NEURAL CORRELATES OF THE LSD EXPERIENCE REVEALED BY MUTLTIMODAL NEUROIMAGING

COGNITIVE SCIENCE WRITTEN ASSIGNMENT 1

BARTO RADMAN

STUDENT NUMBER: 2062836

COMMITTEE

dr. Michal Klincewicz

LOCATION

Tilburg University
School of Humanities and Digital Sciences
Department of Cognitive Science &
Artificial Intelligence
Tilburg, The Netherlands

DATE

October 13, 2023

i want to thank my mom

NEURAL CORRELATES OF THE LSD EXPERIENCE REVEALED BY MUTLTIMODAL NEUROIMAGING

COGNITIVE SCIENCE WRITTEN ASSIGNMENT 1

BARTO RADMAN

1 INTRODUCTION

Lysergic acid diethylamide (LSD) is a potent, prototypical psychedelic drug. Its prototypical hallucinogenic nature is unique among other psychoactive substances due to the magnitude of its effect on science, on art, and on society as a whole. The discovery of the drug marked the begging of exploration of altered states of consciousness. LSD alters consciousness in a profound, often life changing way. The introduced paper by Carhart-Harris et al., (2016) explores potential neural correlates and effects of LSD on brain activity using modern neuroimaging techniques. The primary motivation for conducting the research was examination of the drugs effects in order to advance the understanding "at the time of growing interest in their scientific and therapeutic value" (Carhart-Harris et al., 2016). From the time that the drug was first synthesized, the paper marks the re-emerging interest in the drugs scientific and medical potential. LSD has a high affinity for different neurotransmitters, most notably serotonin 2A receptor which is thought to give the drug its signature psychological effects. Previous research on LSD was limited to using EEG recordings on rodent brains and fMRI scans with psilocybin. The studies conducted with psilocybin reported decreased cerebral blood flow and decreased resting state functional connectivity in resting state networks (RSN). These previous studies remained consistent in the effects on spatial locations measured. Most notably, the effects of psilocybin on the major RSN default-mode network (DMN) displayed novel patterns of communication and suggested an "entropic effect" on the cortical activity. The "entropic effect", which measures the degree of disorder or uncertainty, is thought of as a key characteristic of the psychedelic state. It was therefore hypothesized that major RSN and hippocampal gyri circuitry activity would be involved in drug's mechanism (Carhart-Harris et al., 2016). With the goal of exploring potential neural correlates of the LSD experience, it is critical to distinguish

the minimal neural processes which are sufficient for the LSD experience against the potential prior and consequent NCCs (Aru et al., 2012). Due to the temporal aspect of the phenomena, it can be difficult to discriminate the exact NCCs responsible for the characteristic experience and the NCCs which might precede or follow the experience. As stated, the study employs advanced state of the art neuroimaging techniques which allow for more precise conclusions and provide more insight on the mechanisms underlying the drugs experience. These insights also explore other aspects of consciousness such as vision and the 'sense of self'. Lastly, effects of LSD on the brain can be characterized as high arousal (neuronal excitation) along with extremely high awareness of the environment and most importantly 'self' (Tononi & Koch, 2008). This unique property of LSD makes it an invaluable tool for exploration of altered states of consciousness.

2 METHOD

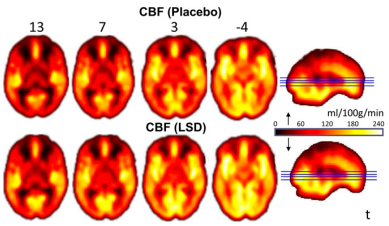
Using a placebo controlled neuroimaging design, the study incorporated three modern techniques: arterial spin labeling (ASL), blood oxygen level-dependent (BOLD) signal measures and MEG resting state scans. ASL is a noninvasive magnetic resonance imaging (MRI) scan measuring tissue perfusion. Tissue perfusion refers to the delivery of oxygen and nutrients to tissue by blood flow (Petcharunpaisan, 2010). Similarly, BOLD signal measures the differences in cerebral blood flow (Sciacca & Gaillard, 2008). Lastly, the study used resting MEG scans which measure the electrical activity of the brain. Twenty participants attended two scanning days two weeks apart which included a LSD and placebo experience. Sessions were comprised of fMRI scans followed by MEG during an eyes closed "resting state" condition. The ASL scans were completed 100 min after the administration of the drug/placebo, correlating with initial peak of the experience. At 135 min two BOLD scans were administered, followed by two resting MEG scans 225 min after infusion (Carhart-Harris et al., 2016). The chosen methods provided a first peak at the LSD experience using modern state of the art neuroimaging techniques. With the primary goal of examining the major RSNs and hippocampal activity, often characterized by wakeful rest, daydreaming, thinking of others (or self) and detailed thoughts, the study rightfully placed the participants in a resting state most suited for the exploration of such states. Furthermore, using the variety of neuroimaging techniques allows for comparison of different temporal aspects along with drawing inferences between the measured phenomena. Thus the techniques complement each other in exploration of underlying neural mechanisms of consciousness during placebo and LSD experience.

3 RESULTS

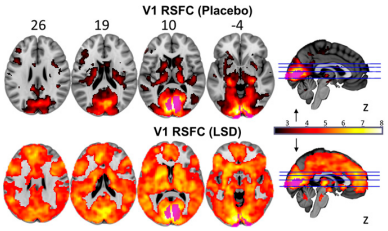
Participants of the study completed an 11-factor "altered states of consciousness (ASC) questionnaire. Some of the factors included feelings of spiritual experience, disembodiment and complex imagery (Studerus et al., 2010). Results of the ASL and BOLD scans in fifteen suitable participants displayed a greater cerebral blood flow (CBF) under LSD in the visual cortex, the magnitude of this increase correlated positively with ratings of complex imagery (Figure 1(a)). Based on previous studies conducted with psilocybin and MDMA, the study observed an increased resting state functional connectivity (RSFC) between V1 and cortical brain regions (Figure 1(b)), along with decreased RSFC between bilateral parahippocampal (PH) and retrosplenial cortex (Figure 1(c)). Increased V1 RSFC correlated positively with ratings of simple and elementary hallucinations along with complex imagery. Decreased PH RSFC correlated positively with ratings on ego-dissolution and altered meaning. Furthermore, the study examined the effects of LSD on twelve brain RSN properties. Four metrics were chosen for each RSN: within RSN CBF, within RSN RSFC ("integrity"), within RSN BOLD signal variance and between RSN RSFC ("segregation"). The study confirmed the predicted hypothesis of decreased DMN integrity correlating with ego dissolution. To test the selectivity of the correlation between decreased DMN integrity and ego dissolution, correlations were calculated for other 11 RSNs and none were significant (Carhart-Harris et al., 2016). Rest of the RSNs observed, notably medial and lateral visual networks, dorsal attention network and parietal cortex network, displayed significant increases in CBF along with significant decreases in integrity and signal variance. MEG scans revealed significantly less oscillatory power for the lower-frequency bands, associated with deep sleep, creativity, mental coordination and overall "slow" processes (Neurohealth, 2019). Decrease in alpha waves significantly correlated with simple hallucinations, decrease in delta waves significantly correlated with ego -dissolution. Thus, the observed results confirmed previously stated expectations and hypothesis of the brain networks involved in the LSD experience.

4 DISCUSSION

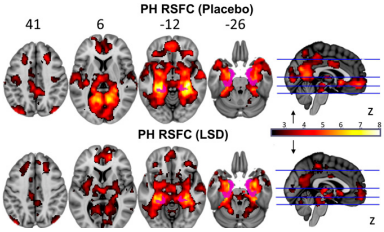
The study provided an extensive description of brain activity during the LSD state. First, the results presented significant increases in CBF in the visual cortex, increased RSFC and decreased alpha power - regions neurally correlated with simple and complex visual hallucinations. Particularly, an increase in V1 RFC suggests that a greater proportion of the brain is being involved in visual processing under LSD. The finding might explain



((a)) CBF Map



((b)) V1 RSFC



((c)) PH RSFC

the reported phenomena of "coloring" of psychological functions such as emotion and cognition, making them more vivid and interpretable. As these areas of the brain are stimulated more under the LSD experience, the consistency with the notion of "seeing with eyes-shut" can be observed, including geometric hallucinations and seeing "as if" visual stimulation. The findings reinforced the view that neuroimaging techniques can be used to inform on on mechanisms underlying visual processing through comparison with psychedelically induced visual state. Neural correlates of visual processing can thus be more precisely explored. In a similar way, the psychedelically induced ego dissolution can inform the neurobiology of the 'self'. Most importantly, the preservation of DMN "integrity", PH desegregation and oscillation rhythms could be critical for maintaining the sense of self. As the LSD experience displays disintegration within different RSNs, but desegregation between the networks, its potential therapeutic use becomes more evident. These RSNs, which are critical for most functions critical to the human experience, can be though of as dissolving within themselves while highly increasing the communication between the networks. Psychedelics such as LSD reduce the stability of the RSNs while at the same time inducing network desegregation, allowing the brain to not be "trapped" within rigid behaviors through dismantling patterns of activity upon which disorders may rest - directly tying to the notion of the "entropic brain".

REFERENCES

[1] Aru, J., Bachmann, T., Singer, W., amp; Melloni, L. (2012). Distilling the neural correlates of consciousness. Neuroscience amp;amp; Biobehavioral Reviews, 36(2), 737–746. https://doi.org/10.1016/j.neubiorev.2011.12.003

[2] Carhart-Harris, R. L., Muthukumaraswamy, S., Roseman, L., Kaelen, M., Droog, W., Murphy, K., Tagliazucchi, E., Schenberg, E. E., Nest, T., Orban, C., Leech, R., Williams, L. T., Williams, T. M., Bolstridge, M., Sessa, B., McGonigle, J., Sereno, M. I., Nichols, D., Hellyer, P. J., … Nutt, D. J. (2016). Neural correlates of the LSD experience revealed by multimodal neuroimaging. *Proceedings of the National Academy of Sciences*, *113*(17), 4853–4858. https://doi.org/10.1073/pnas.1518377113

[3] Petcharunpaisan, S. (2010). Arterial spin labeling in neuroimaging. *World Journal of Radiology*, *2*(10), 384. https://doi.org/10.4329/wjr.v2.i10.384

[4] Sciacca, F., & Gaillard, F. (2008). Bold imaging. *Radiopaedia.Org*. https://doi.org/10.53347/rid-958

[5] Studerus, E., Gamma, A., & Vollenweider, F. X. (2010). Psychometric evaluation of the Altered States of Consciousness Rating Scale (OAV). *PLoS ONE*, *5*(8). https://doi.org/10.1371/journal.pone.0012412

[6] Tononi G, Koch C. The neural correlates of consciousness: an update. Ann N Y Acad Sci. 2008 Mar;1124:239-61. doi: 10.1196/annals.1440.004. Erratum in: Ann N Y Acad Sci. 2011 Apr;1225:200. PMID: 18400934.

[7] Neurohealth, The Science of Brainwaves - the language of the brain. NeuroHealth Associates. (2019, December 2). https://nhahealth.com/brainwaves-the-language/