PhiMiSci
Philosophy and the Mind Sciences

Introduction: Psychedelic Science Needs Philosophy

Matthew W. Johnson[a,b,c](mwj@jhu.edu)

This article is part of a symposium on Chris Letheby's book "Philosophy of Psychedelics" (OUP 2021), edited by Chiara Caporuscio and Sascha Benjamin Fink.

I highly recommend *Philosophy of Psychedelics* by Chris Letheby (2021) to both the public and academics who want to dig deeper into the modern therapeutic science of psychedelics. I have been conducting clinical research with psychedelics since 2004, including trials suggesting the efficacy of psilocybin for treating tobacco use disorder (Garcia-Romeu et al., 2014), major depressive disorder (Davis et al., 2020), and cancer-related distress (Griffiths et al., 2016). Many of these studies have examined relatively high doses of psychedelics in the context of the screening, preparation, monitoring, and follow-up discussion in the days following the session (the so-called "integration" phase). An aspect that has long drawn me to this field is its cross-disciplinary nature. Indeed, it is hard to imagine a more cross-disciplinary area of interest than psychedelics. These compounds are fascinating through the lenses of history, prehistory, anthropology chemistry, medicine, neuroscience, and psychology, to name a few. However, the clinical trials and other studies conducted in the modern psychedelic research era have typically lacked professional representation from philosophy, despite a number of ways in which philosophy is particularly critical to understanding psychedelic effects. This book constitutes a significant advance in the philosophy surroundings psychedelic therapy. In this piece, I will draw attention to key topics covered in the book that I

[a] Center for Psychedelics and Consciousness Research.
[b] Department of Psychiatry and Behavioral Sciences.
[c] Johns Hopkins University School of Medicine.

Johnson, M. W. (2022). Psychedelic Science Needs Philosophy. *Philosophy and the Mind Sciences*, *3*, 3. https://doi.org/10.33735/phimisci.2022.9452

judge as particularly compelling and likely to influence psychedelic therapy and our understanding of it going forward.

After an introduction and overview of book structure in chapter 1, chapter 2 catches the reader up on the state of psychedelic therapy science, including a description of how psychedelic therapy is performed, and evidence suggesting safety and efficacy in the treatment of multiple psychiatric disorders. The treatment model is unique, with only one to a few monitored drug administrations, along with a number of preparatory and follow-up discussion sessions. This stands in contrast to typical psychiatric medications taken on a regular basis to address symptoms such as depressed mood or cravings for an addictive substance. The efficacy data is remarkable, with studies suggesting that these limited number of psychedelic administration sessions lead to large clinical improvements 6 months or more after treatment. And research suggests that session experiences, in particular "mystical experiences" are associated with long term treatment success, suggesting a causal role in behavior change.

Letheby argues, successfully in my opinion, that the core mechanism of psychedelic therapy benefit is not the provision of a comforting delusion, for example, one in which people shift to a more supernatural worldview. He argues instead that "naturalism" is the lens through which the key mechanisms of psychedelic therapy can be understood by combining empirical evidence across multiple disciplines through scientific reasoning. Chapter 3 explores the experiences that people report from psychedelic therapy sessions and their lay ideas as to how psychedelics work as therapeutics. While some such patient explanations refer to supernatural mechanisms (e.g., intervention from a deity), others refer to naturalistic explanations. These naturalist explanations may in fact account for efficacy in the individuals making supernatural claims. Naturalistic explanations, therefore, seem to be fundamental. As an empirical scientist it is likely little surprise that I agree with this orientation toward naturalistic approaches to understanding psychedelic therapeutic mechanisms.

Chapter 4 is noteworthy as it provides a thorough exploration of a question that will be familiar to those who follow psychedelic science: Are the long-term therapeutic benefits of psychedelics dependent on the subjective experiences during the drug effect (the "altered state of consciousness"), or are those benefits caused by a more direct pharmacological effect independent of subjective effects? Letheby argues based on the evidence that subjective experience does play a causal role in long-term benefit. This is supported by studies showing that the mystical-type nature of the experience can predict how therapeutic or otherwise positive the sessions will be in the long term, providing information in some cases that is above and beyond the predictive value of the dose itself or the participants' ratings of drug intensity (Garcia-Romeu et al., 2014; e.g., Griffiths et al., 2016; MacLean et al., 2011). Letheby posits that the subjective experience causes lasting therapeutic benefit independent of whether the session involved or left patients with supernatural ideation. These conclusions are consistent with my view. However, like Letheby, I recognize that more definitive experimental tests are in order to determine if sub-

Johnson, M. W. (2022). Psychedelic Science Needs Philosophy. *Philosophy and the Mind Sciences*, *3*, 3. https://doi.org/10.33735/phimisci.2022.9452

jective psychedelic effects are necessary for lasting benefit from psychedelic therapy sessions. For example, one approach is to examine non-psychedelic analogs that share similar neuroplastic effects as psychedelics and determine if they would have therapeutic effects when conducting "psychedelic" therapy sessions. Yet another example is to administer the psychedelic under anesthesia in order to block the subjective experience (Olson, 2021).

It is also important to note that such views are not mutually exclusive. If the proponents of what Letheby calls the "Molecular Neuroplasticity Theory" are correct that the forms of neuroplasticity identified in rodents are also relevant to human therapeutics (e.g., Olson, 2022), then, as Letheby points out, this might underlie the so called "after-glow" effect in humans that has been reported since the early days of psychedelic therapy. I would also add that inducing neuroplastic effects, be it via non-psychedelic analogs of psychedelics (Olson, 2022) or via "microdoses" of psychedelics (Wit et al., 2022, in press), may also have a therapeutic future in more of a chronic dosing regimen (e.g., a daily pill) analogous to traditional psychiatric medications. If so, one can imagine a future treatment model where the patient has a full psychedelic therapy experience, but then takes non-psychedelic analogs in the days and weeks following the session to prolong the temporal window of potential neuroplasticity and resultant increased learning propensity. If the subjective effects are not critical to psychedelic therapy, then this would lead to drastically different future treatment models that are less clinically intensive regarding personnel time. If the subjective effects are necessary, then experimentally interrogating how this works will be critical for optimizing treatments. Examining the importance of subjective effects is therefore critical for optimizing psychedelics as therapeutics.

Chapter 5 explores ground not typically covered in the literature on psychedelic medicines by asking the question: What is the quintessential psychological mechanism underlying psychedelic therapy, regardless of which disorder is being treated? Letheby's answer, drawing across studies using clinical trial and survey self-report data and network-level brain imaging research, is a in change self-representation, or put differently, or a change in the person's mental model of her or himself. Letheby believes that changes in self-representation are the missing link connecting mystical experiences to therapeutic outcomes. This is a bold and empirically addressable proposition that constitutes an important advance in the field. It can be difficult to reconcile across studies and the diversity of outcome measures, but Letheby's analysis strikes me a credible first approximation suggestive of his hypothesis. An attractive feature is that this framework is consistent with the extended process of psychedelic therapy. The psychological features during the acute subjective drug effects may play a particular causal role in ultimately leading to long-term therapeutic outcomes. However post-acute and perhaps temporary shifts in psychology (e.g., self-representation) play a separate causal role later in the process.

The role for self-representation suggested by Letheby fits with my personal judgement from having supervised hundreds of psilocybin sessions and having

Johnson, M. W. (2022). Psychedelic Science Needs Philosophy. *Philosophy and the Mind Sciences*, *3*, 3. https://doi.org/10.33735/phimisci.2022.9452

been a session guide (who prepares the participant, monitors the session in the room with the participant, and conducts follow-up discussion sessions) for dozens of sessions. It fits with the work our laboratory conducted using in-depth qualitative interviews with participants in our psilocybin for tobacco smoking cessation pilot study (Noorani et al., 2018). In these interviews we asked participants their thoughts on: If the psilocybin session helped them quit smoking, how did it do so? Eleven of the 12 participants who quit smoking on the day of the first psilocybin session indicated that the psilocybin session was an essential element in their success. Seven out of the twelve participants spontaneously indicated that the psilocybin sessions led to insights in self-identity, in other words, advances in their understanding of themselves. Or in Letheby's language, changes in self-representation. And these were just the spontaneous reports. It is very possible that other answers provided by several participants, such as insights into their own smoking behavior, may have also led to (or perhaps are synonymous descriptions with) changes in self-representation. Perhaps the most important thing for the clinical psychedelic research field is that Letheby has provided a testable hypothesis for future laboratory and survey studies. One definition of a useful theoretical framework is whether it leads to empirically testable experiments that will advance the science, regardless of whether the theory is ultimately supported. In that respect, I strongly suspect that the self-representation hypothesis will have a positive impact on the field.

Chapters 6 introduces the concept of predive self-binding. Drawing from predictive processing, this refers to a biological and psychological account of how psychedelics temporarily relax top-down expectations by changes in brain network connectivity, and this allows for an updating of self-representation by altering the "binding" or integration of diverse data that converge on the representation of the self. This value-neutral framework with its focus on the relaxation of mental priors and fluidity of the self is consistent with the clinical observation that efficacy is dependent on set and setting, and that the same compounds sometimes cause harms in suboptimal settings and by vulnerable individuals.

Chapters 7 and 8 continue further into realms rarely considered by clinical researchers and basic scientists. The central question is whether there are epistemic benefits of psychedelic therapy. Even if the comforting delusion hypothesis discussed above is not the key to psychedelic therapy efficacy, some people do interpret their psychedelic sessions from a supernatural perspective, and such beliefs are likely increased by psychedelics for at least a subset of individuals. Chapter 8 concludes based on the available evidence that the epistemic benefits of psychedelic therapy do outweigh potential epistemic harm. These are critical domains to explore as they have ethical implications. As we discussed in Nayak and Johnson Nayak & Johnson (2021) psychedelic therapy can potentially cause epistemic harm by prompting a non-scientific worldview, and this can have implications for other public health and policy domains. This potential could exist even without explicit endorsement of supernatural beliefs by the clinician, but they may be even more likely when clinicians impose supernatural beliefs (Johnson, 2021).

Johnson, M. W. (2022). Psychedelic Science Needs Philosophy. *Philosophy and the Mind Sciences*, *3*, 3. https://doi.org/10.33735/phimisci.2022.9452

In chapter 9 Letheby argues for the concept of naturalized spirituality, which is essentially the positive psychological aspects that people associate with the term "spirituality," including meaning and purpose, but that do not involve supernatural beliefs. This is an area where the adoption of lay terms without specifically anchoring them as scientific constructs is dangerous, for example as we argued for the concept of "impulsivity" in psychological science (Strickland & Johnson, 2021). This has practical implications for how experiences are measured. If one patient is asked if their psychedelic session was spiritual, he or she might say that it was full of reflections on the purpose of life and on connections with loved ones, but no, it was not "spiritual" as no angels or spirits were seen. A different participant might describe an extremely similar experience involving life purpose and connections with loved ones, and when asked if it were "spiritual," he or she might say "Were you not listening to my description? Of course it was spiritual!" Diverging implicit definitions of term such as "spiritual" might therefore invite substantial variance into analyses investigating the mechanisms and processes of psychedelic therapy.

The tenth and concluding chapter includes a discussion of testable predictions. Here, Letheby briefly reports on a survey study that was in preparation during the writing of the book but that has since been published (Timmermann et al., 2021). Surprisingly, the study found that after a psychedelic experience, on average people shifted away from physicalist and materialist views (both consistent with naturalism) and toward panpsychism and fatalism (which can be seen as deviations from naturalism). Moreover, these shifts were correlated with long term mental health benefits. While these results initially seem to contradict the naturalistic understanding of psychedelic healing hypothesized by Letheby, the chapter also describes the limitations of this initial investigation, for example, the possible confounding factor of having a ceremonial environment, in shaping the results. As described by Letheby, there are ethical concerns if therapeutic benefits of psychedelic therapy are fundamentally dependent on causing epistemic harm. Therefore, additional research on the metaphysical outcomes of psychedelic therapy is critical for fully evaluating the societal effects of these treatments.

Perhaps the biggest picture "take home" message for me personally is that to truly understand psychedelic therapeutics, clinical and basic scientists should be better informed by the field of philosophy. Philosophy can provide more accurate and relevant frameworks, concepts, and language, for example, regarding states of mind and metaphysical beliefs. It may also be critical in understanding how psychedelics work. Traditional psychiatric medications typically do not exert efficacy by changing the way people define themselves or how they evaluate the nature of knowledge, for example, so we can use some help beyond that provided by pharmacology, neuroscience, and clinical psychology. Philosophy can help in providing descriptions of psychedelic experiences and their lasting effects on individuals and society, and provide a valuable perspective for evaluating epistemic risk/benefit ratio information for society on how these treatments should be potentially regulated. Clearly, the importance of philosophy in the modern psychedelic therapy renaissance will increase, and Letheby's *Philosophy of Psychedelics* will hold a place as a foundational work helping to shape this future.

Johnson, M. W. (2022). Psychedelic Science Needs Philosophy. *Philosophy and the Mind Sciences*, *3*, 3. https://doi.org/10.33735/phimisci.2022.9452

Acknowledgments
Effort was supported by the Johns Hopkins Center for Psychedelics and Consciousness Research which is funded by the Steven and Alexandra Cohen Foundation and the Tim Ferriss, Matt Mullenweg, Craig Nerenberg, and Blake Mycoskie Collaborative. The author serves as an advisor to the following organizations regarding the medical development of psychedelics and related compounds: AJNA Labs LLC, AWAKN Life Sciences Inc., Beckley Psychedelic Ltd., Entheogen Biomedical Corp., Field Trip Psychedelics Inc., Mind Medicine Inc., and Otsuka Pharmaceutical Development & Commercialization Inc.

References

Davis, A. K., Barrett, F. S., & Griffiths, R. R. (2020). Psychological flexibility mediates the relations between acute psychedelic effects and subjective decreases in depression and anxiety. *Journal of Contextual Behavioral Science*, *15*, 39–45. https://doi.org/https://doi.org/10.1016/j.jcbs.2019.11.004

Garcia-Romeu, A., Griffiths, R. R., & Johnson, M. W. (2014). Psilocybin-occasioned mystical experiences in the treatment of tobacco addiction. *Current Drug Abuse Reviews*, *7*(3), 157–164. https://doi.org/10.2174/1874473708666150107121331

Griffiths, R. R., Johnson, M. W., Carducci, M. A., Umbricht, A., Richards, W. A., Richards, B. D., Cosimano, M. P., & Klinedinst, M. A. (2016). Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial. *Journal of Psychopharmacology (Oxford, England)*, *30*(12), 1181–1197. https://doi.org/10.1177/0269881116675513

Johnson, M. W. (2021). Consciousness, religion, and gurus: Pitfalls of psychedelic medicine. *ACS Pharmacology & Translational Science*, *4*(2), 578–581. https://doi.org/10.1021/acsptsci.0c00198

Letheby, C. (2021). *Philosophy of Psychedelics*. Oxford University Press.

MacLean, K. A., Johnson, M. W., & Griffiths, R. R. (2011). Mystical experiences occasioned by the hallucinogen psilocybin lead to increases in the personality domain of openness. *Journal of Psychopharmacology (Oxford, England)*, *25*(11), 1453–1461. https://doi.org/10.1177/0269881111420188

Nayak, S., & Johnson, M. W. (2021). Psychedelics and psychotherapy. *Pharmacopsychiatry*, *54*(4), 167–175. https://doi.org/10.1055/a-1312-7297

Noorani, T., Garcia-Romeu, A., Swift, T. C., Griffiths, R. R., & Johnson, M. W. (2018). Psychedelic therapy for smoking cessation: Qualitative analysis of participant accounts. *Journal of Psychopharmacology (Oxford, England)*, *32*(7), 756–769. https://doi.org/10.1177/0269881118780612

Olson, D. E. (2021). The subjective effects of psychedelics may not be necessary for their enduring therapeutic effects. *ACS Pharmacology & Translational Science*, *4*(2), 563–567. https://doi.org/10.1021/acsptsci.0c00192

Olson, D. E. (2022). Biochemical mechanisms underlying psychedelic-induced neuroplasticity. *Biochemistry*, *61*(3), 127–136. https://doi.org/10.1021/acs.biochem.1c00812

Strickland, J. C., & Johnson, M. W. (2021). Rejecting impulsivity as a psychological construct: A theoretical, empirical, and sociocultural argument. *Psychological Review*, *128*(2), 336–361. https://doi.org/10.1037/rev0000263

Timmermann, C., Kettner, H., Letheby, C., Roseman, L., Rosas, F. E., & Carhart-Harris, R. L. (2021). Psychedelics alter metaphysical beliefs. *Scientific Reports*, *11*(1), 22166. https://doi.org/10.1038/s41598-021-01209-2

Wit, H. de, Molla, H. M., Bershad, A., Bremmer, M., & Lee, R. (2022). Repeated low doses of LSD in healthy adults: A placebo-controlled, dose-response study. *Addiction Biology*, *27*(2), e13143. https://doi.org/10.1111/adb.13143