.1007/s11011-020-00547-w
33. Marques AA, Bevilaqua MC, da Fonseca AM, Nardi AE, Thuret S, Dias GP. Gender differences in the neurobiology of anxiety: focus on adult hippocampal neurogenesis. Neural Plast. (2016) 2016:14. doi: 10.1155/2016/5026713
34.)Bath KG, Schilit A, Lee FS. Stress effects on BDNF expression: effects of age, sex, and form of stress. Neuroscience. (2013) 239:149– 56. doi: 10.1016/j.neuroscience.2013.01.074 78.
35. Oberlander XJG, Woolley CS. Erratum: 17β-Estradiol acutely potentiates glutamatergic synaptic transmission in the hippocampus through distinct mechanisms in males and females (The journal of neuros-

cience, (2016) 36, 9, (2677-2690), 10.1523/JNEUROSCI.4437-15.2016). J Neurosci. (2017) 37:12314–27. doi: 10.1523/JNEUROSCI.3011-17.2017

36. arrier N, Kabbaj M. Sex differences in the antidepressantlike effects of ketamine. Neuropharmacology. (2013) 70:27– 34. doi: 10.1016/j.neuropharm.2012.12.009 80.
37. Kokras N, Dalla C. Preclinical sex differences in depression and antidepressant response: implications for clinical research. J Neurosci Res. (2017) 95:731–6. doi: 10.1002/jnr.23861
38. Lepack AE, Bang E, Lee B, Dwyer JM, Duman RS. Fast-acting antidepressants rapidly stimulate ERK signaling and BDNF release in primary neuronal cultures. Neuropharmacology. (2016) 111:242–52. doi: 10.1016/j.neuropharm.2016.09.011
39. Central Tenets of Neuro Reality Processes; Garnet Dupuis; July 6, 2018; amended July 31, 2021
40.)Barry E. Stein and Benjamin A. Rowland, Organization and Plasticity in Multisensory Integration: Early and Late Experience Affects its Governing Principles, Prog Brain Res. 2011; 191: 145–163., doi: 10.1016/B978-0-444-53752-2.00007-2
41. Evangelos Paraskevopoulos and Sibylle Herholz, Multisensory integration and neuroplasticity in the human cerebral cortex, From the journal Translational Neuroscience, https://doi.org/10.2478/s13380-013-0134-1
42. https://microdosinginstitute.com/microdosing-101/james-fadiman/

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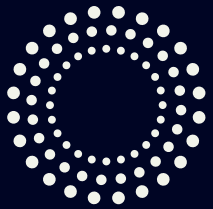

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