

The Effects of D-Lysergic Acid Diethylamide (LSD) On The Brain

Curtis Menon, Yhameen Hamid, Harleen Kaura, Bosco Xu,
Aravind Rajendran



LIFESCI 4M03

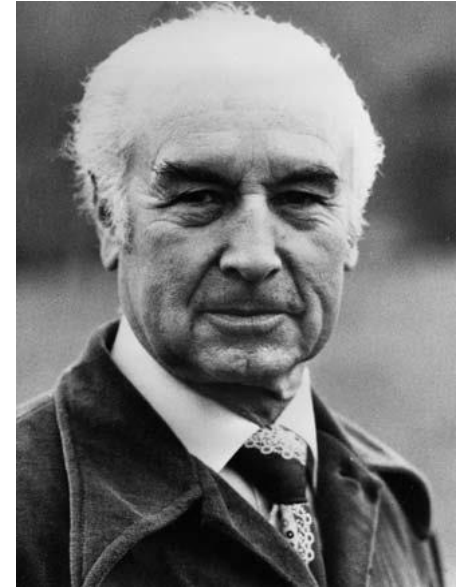


Outline

1. History of LSD
2. LSD Users and Classification
3. Demographics
4. Biochemical Properties and Mechanism of Action
5. Effects on the Brain
6. Uses and Potential as a Therapeutic Agent
7. Short Term Effects/Overdosing
8. Long Term Effects
9. Current Research
10. Social Implications/Conclusion

History

- Albert Hofmann ingests experimental drug LSD-25 in 1938
- Retook the drug intentionally again and bicycled home while undergoing its effects
- Origin of 'Bicycle Day'
- Usage of LSD began in 1960s



<https://www.britannica.com/biography/Albert-Hofmann>

("Hallucinogenic Effects of LSD Discovered", n.d., Horgan, 2014)

“Last Friday, April 16, 1943, I was forced to interrupt my work in the laboratory in the middle of the afternoon and proceed home, being affected by a **remarkable restlessness**, combined with a **slight dizziness**. At home I lay down and sank into a **not unpleasant, intoxicated-like condition** characterized by an **extremely stimulated imagination**. In a **dreamlike state**, with eyes closed (I found the daylight to be unpleasantly glaring), I perceived an uninterrupted stream of **fantastic pictures, extraordinary shapes with intense, kaleidoscopic play of colors**. After some two hours this condition faded away.” --- Albert Hofmann

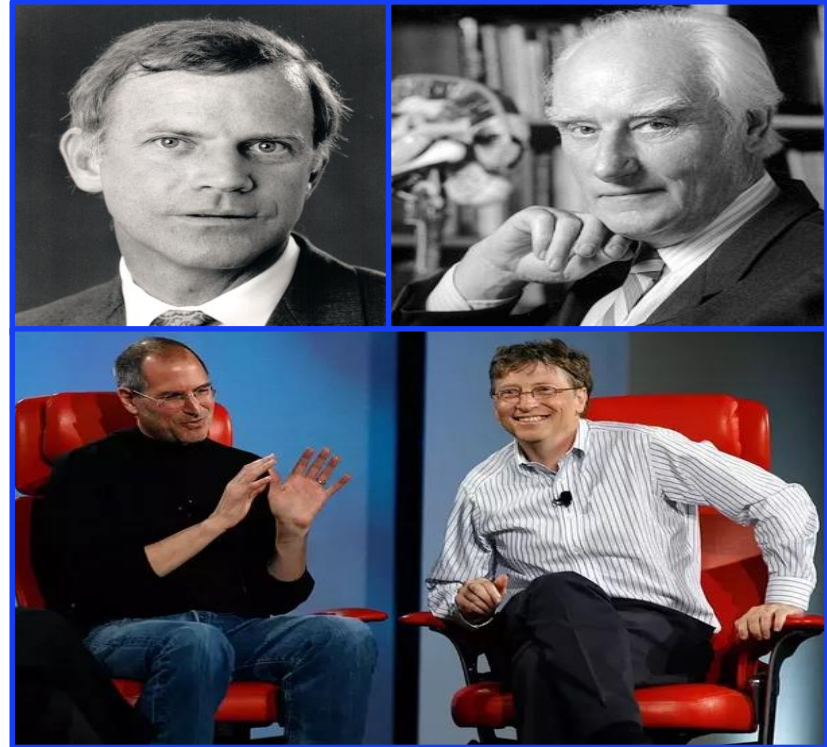
(“Hallucinogenic Effects of LSD Discovered”, n.d.)

Famous LSD Users

http://gairdner.org/award_winners/kary-b-mullis/

<http://www.sciography.com/francis-crick.htm>

- Bill Gates
- Steve Jobs
- The Beatles
- Francis Crick
- Kary Mullis



<https://www.quora.com/Did-Steve-Jobs-hate-Bill-Gates-What-happened-when-two-of-the-biggest-names-in-the-field-of-technology-met>

Classification

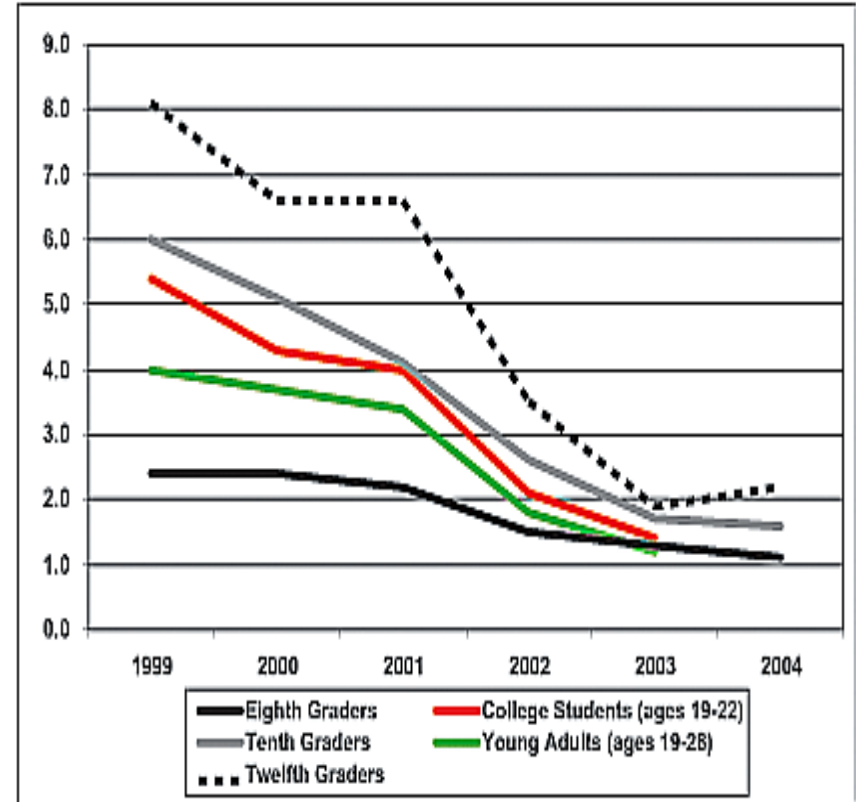
- A psychedelic drug (psychological effects)
- Hallucinogenic
- Recreational
- Over 40 Street Names
- Tolerance Building



<http://brokeasstuart.com/blog/2015/09/25/30-days-micro-dosing-with-ld/>

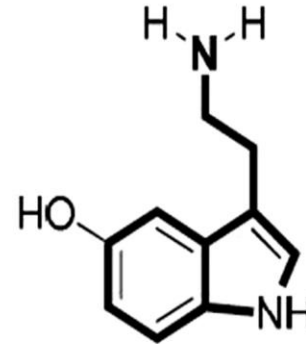
Demographics

- Middle/Upper-Middle Class Whites
- Men Use More Often
- Rarely Taken Beyond Age 28
- Declining Usage Rates
- One Time Use Common

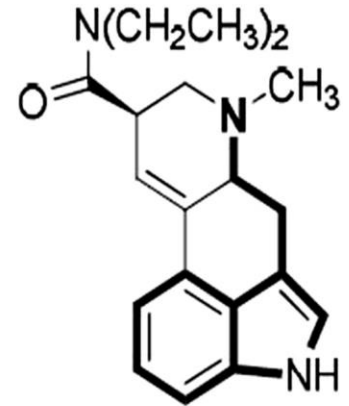


Biochemical Properties

- Tasteless odorless and colorless
- Water Soluble
- Decomposes in light and high temperature
- Similar structure to serotonin



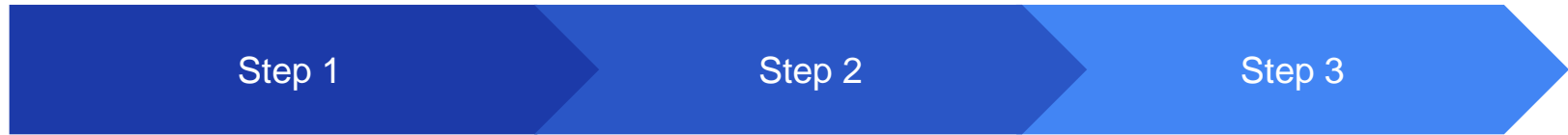
Serotonin; 5-HT



LSD

<http://www.themindcentre.com.au/microdosing-ld-psychedelic-drugs-treatment-future/>

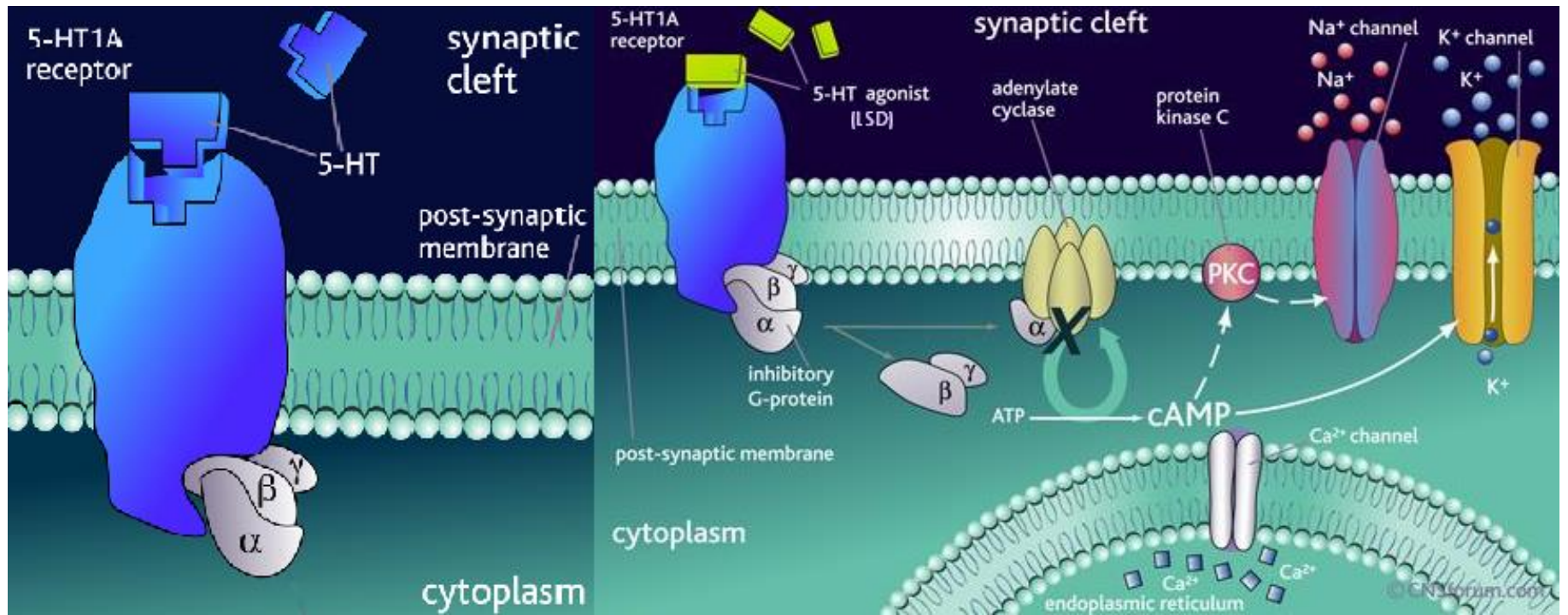
Mechanism of Action



LSD interacts with 5-HT receptors

Interaction with the 5-HT receptors results in an agonist or partial antagonist on serotonin activity

Glutamate release in thalamocortical terminals



<http://flipper.diff.org/apprulesitems/items/4051>

Effects on the Brain



<https://developingchild.harvard.edu/science/key-concepts/brain-architecture/>

- More “unified” brain
- Network(s) break down leading the activity to become entropic
- Disconnections between the parahippocampus and retrosplenial complex
- Feeling of “ego dissolution”
- Psychologically addictive not physically

(Carhart-Harris et al., 2016; Cormier, 2016; Das et al., 2016)

Uses of LSD

Recreational Purposes

- Mood-changing
- Delusions
- Hallucinations
- Boosts creativity

Spiritual Purposes

- Enhances religious experiences
- Cleansing
- Display love for God



<https://thethirdwave.co/lsd-myths/>

Therapeutic Agent?



<http://curioustendency.blogspot.ca/2012/05/psychoanalysis-part-i-transference-and.html#.WfPyxdenHIU>

- LSD + counseling → reduced anxiety, depression and pain in patients with advanced cancer
- Research potential in psychiatry, psychology & psychotherapy
- Antianxiety agent
- Helped with
 - Addictions
 - Obsessive-compulsive disorders
 - Severe depression

LSD Dosage Effects

- Moderate effects: 0.5 mg
- Lethal dose: 20 mg

Effects First Observed



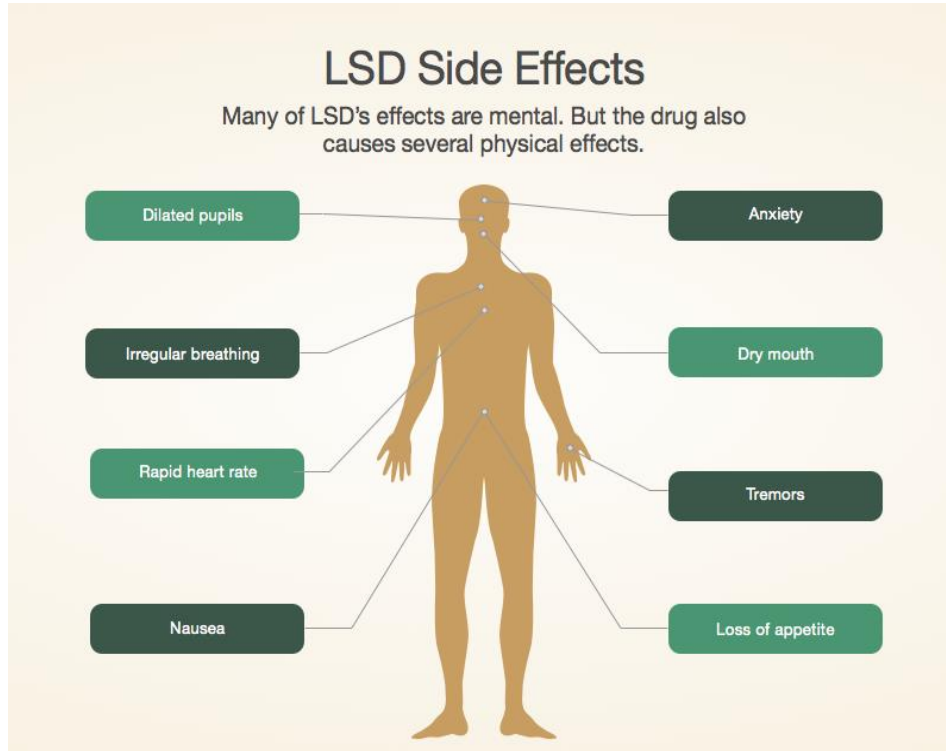
Peak



Dissipate



Acute Toxicity Effects



- Upset GI system
- Causes chills
- Hypothermia
- Palpitation
- Hypertension
- Hyperglycemia
- Tachycardia
- Panic
- Rapidly changing emotions
- Muscle incoordination

(NIDA, 2016; Das et al., 2016; NIDA, 2009)

Effects of Overdosing

- Delusions and visual hallucinations
- Altered sense of self
- Cross-over of senses
- Feelings of despair, insanity, death etc.
- Impaired perception of depth, time, size, movements, etc.
- Sudden or delayed flashbacks (HPPD)
- “Bad trips”



<https://b.passagesmalibu.com/tag/side-effects-of-lsd/>

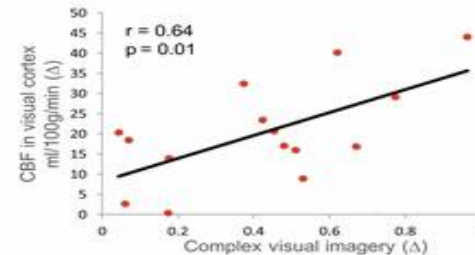
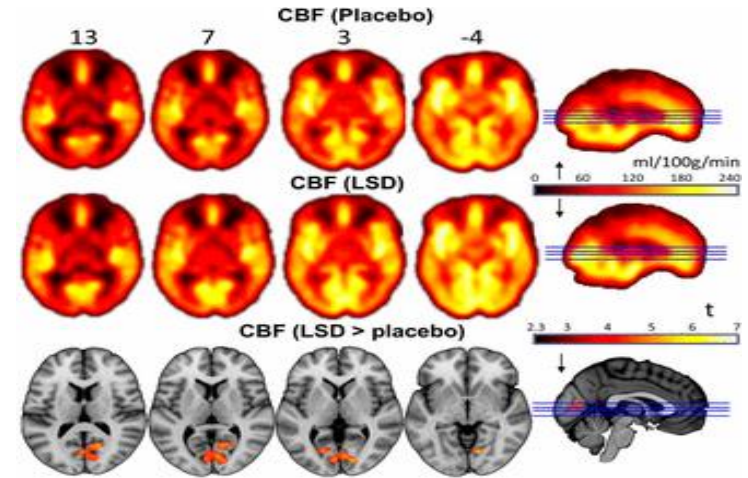
(NIDA, 2009; Das et al., 2016; NIDA, 2016)

Current Research

- LSD Effect on Brain
- LSD to Treat Alcoholism
- Studies on LSD Effects on Thoughts
- LSD as Treatment for End-of-Life Anxiety/Pain
- LSD as Treatment for Cluster Headaches

LSD Effects on Brain

- Cerebral Blood Flow (CBF) Tracking
- Positron Emission Tomography (PET) and Functional Magnetic Resonance Imaging (fMRI)
- Complex Imagery in Altered State of Consciousness (ASC)



<http://www.pnas.org/content/113/17/4853.full>

LSD to Treat Alcoholism

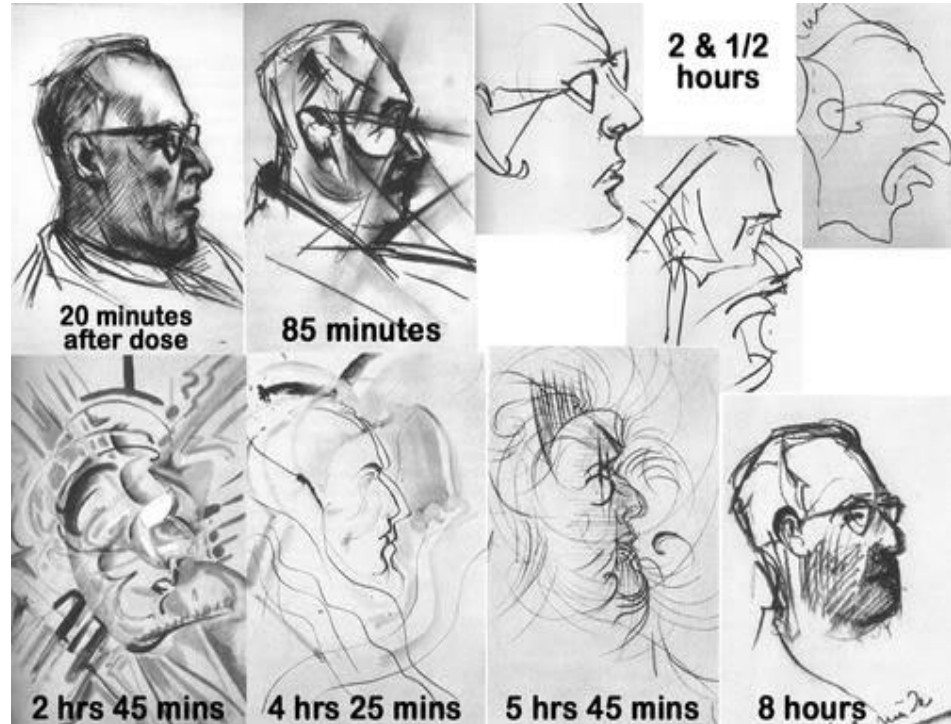
<https://www.pinterest.ca/explore/psychedelic-drugs/>

- Meta-Analysis
- Significant Decrease in Short-Term
- No Success in Long-Term
- Similar With Other Addictions



LSD Effects on Thoughts

- Only required 1/10 dosage
- Increased:
 - Optimism
 - Openness
 - Creativity
 - Imagination



(Lebedev et al., 2014)

<http://www.openculture.com/2013/10/artist-draws-nine-portraits-on-lsd-during-1950s-research-experiment.html>

LSD Treatment for End-of-Life Anxiety & Pain

- Reduction in Anxiety
- Rise in Their Quality of Life
- Decreased Blood Pressure and Heart Rate

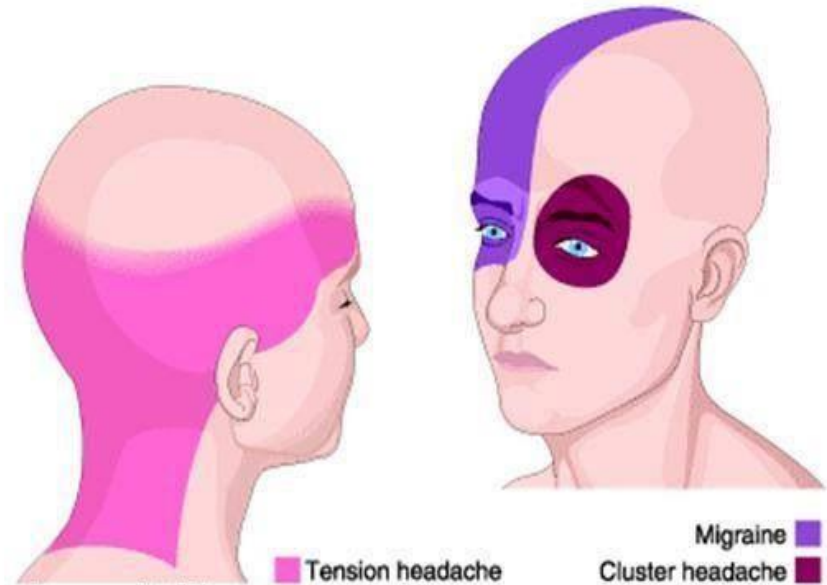
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4086777/>

Time Post-LSD (hour)	Experimental Dose Group (n = 8)						Active Placebo Group (n = 4)					
	HR (bpm)		SBP (mm Hg)		DBP (mm Hg)		HR (bpm)		SBP (mm Hg)		DBP (mm Hg)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
0	74.8	10.0	130.3	13.5	80.0	9.3	82.0	17.1	136.7	7.5	85.0	7.1
4	73.0	9.9	129.1	16.3	80.3	10.2	78.0	18.4	134.7	13.9	87.0	4.7
8	73.3	12.5	126.3	9.0	77.5	9.10	77.3	15.5	137.5	7.6	87.5	4.2

bpm indicates beats per minute; DBP, diastolic blood pressure; HR, heart rate; SBP, systolic blood pressure.

LSD Treatment for Cluster Headaches

- Reduce Cluster Pain
- Interrupt the Cluster-Headache Cycle
- Micro-Dosage (Sub-Psychedelic)



<https://www.pinterest.ca/louise3816/headaches-and-migraine/>

Conclusion/Social Implications

- LSD is a hallucinogenic drug
- Recreational usage prevalent
- Potential for 'more'...
- *Don't Do Drugs!*



<http://www.nomeatathlete.com/long-run-bad/>



MAPS
MULTIDISCIPLINARY ASSOCIATION FOR PSYCHEDELIC STUDIES

<http://www.maps.org/>

Multiple Choice #1:

LSD (Lysergic Acid Diethylamide) has a similar structure to which neurotransmitter?

- a) Serotonin
- b) Histamine
- c) Dopamine
- d) Epinephrine
- e) Norepinephrine

Multiple Choice #1 (Answer):

LSD (Lysergic Acid Diethylamide) has a similar structure to which neurotransmitter?

- a) **Serotonin ##**
- b) Histamine
- c) Dopamine
- d) Epinephrine
- e) Norepinephrine

Multiple Choice #2:

Which of the following statements is incorrect?

- a) Dustin Hoffman was credited with being the first to synthesize LSD
- b) LSD is classified as an Hallucinogenic drug
- c) LSD interacts with 5-HT receptors
- d) Ego Dissolution is an effect LSD has on the brain
- e) LCD is psychologically addictive

Multiple Choice #2 (Answer):

Which of the following statements is incorrect?

- a) **Dustin Hoffman was credited with being the first to synthesize LSD ##**
- b) LSD is classified as an Hallucinogenic drug
- c) LSD interacts with 5-HT receptors
- d) Ego Dissolution is an effect LSD has on the brain
- e) LCD is Psychologically addictive

References

Blachford, S.L., & Krapp, K. (2010). LSD (lysergic acid diethylamide). *Drugs and Controlled Substances: Information for Students*. Detroit: Gale. Retrieved from

<http://sproxy.glenbrook225.org/login?url=http://link.galegroup.com/apps/doc/CV2645000028/SCIC?u=gotitans&xid=8a0a151>

Carhart-Harris, R.L., Muthukumaraswamy, S., Roseman, L., Kaelen, M., Droog, W., Murphy, K., . . . Nutt, D.J. (2016). Neural correlates of the LSD experience revealed by multimodal neuroimaging. *PNAS*, *113*(17), 4853-4858.

<https://doi.org/10.1073/pnas.1518377113>

Cormier, Z. (2016). Brain scans reveal how LSD affects consciousness. *Nature*. <http://dx.doi.org/10.1038/nature.2016.19727>

Das, S., Barnwal, P., Ramasamy, A., Sen, S., & Mondal, S. (2016). Lysergic acid diethylamide: a drug of 'use'?. *Therapeutic Advances In Psychopharmacology*, *6*(3), 214-228. <http://dx.doi.org/10.1177/2045125316640440>

Davis, K. (2017). *LSD: Effects and hazards*. [online] Medical News Today. Available at:

<https://www.medicalnewstoday.com/articles/295966.php> [Accessed 1 Nov. 2017].

Erowid LSD (Acid) Vault : Fatalities / Deaths. (2010). *Erowid.org*. Retrieved 1 November 2017, from

https://erowid.org/chemicals/lsd/lsd_death.shtml

European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) (2011). *Drug Profiles: Lysergide (LSD)*.

Gasser, P., Holstein, D., Michel, Y., Doblin, R., Yazar-Klosinski, B., Passie, T., . . . Brenneisen, R. (2014). Safety and efficacy of lysergic acid diethylamide-assisted psychotherapy for anxiety associated with life-threatening diseases. *The Journal of Nervous and Mental Disease*, *202*(7), 513–520. <https://doi.org/10.1097/NMD.0000000000000113>

References

- Haddad, L.M. (1990). *Clinical Management of Poisoning and Drug Overdose*. 2nd ed. Philadelphia, PA: W.B. Saunders Co., p. 759
- Lewis, R.J. (2004). *Sax's Dangerous Properties of Industrial Materials*. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. p. 1277
- Hawkins, J. D., Catalano, R. F., & Miller, J. Y. (1992). Risk and protective factors for alcohol and other drug problems in adolescence and early adulthood: implications for substance abuse prevention. *Psychological bulletin*, 112(1), 64.
- HISTORY.com. (n.d.). *Hallucinogenic effects of LSD discovered - Apr 16, 1943 - HISTORY.com*. [online] Available at: <http://www.history.com/this-day-in-history/hallucinogenic-effects-of-ldd-discovered> [Accessed 1 Nov. 2017].
- Horgan, J. (2014). *Tripping in LSD's Birthplace: A Story for "Bicycle Day"*. [online] Scientific American Blog Network. Available at: <https://blogs.scientificamerican.com/cross-check/tripping-in-lsds-birthplace-a-story-for-e2809cbicycle-daye2809d/> [Accessed 1 Nov. 2017].
- Kast, E. C., & Collins, V. J. (1964). STUDY OF LYSERGIC ACID DIETHYLAMIDE AS AN ANALGESIC AGENT. *Anesthesia and Analgesia*, 43, 285–291.
- Krebs, T.S. & Johansen, P.O. (2012). Lysergic acid diethylamide (LSD) for alcoholism: meta-analysis of randomized controlled trials. *Journal of Psychopharmacology*, 26(7), 994-1002. <https://doi.org/10.1177/0269881112439253>
- Krebs, T. S., & Johansen, P.-Ø. (2013). Over 30 million psychedelic users in the United States. *F1000Research*, 2, 98. <http://doi.org/10.12688/f1000research.2-98.v1>
- Lebedev, A.V., Kaelen, M., Lövdén, M., Nilsson, J., Feilding, A., Nutt, D.J., . . . Carhart-Harris R.L. (2016) LSD-induced entropic brain activity predicts subsequent personality change. *Human Brain Mapping*, 37(9), 3203–3213. <https://doi.org/10.1002/hbm.23234>

References

Lewis, R.J. (2007). *Hawley's Condensed Chemical Dictionary 15th Edition*. John Wiley & Sons, Inc. New York, NY., p. 773

MAPS (n.d.). What Is MAPS? Retrieved from <http://www.maps.org/>

National Institute on Drug Abuse (NIDA). (2009). *Hallucinogens: LSD, Peyote, Psilocybin, and PCP*. *Drugabuse.gov*. Retrieved 28 October 2017, from <https://www.drugabuse.gov/sites/default/files/hallucinogens09.pdf>

NIDA. (2015). Hallucinogens and Dissociative Drugs. Retrieved from <https://www.drugabuse.gov/publications/research-reports/hallucinogens-dissociative-drugs> on 2017, October 30

Passie, T., Halpern, J.H., Stichtenoth, D.O., Emrich, H.M., & Hintzen, A. (2008). The pharmacology of lysergic acid diethylamide. *CNS Neuroscience & Therapeutics*. 14 (4), 295–314. <https://doi.org/10.1111/j.1755-5949.2008.00059.x>

PubChem. (2017). Lysergide. Retrieved from <https://pubchem.ncbi.nlm.nih.gov/compound/5761> on 2017, October 30

Samhsa.gov. (2015). *Substance Use Disorders | SAMHSA - Substance Abuse and Mental Health Services Administration*. [online] Available at: <https://www.samhsa.gov/disorders/substance-use> [Accessed 1 Nov. 2017].

Schiff, P. (2006). Ergot and Its Alkaloids. *American Journal Of Pharmaceutical Education*, 70(5), 98. <http://dx.doi.org/10.5688/aj700598>

Smith, P. (2015). 7 People Who Say They Owe Their Huge Success to Psychedelics. *Alternet*. Retrieved from <https://www.alternet.org/drugs/seven-high-achievers-credit-psychedelics-their-success>

Zhuyin Li, A.J. McNally, Haiying Wang, S.J. Salamone; Stability Study of LSD Under Various Storage Conditions, *Journal of Analytical Toxicology*, Volume 22, Issue 6, 1 October 1998, Pages 520–525, <https://doi.org/10.1093/jat/22.6.520>