The connection between psilocybin and dreaming

Sarah Pekar
Department of Biology
Lake Forest College
Lake Forest, Illinois 60045

Introduction

Dreaming is a universally shared concept between humans. The study of dreaming offers unique insights into human consciousness. There are five stages of sleep: stages 1-4 and rapid eye movement (REM) sleep. REM sleep is also known as active or desynchronized sleep and is when dreams typically occur. The stage of REM occurs about 90 minutes after a person has fallen asleep. Typical REM stages usually last about 10 minutes, but increase the longer a person is asleep; it is possible for REM sleep to occur for up to an hour. In previous studies, subjects that were awakened during the REM stage would report hallucinatory experiences that would follow a narrative (Nir & Tonioni, 2010; Hobson et al., 2000). Moreover, it was reported that these hallucinations involved vivid sensory and motor functions (Nir & Tonioni, 2010; Hobson et al., 2000). To be more specific, subjects would describe dreams as highly colorful. At the same time, subjects would report seeing familiar faces and objects (Nir & Tonioni, 2010; Hobson et al., 2000; Hall & Castle, 1966). Dream research offers a field of study to gain knowledge about the function of specific brain regions. With this understanding of the dream state, researchers believe there is a future in using REM sleep for the maintenance of waking consciousness.

Similar experiences have been described by patients under the influence of psilocybin. Out of the four groups of psychoactive mushrooms, the Psilocybe genus of mushrooms produces the chemical compound psilocybin. The history of psilocybin is to be used in healing rituals that date back about 3,000 years. It was also used in Western medicine until 1971 when it was listed as a Schedule I substance, with Psilocin being responsible for the psychedelic effects (Passie et al., 2002). These mushrooms can be consumed in their fresh or dried forms, as capsules, and sometimes brewed into a tea. After consuming the mushroom, users report mild euphoria and increased feeling of the five senses. Psilocybin mushrooms are not known to cause addiction (Passie et al., 2002). Once a person consumes psilocybin, it is converted into psilocin in the body. Psilocybin (O-phosphoryl-4-hydroxy-N,N-dimethyltryptamine) is converted into psilocin, a pharmacologically active compound. This conversion process takes place through a dephosphorylation reaction under strongly acidic conditions. Alkaline phosphatase is the enzyme which drives the reaction (Fig. 1) (Passie et al., 2002). Psilocin mimics the effect of serotonin. It attaches to serotonin receptors and stimulates the excessive release of the neurotransmitter (Passie et al., 2002).

Studies have shown that psilocybin has a major effect on the default mode network (DMN) (Carhart-Harris et al., 2012). The default mode network consists of the medial temporal lobe, medial prefrontal cortex (vmPFC), posterior cingulate cortex (PCC), and parts of the parietal cortex (Carhart-Harris et al., 2012). These parts of the brain working together are important for integration of sensory information. The default mode network is engaged during self-reflection, complex mental imagery, and theory of mind. When in a normal conscious state, the default mode network allows us to perceive images around us in a precise and constrained way. Normal integration of these key brain networks also gives people their sense of self (Carhart-Harris et al., 2012). Based on research, it can be seen that psilocybin produces similar physiological and neurobiological similarities in the body as dreaming during REM sleep.

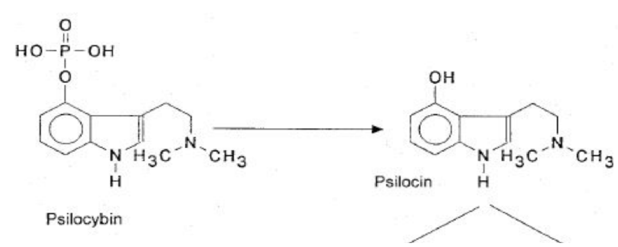

Figure 1. Molecular structures of psilocybin and psilocin. Dephosphorylation of psilocybin into psilocin

Physiological changes during REM and psilocybin

The study and report of the effects of psilocybin usage strongly focus on the neurobiological changes. There are a few reports of physiological changes in studies of psychedelic mushroom use, but the changes are distinct and very common. Fortunately, the physiological changes during REM sleep are well studied. The body experiences many physiological changes during dreams compared to the normal state. REM is categorized by eye movements during the stage. In slow-wave sleep the eyes drift apart, but in REM the eyes move in tandem, similar to their behavior in the awake state. Moreover, it is hypothesized that in order to conserve energy, a person's body temperature drops to its lowest point of the night during REM, which can be as low as 96.5 °F (Brands et al., 1998). Subjects using psilocybin have been found to have the opposite effect. When using psilocybin, it is reported that the person will have an increased body temperature (Brands et al., 1998). Before REM sleep, blood pressure and heart rate decrease in order to adapt to reduced metabolic needs (Penzel et al., 2003; Purves et al., 2001). However, when the body reaches REM, these activities increase to levels that are almost as high as the awake state. Although the reason is not well understood, subjects using psilocybin have been found to have increased heart rate and blood pressure, just like during REM sleep (Brands et al., 1998). In REM there is also a paralysis of large muscles and twitching of the fingers and toes during REM (Purves et al., 2001). Similarly, research shows that the use of psilocybin causes muscle relaxation, weakness, and twitching (Brands et al., 1998).

Neurobiological changes during REM

Recent studies have revealed the potential use of psilocybin mushrooms in both research and therapies. The research done under Dr. Carhart-Harris has revealed astounding results on the effects of psychedelics on the brain. In Harris' study done in 2012, researchers used psilocybin to study the neural correlates of the brain on the psychedelic. Fifteen subjects were intravenously given either a placebo (10 mL of saline) or psilocybin (2 mg in 10 mL of saline). The infusion was done over a sixty second time period and the subjects would feel the results almost immediately. Before the infusion, the subjects were placed in an MRI. The study was done using an arterial spin labeling perfusion, and was done again using a blood- oxygen level dependent fMRI. In both cases, the subject was asked to rate the intensity of the image of a fixation cross at specific

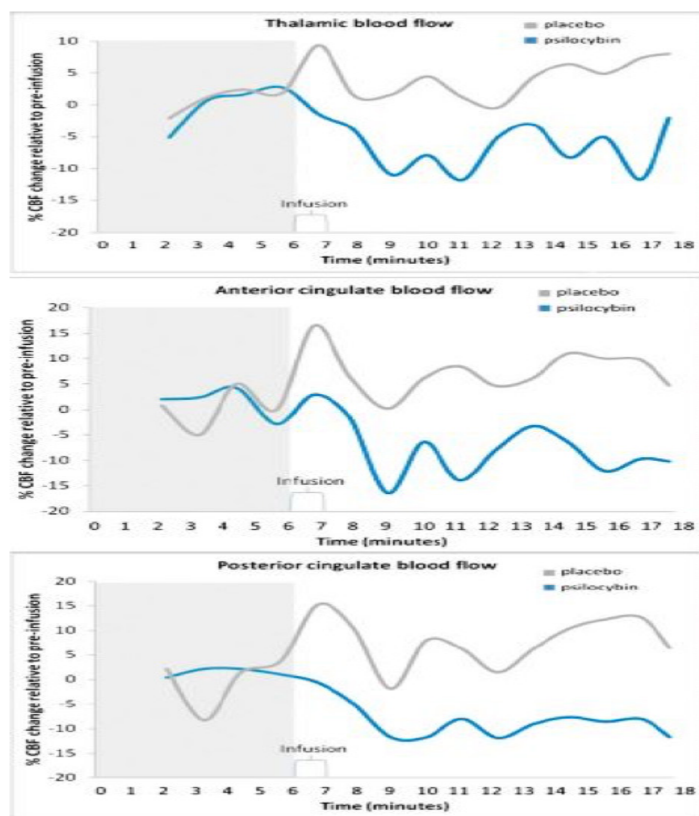

Figure 2. Cerebral blood flow in brain regions.
Cerebral blood flow in the thalamus, anterior cingulate, and posterior cingulate cortex before and after psilocybin infusion, compared to placebo infusion.

times; once immediately after the start of the MRI, prior to the infusion, six minutes after the infusion, and finally twelve minutes after the infusion. The results were not what they expected. Studies researching the neuronal functionality agree that activation of the amygdala is higher during dreaming (Braun et al., 1997; Maquet et al., 1996; Nofzinger et al., 1997). In addition, during the dream state there is a partial activation of limbic regions of the forebrain, which are involved in memory and emotion. In research done by John Hobson (2009), there was a focus on the activation of the default mode network, compared to the brain regions previously discussed. Multiple studies done using PET by Hobson have shown a decrease in activity in the lateral prefrontal cortex and posterior cingulate cortex during REM The study revealed that there was a significant decrease in cerebral blood flow in the regions that made up the default mode network, as previously discussed. Both MRI's showed decreases in blood flow in the thalamus, prefrontal cortex, posterior cingulate cortex, and anterior cingulate cortex (Fig. 2). The study also found that there was increased brain activity in the parts of the brain that play a role in visual imagery (Carhart-Harris et al., 2012). Based on these results, researchers were able to make conclusions about the neural correlates of the brain. Moreover, they were able to understand why the default mode network had decreased cerebral flow and other parts of the brain involved in the senses had increased blood flow. Dr. Carhart-Harris describes the DMN as a central hub for the rest of the brain. When there is normal activity to the DMN and normal integration of the key brain networks, the senses are constrained and precise. Therefore, all humans are able to see the world in a similar way if these brain networks are functioning correctly. However, when there is decreased integration of the key brain networks, like after consuming psilocybin, cognition and the senses are unconstrained, giving a sense of euphoria. Studies have suggested that consuming psilocybin places a person in a "waking dream state".

Similar fMRI and PET studies have been done to map the brain and its functionality during dreaming. PET technique in 1996 showed a decrease in neuronal activity at the orbitofrontal cortex and posterior cingulate cortex and an increase of activity at the thalamus, anterior cingulate cortex, and amygdala during REM sleep (Braun et al., 1997; Maquet et al., 1996; Nofzinger et al., 1997). In a study done in 1997, it was found that there was a decrease of neuronal activity at the posterior cingulate cortex and increase of activity at the amygdala, thalamus, and medial prefrontal cortex during REM sleep (Braun et al., 1997; Nofzinger et al., 1997). Based on PET results, there was an increase of activity at the anterior cingulate cortex (Fig. 3) (Nir & Tonioni, 2010).

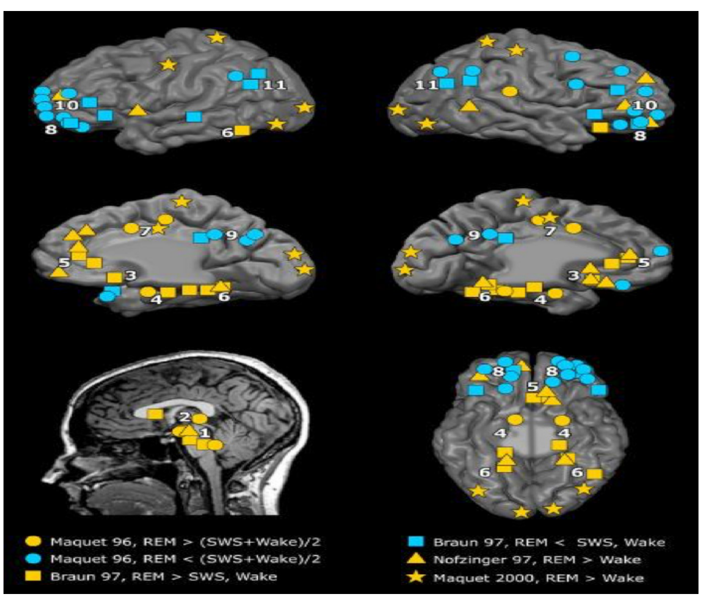

Figure 3. Meta-analysis of PET results.
Circles, squares, triangles, and stars signify significant changes in activity as reported by Maquet (1996), Braun, Nofzinger, and Maquet (2000), respectively. Yellow denotes an increase in neuronal activity, while blue denotes a decrease in neuronal activity in the region tagged.

Studies researching the neuronal functionality agree that activation of the amygdala is higher during dreaming (Braun et al., 1997; Maquet et al., 1996; Nofzinger et al., 1997). In addition, during the dream state there is a partial activation of limbic regions of the forebrain, which are involved in memory and emotion. In research done by John Hobson (2009), there was a focus on the activation of the default mode network, compared to the brain regions previously discussed. Multiple studies done using PET by Hobson have shown a decrease in activity in the lateral prefrontal cortex and posterior cingulate cortex during REM sleep, compared to the waking state and lucid dreaming (Fig. 4) (Hobson et al., 2009). The similarities and differences of these findings, compared to psilocybin, could lead to a deeper understanding of the functionality of certain brain regions.

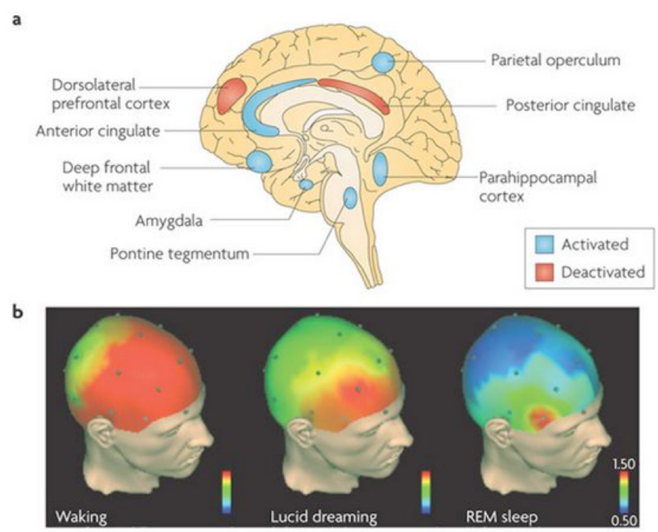

Figure 4. PET results of brain activation.
A. Red signifies the deactivation in brain regions. Results showed a deactivation of the lateral prefrontal cortex and posterior cingulate cortex. All other brain regions studied showed an increase of activity, denoted by the color blue.

The studies discussed reveal strong similarities, as well as some differences, between the neuronal activity during REM sleep and psilocybin use. While psilocybin research reveals a decrease in activity in the thalamus, prefrontal cortex, posterior cingulate cortex, and anterior cingulate cortex, REM studies find deactivation only at the lateral prefrontal cortex and posterior cingulate cortex during dreaming. Conversely to the psilocybin research, REM studies show an activation of the anterior cingulate cortex and amygdala. These conclusions place a focus on the function of the posterior cingulate cortex and prefrontal cortex. Research shows that tasks such as memory and learning depend on the function of the prefrontal cortex (Puig & Gulledge, 2011). The function of the posterior cingulate cortex is not understood as well as other brain region, however, it is hypothesized that its deactivation during cognitively demanding tasks could mean that its function is to control the activity of brain regions involved in the senses (Leech & Sharp, 2014; Sing & Fawcett, 2008).

Conclusion

Scientists believe that psilocybin mushrooms place people into a 'waking' dream state. The reasons for this are that these mushrooms create brain states that usually only occur when a person is sleeping. Research done by Dr. Carhart-Harris concludes that there is increased brain function in areas of the brain that are associated with emotion, due to the lack of cerebral blood flow to the default mode network. These same areas that are associated with emotion and memory also have increased functionality during dreaming.

Analyzing the biological similarities and differences of psilocybin use and dreaming not only allows researchers to gain an understanding of the functionality of the brain, but also opens up the doors for using psilocybin mushrooms as a therapy for diseases like depression and anxiety. It may seem counterintuitive to prescribe a drug that would increase functionality in the part of the brain that controls emotions, but the neural connectivity studied by Dr. Carhart-Harris speaks to its possible efficacy. Studies have shown that depression can be linked to REM sleep dysregulation (Palagini et al., 2013). A possible area of study for the future would be to see if placing people into a waking dream state using psilocybin could treat depression and anxiety.

Another possible area to study would be the default modes network role in depression and anxiety. Carhart-Harris believes that people with these diseases suffer from a strict theory of mind and sense of self due to increased areas of the DMN, such as the posterior cingulate cortex and prefrontal cortex. If psilocybin could reduce the functionality of these brain regions, it is possible that people with depression and anxiety would see the world in a different way.

This research on psychedelic mushrooms gives the possibility for future use of psychedelics in the scientific and medical community. Its current legal status, however, makes future studies on psychedelics difficult. Yet, researchers remain hopeful that these studies will shift community attitudes towards psychedelics.

References

Brands, et al.1998. DEA, club drugs: An update; DEA, drugs and chemicals of concern: psilocybin; Partnership for Awareness, Mushrooms.

Braun A.R., et al. 1997. Regional cerebral blood flow throughout the sleep-wake cycle. An H2(15)O PET study. 120: 1173–1197.

Carhart-Harris, et al. 2012. Implications for psychedelic-assisted psychotherapy: functional magnetic resonance imaging study with psilocybin. The British Journal of Psychiatry 200: 238-244.

Carhart-Harris, et al. 2012. Neural correlates of the psychedelic state as determined by fMRI studies with psilocybin. Proceedings of the National Academy of Sciences 109: 2138-2143.

Gennaro, L. D., et al. 2011. Amygdala and hippocampus volumetry and diffusivity in relation to dreaming. Human Brain Mapping 32: 1458-1470.

Hall, C., and R. Van de Castle. 1966. The content analysis of dreams. Appleton-Century-Crofts.

Hobson, J. A. 1988. The Dreaming Brain. Basic Books.

Hobson, J. A., E. F. Pace-Schott, and R. Stickgold. 2000. Dreaming and the brain: toward a cognitive neuroscience of conscious states. Behavioral and Brain Sciences 23: 793-842.

Hobson J., et al. 2009. The neuropsychology of dreaming: Studies and observations. Nature Reviews Neuroscience 10: 803-813

Maquet P., et al. 1996. Functional neuroanatomy of human rapid-eye-movement sleep and dreaming. Nature 383: 163–166.

Maquet, P. 2000. Functional neuroimaging of normal human sleep by positron emission tomography. Journal of Sleep Research 9: 207–231.

Nir, Y., and G. Tonioni, 2010. Dreaming and the brain: from phenomenology to neurophysiology. Trends in Cognitive Sciences 14: 88-100.

Nofzinger E.A., et al. 1997. Forebrain activation in REM sleep: an FDG PET study. Brain Research 770: 192–201.

Palagini, L., C. Baglioni, A. Ciapparelli, A. Gemignani, and D. Riemann. 2013. REM sleep dysregulation in depression: state of the art. Sleep Medicine Reviews 17: 377-390.

Passie, T., J. Seifert, U. Schneider, and H.M. Emrich. 2002 . The pharmacology of psilocybin. Addiction Biology 7: 357-364.

Penzel, T., J. W. Kantelhardt, L. Chung-Chang, V. Karlheinz, C. Vogelmeier. 2003. Dynamics of heart rate and sleep stages in normals and patients with sleep apnea. Neuropsychopharmacology 28: 48-53.

Puig, M. V., and A. T. Gulledge. 2011. Serotonin and prefrontal cortex function: neurons, networks, and circuits. Molecular Neurobiology 44: 449-464.

Purves D., et al. 2001. Physiological changes in sleep states. Neuroscience 2.

Singh K.D., and I.P. Fawcett. 2008. Transient and linearly graded deactivation of the human default-mode network by a visual detection task. Neuroimage 41:100-12

Wehrle R., C. Kaufmann, T.C. Wetter, F. Holsboer, D.P. Auer, T. Pollmacher, M. Czisch. 2007. Functional microstates within human REM sleep: First evidence from fMRI of a thalamocortical network specific for phasic REM periods. European Journal of Neuroscience 25: 863–871.