ALIUS BULLETIN

exploring the diversity of consciousness

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Foreword

About ALIUS

ALIUS is an international and interdisciplinary research group dedicated to the investigation of all aspects of consciousness, with a specific focus on non- ordinary or understudied conscious states traditionally classified as *altered states of consciousness*.

In Latin, *alius* means “different”. This lexical choice reflects the group’s mission to study the diversity of consciousness in a systematic manner. ALIUS puts a particular stress on the need for a naturalistic approach to all aspects of consciousness, including states and experiences which have long been unduly associated to parapsychology and pseudoscientific hypotheses.

To this end, it fosters a unique interdisciplinary collaboration of researchers, involving neuroscientists, psychologists, philosophers of mind, psychiatrists and anthropologists, towards the development of a systematic and scientific model of consciousness supported by both theoretical work and experimental studies. This collaboration may take the form of joint articles, blog posts, editorial work on special issues, thematic workshops and international conferences.

Find out more about the group on the website: aliusresearch.org `

About the Bulletin

The ALIUS Bulletin is an annual publication featuring in-depth interviews with prominent scholars working on consciousness and its altered states (ASCs). The goal of the Bulletin is to present a clear outline of current research on ASCs across a variety of disciplines, with an emphasis on empirical work. It also aims at dispelling the widespread stigma that still plagues the notion of ASC, while allowing a wider audience to discover rigorous scientific work on the topic presented by authors in their own words.

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Near-death experiences in the public debate:

A scientific perspective

by Charlotte Martial

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Abstract

On January 6th 2021, Netflix released a new docu-series called "Surviving Death", whose first episode is dedicated to near-death experiences (NDEs). We asked ALIUS member and NDE expert Charlotte Martial (neuropsychologist and post-doctoral researcher at the Coma Science Group) to share her perspective about this episode. She watched it with great interest and shares her enthusiasm that popular media addresses this fascinating and growing area of research, which has not received the scientific and medical attention it deserves. She would like to raise several concerns about some statements and comments and address further points to move the debate about NDEs forward.

keywords: *near-death experiences, public debate, consciousness, EEG*

Commentary on: first episode of *Surviving Death* (2021) Netflix

NDE is a particular and touchy topic, in the sense that these experiences touch upon the notion of boundary of life and death. The existence of NDE is, to date, no longer debated in the scientific community, however, their origin is still a matter of controversy (Peinkhofer et al., 2019). To move the debate forward, it is essential that scientists consider available empirical evidence clearly and exhaustively. The significance and interpretation that experiencers give to their NDE have also been the subject of debate; they can be studied by scientists, but it is a matter of belief. We, as humans, have our own beliefs regarding death – and this is so precious! Whatever the personal beliefs regarding NDEs and what they represent, I, as a researcher, will only discuss the scientific evidence that exists to date.

> “To move the debate forward, it is essential that scientists consider available empirical evidence clearly and exhaustively.”

To this day, much of the ambiguity in the definition of NDEs mainly stems from the confusion over how to define death itself and the failure to mention the distinction between “clinical death”, *i.e.,* the cessation of heartbeat and respiration, and “brain death”, *i.e.,* the permanent cessation of functioning of the entire brain. Importantly, since the establishment of the brain death’s criteria in the 1950s, no patient with these criteria has ever recovered from death. Surprisingly, at no point in this episode they mention the distinction between “clinical death” and “brain death”. This might lead a viewer to envision the possibility that the experiencer may be dead, while it is not the case. They also claim that during a NDE, the brain functions are stopped. According to the best of my knowledge, there is no empirical scientific evidence of this statement.

This is related to another statement that is also expressed in the episode, namely that getting EEG flatlining is necessary evidence of the complete absence of brain activity. So far, we know that current scalp-EEG technologies detect only activity common to neurons mainly in the cerebral cortex, but not deeper in the brain. Consequently, an EEG flatline might not be a reliable sign of complete brain inactivity; this limits the conclusion that can be drawn only based on EEG results. The show also discusses the case of Pamela Reynolds, which is fascinating—as all other similar testimonies. In the episode, it is claimed that she experienced her NDE when there was no brain activity. Nevertheless, the EEG data we have from this case does not permit to exclude a (neuro)physiological explanation of her NDE. In fact, we would have needed a rigorous scientific methodology to explore this case and draw any reliable conclusion about the potential (absence of) link between her NDE and underlying (neuro)physiological mechanisms. Considering the two empirical studies published by Chawla and colleagues (2009, 2017) identifying transient electrical spikes in critically ill patients just after cardiac arrest, a likely possibility would be that Pamela Reynolds has had he NDE during such electrical surges. However, this remains a hypothesis and we will never know what exactly happened to her.

> “They claim that during a NDE, the brain functions are stopped. To the best of my knowledge, there is no empirical scientific evidence of this statement (…). So far, we know that current scalp-EEG technologies detect only activity common to neurons mainly in the cerebral cortex, but not deeper in the brain.”

Moreover, an important issue is that it is still unclear when NDEs are experienced exactly, that is, before, during and/or after (i.e., during recovery) the cardiac arrest for example. Indeed, the exact time of onset within the condition causing the NDE has not yet been determined. So far, based on the current scientific literature on consciousness, the most likely hypothesis is that NDEs arise when cerebral functions are still sufficiently operating. Several empirical studies also suggest the implications of various other causal agents, such as the release of endogenous neurotransmitters (see Martial et al., 2020). However, future studies are still needed to explore this issue further.

In this episode, there is also a discussion about the fact that Pamela Reynolds subsequently reported elements from her environment during her operation while she was supposed to be completely unaware of external stimuli. It is important to note that, although many similar intriguing anecdotes have been reported in the literature, so far no empirical study is “methodologically strong” enough for reliably testing whether NDE experiencers did report some actual (real-life-based) events happening in the surrounding during their NDE. Taking the example of one of the most rigorous scientific studies we have so far, Parnia and co-authors (2014) claimed that one experiencer (out of a total of 330 cardiac arrest survivors) reported some elements from the surroundings during his/her cardiopulmonary resuscitation. However, it is noteworthy to mention that their protocol does not permit to exclude that those retrieved memories were not based on retrospective imaginative (re)constructions built up from other memories, expectation about the world and/or prior knowledge (see Martial et al., 2020).

> “ it is still unclear when NDEs are experienced exactly, that is, before, during and/or after (i.e., during recovery) the cardiac arrest for example. Indeed, the exact time of onset within the condition causing the NDE has not yet been determined. ”

The memory literature has repeatedly demonstrated the malleability of the human memory and that our previous memories, expectation about the world and/or prior knowledge may influence the formation of our memories. Currently, the empirical literature has not been able to confirm the accuracy of these reports. We clearly need to conduct studies with more refined methodologies to objectively examine the validity of these intriguing memories. Such methodologies could, for example, include target salient items/objects unexpected to be present in a resuscitation room and see if the patient will report it. This could be filmed by video recordings permitting to objectively examine the claims' validity of visual and auditory perception subsequently reported. I would like to stress that I do not exclude here the possibility that experiencers do report actual real-life-based events happening in the surrounding during their NDE, but I rather remind that convincing empirical evidence of this hypothesis is currently lacking. It is worth noting that if actual real-life-based events are confirmed, this will have important implications in the consciousness field and this will notably corroborate the existing empirical literature showing that unresponsiveness does not equal unconsciousness (see Sanders et al., 2012 for a review).

Undoubtedly, the scientific literature on NDE has long suffered from a lack of a structured framework for analyzing the phenomenon, and especially for studying the seemingly paradoxical dissociation between the trigger event and the richness of the subjective experience, that probably occurs during a moment of brain dysfunction. Due to this lack of framework modelling this dissociation, many publications have been devoted to discussing the fact that NDEs are in support of the nonlocal consciousness theories (*e.g.*, Carter, 2010; van Lommel, 2013; Parnia, 2007) suggesting that consciousness may not always coincide with the functioning of the brain.

> “ it is still unclear when NDEs are experienced exactly, that is, before, during and/or after (i.e., during recovery) the cardiac arrest for example. Indeed, the exact time of onset within the condition causing the NDE has not yet been determined. ”

Some of their proponents claim that NDE is precisely what it seems to be to the individual experiencing it: an experience which can be considered as evidence of a “dualistic” model toward the mind-brain relationship. Nonetheless, to date, convincing empirical evidence of this hypothesis is lacking. It is an intriguing fact that several authors, including cardiologists (*e.g.*, van Lommel, 2013), debating NDEs do not appear to recognize that they are states of disconnected consciousness likely underlined by brain functions, while this is currently the most likely hypothesis based on the current scientific state of the art.

In reality, NDE is far from being the only example of such seemingly paradoxical dissociation and research has repeatedly shown that consciousness and behavioral responsiveness (*i.e.*, behavioral interactions with the outside world, excluding reflex behaviors) may decouple, notably using brain imaging techniques in severe brain injury or pharmacologically induced states (*e.g.*, Monti et al., 2010). For instance, complex patterns of cortical activity and interactions which are typically observed in awake conscious states can be observed throughout ketamine-induced unresponsiveness states after which reports of subjective experience have been recalled (Bonhomme et al., 2016; Sarasso et al., 2015). Nevertheless, it is true that NDEs are particularly intriguing due to their rich phenomenology subsequently reported.

> “ Some proponents of this hypothesis claim that NDEs are evidence of a “dualistic” model toward the mind-brain relationship. Nonetheless, to date, convincing empirical evidence of this hypothesis is lacking. ”

We recently published an opinion article examining the NDE phenomenon in light of a novel framework (Martial et al., 2020), hoping that this will facilitate the development of a more nuanced description of NDEs in research, as well as in the media (see figure below).

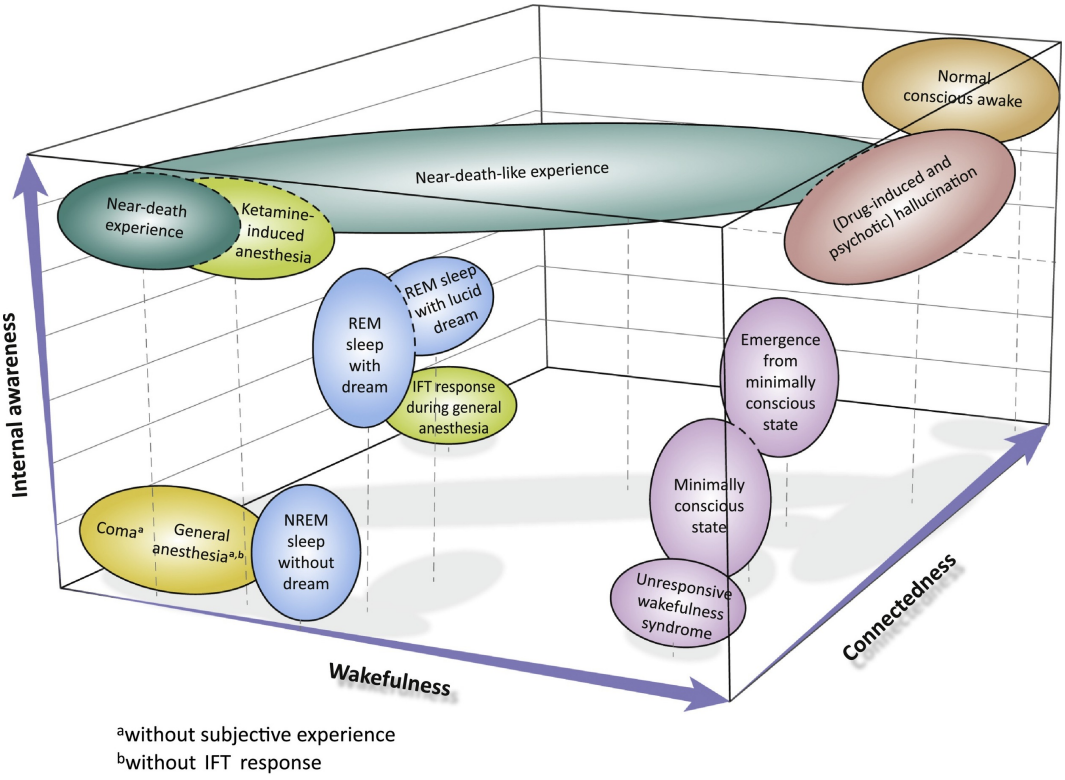

Illustration of Different States and Conditions Based on Wakefulness, Connectedness, and Internal Awareness. Reproduced from Martial et al. (2020)

Research on NDEs has also long suffered from a dearth of empirical evidence regarding the NDE event itself because of its unpredictable aspect, which makes its scientific investigation extremely difficult. Nonetheless, experimental methods have been recently developed to go beyond limitations inherent in NDE research. For example, it is possible to induce resembling subjective experiences through the use of psychedelic substances (Timmermann et al., 2018), hypnosis (Martial et al., 2019) or syncope (*i.e.*, transient cerebral hypoxia; Lempert et al., 1994a,b).

> “ NDE is far from being the only example of such seemingly paradoxical dissociation and research has repeatedly shown that consciousness and behavioral responsiveness (...) may decouple. ”

Contrary to what is said in the episode, we know that low cerebral oxygen levels can lead to very pleasant experiences – sometimes even intentionally induced by teenagers using the so-called "fainting lark" manoeuvre (Johnson et al., 1984). Notably, while investigating motor phenomena of syncope in a cohort of healthy young adults, Lempert and colleagues (1994a) were one of the first to report pleasant syncopal hallucinations. Out of 42 young adults volunteers who experienced complete syncope with falling, 25 subsequently reported visual and auditory hallucinations, such as out-of-body experiences, perceptions of lights which in some cases intensified to a glaring brightness, encountering relatives or more blurred entities, and hearing human voices (Lempert et al., 1994a,b). Seven volunteers described their experience of syncope as a negative one (notably due to disorientation), while all others had neutral or pleasant emotions – sometimes comparing them to drug-induced or meditation experiences. Some of them admitted being reluctant to "return to reality" (Lempert, 1996). In their paper, the authors qualified those memories as similar to NDEs as described by R. A. Moody in his book "Life after Life" (Moody, 1975), because of their close resemblance to subjective experiences reported after pathological severe prolonged periods of cerebral hypoxia, i.e., cardiac arrest. We should nonetheless bear in mind that these experiences are not considered as "classical" NDE, *i.e.,* occurring in a life-threatening situation; however, these convincing experimental manipulations may help to understand the underlying mechanisms of classical NDEs. More generally than this example, the current neuroscience hypotheses are lacking (or not sufficiently described) in this episode.

Finally, I would like to recall that it is too early to speculate on the universality of NDE features. Although historical descriptions of NDEs from diverse sources reveal sufficient common features which suggests a prototypical core experience that seems to be independent from cultures, societies and religions (Belanti et al., 2008; Blackmore, 1993; Greyson, 2006), large scale cross-cultural studies recruiting individuals from different cultural and religious backgrounds are currently missing. To date, publications are centrated in North America and Western Europe (Sleutjes et al., 2014). So far, it is still not clear to what extent the NDE experiencers' religiosity and cultural background influence the content of NDEs and the

interpretation of their features (Belanti et al., 2008; Blackmore, 1993). Some studies have shown a culture-related incidence of certain features, i.e., tunnel vision (Belanti et al., 2008; Kellehear, 1993; Pasricha & Stevenson, 1986). However, most studies are case reports, thus limiting the generalizability and the conclusions that can be drawn at a cultural level.

It is clear that the topic of NDE fascinates people around the world. I therefore invite media actors and scientists to be exhaustive when presenting the perspectives on NDEs, e.g., interview researchers from different laboratories testing different types of hypotheses and who recently published scientific publications in the field and have neuroscientific expertise. No matter what scientists will discover, it does not take anything away from the fact that NDE testimonies are intriguing and are identifiable as a psychological and physiological reality of clinical significance. NDE testimonies presented in the episode are, as often, moving and fascinating. I would like to use this opportunity to thank these NDE experiencers, as well as all other NDE experiencers who have shared their experience with researchers and/or journalists.

> “ It is too early to speculate about the universality of NDE features. (...) Large scale cross-cultural studies recruiting individuals from different cultural and religious backgrounds are currently missing. ”

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How culture breaks down the mind-body divide

An interview with Maddalena Canna and Rebecca Seligman

by Matthieu Koroma

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Abstract

In this interview, anthropologists Maddalena Canna and Rebecca Seligman explain their recent research agenda investigating how culture shapes the relationship between the body and mind. After having studied trance, they shift their focus to Functional Neurological Disorder (FND), an illness in which sensory or motor symptoms do not match any identified physiological causes. Their approach relies on a mix of anthropological and psychophysiological methods to unravel the mechanisms by which cultural expectations influence the perception and meaning of bodily sensations, a phenomenon that they call "interoceptive affordance". The cultural contextualization of psychophysiological processes puts into question our conceptions of the body and mind divide, and what we consider as normal or pathological. By emphasizing how social factors such as gender, race and medical categorization impact the symptomatology of FND, they highlight how anthropological research can lead to a more encompassing and humanized vision of treatment and care that replaces the category of patient with a participatory actor of the scientific investigation of conscious states and their modification.

keywords: *Functional Neurological Disorder*, *trance*, *psychophysiology*, *interoception*, *interoceptive affordance*, *social science*, *medical ethics*

Dr. Maddalena Canna is a Postdoctoral researcher at Northwestern University and Dr. Rebecca Seligman is an Associate professor of anthropology at Northwestern University. You are both part of the ALIUS research group

devoted to fostering interdisciplinary research about the diversity of consciousness. What types of conscious phenomena have you been primarily interested in? Could you illustrate how transcultural research has helped you better understand some aspects of consciousness?

We both conducted our PhD research on spirit possession; Maddalena Canna on demonic possession in Nicaragua, and Rebecca Seligman on religious possession in Brazilian Candomblé. Spirit possession has been frequently exoticized, as something exclusively bounded to localized systems of beliefs. Also, it has been medicalized and conflated with a wide array of psychiatric constructs, from hysteria to conversion disorder. We both reacted to these two lines of misconception—exoticization and pathologization—by deconstructing their underlying implicit assumptions. Both exoticization and pathologization of trance and possession rest on interrelated assumptions about the nature of consciousness and the relationship between mind and body.

Possession—in whatever form—is a compelling example of how consciousness cannot be reduced to the mind-body binarism dominating Western lay models of health. Studying the complex physiological, emotional and cognitive underpinnings of possession across cultures requires a model of the interplay between mind and body not relying on an implicit assumption of their ontological separation. As anthropologists, we acknowledge that diverse societies elaborate diverse conceptions of consciousness. This diversity operates not only at the conceptual level, but also in shaping experiences. The subtle line between normal and abnormal, progressive and regressive, healthy and pathological is highly variable not only across societies, but also across different moments and spaces within the same society or individual.

The way in which a state of consciousness is appraised (e.g., healthy vs. pathological) and reappraised shapes the core of its phenomenological experience. For example, a trance episode can be lived as pathological *before* religious initiation but healthy *after* it. The appraisal shapes the experience of trance, including its physiological components (e.g., hormonal and neuronal correlates) (Seligman 2018). This is why, as anthropologists, we put

> The way in which a state of consciousness is appraised (e.g., healthy vs. pathological) and reappraised shapes the core of its phenomenological experience.

in brackets the term "altered" when talking about states of consciousness. Transcultural research helps us better understand that the relationship between what is deemed normal and what is deemed altered is a matter of continuous negotiation, re-invention and transformation. Questioning the subtle line between normal and abnormal, relativizing the systems of normativity shared by any society, allows for a culturally attuned understanding of the diversity of consciousness. One of the foundations of anthropological practice is familiarizing the unknown and deconstructing the familiar. This paves the way for experimentation with the full range of potentialities of our own consciousness.

In your collaboration, you propose to explore how body-mind relationships are shaped by cultural factors. You do so by studying the case of Functional Neurological Disorder (FND), also known as Conversion Disorder (CD), which consists in the presence of sensory or motor symptoms that do not match any identified physiological causes (Canna & Seligman, 2020). For example, you introduce the case of Alice. Alice is a biomedical doctor who became anxious after being diagnosed with breast cancer. After her tumor was removed and no trace of propagation of cancer was found, she developed a series of symptoms such as an intense chest pain, arm paralysis and non-epileptic seizure despite her physiological state being diagnosed as normal. To account for these phenomena, you propose a framework in which bodily sensations depend on the embodiment of cultural models, explaining how expectations, for example Alice's medical knowledge about the spreading of cancer, are converted into the experience of somatic symptoms.

You both have been studying non-pharmacological trance in your research (Canna, 2016; Seligman, 2010). Trance is a conscious state during which physiological alterations are typically induced without apparent physiological cause and occurs within a cultural context, for example a ritual practice (Seligman, 2014). Trance is commonly practiced for healing purposes by shamans (Winkelman, 1989). By working on the way people frame the meaning and live their somatic experiences, body-mind relationships can be

altered and allow therapeutic processes to happen. If FND and trance share some commonalities, do you think trance can be relevant in a way to help FND patients? Which continuities and discontinuities do you draw between these two phenomena?

The parallel between FND and trance is fascinating. It is fascinating because there are some common processes involved both in trance and in FND. In particular, we think these phenomena may both involve processes associated with what is known as dissociation. FND have been removed from the spectrum of dissociative disorders in the last DSM-5, where they are now listed under the broader category of Somatic Symptom Disorders (APA 2013). Nevertheless, if we adopt a larger, non-biomedically bounded notion of what dissociation is, we can recognize important overlaps.

Dissociation, as described cross-culturally by Seligman and Kirmayer, is the dis-integration of processes or components of the persona that are usually integrated (Seligman and Kirmayer, 2008). In this sense, FND symptoms and trance entail both dissociative components, as they rely on the temporary dis-integration of processes that are integrated in a state that is deemed normal. In both cases, the experience seems to be related to a shift in the allocation of attention or regulation of information that is available to the self-conscious mind. For example, during a non-epileptic seizure (a form of FND) a person can lose control of their limb movements, and still remain in a state of conscious awareness. Something similar happens during trance, when bodily movements are perceived to happen beyond personal control, even though the individual conscious awareness is still intact (Seligman 2014; Halloy 2015; Canna 2017).

To return to the idea of what is normative and what is pathological, dissociation has typically been interpreted as pathological within the context of Euro-American psychiatry, and people living with FND may reject the connection as a result. But what our research shows is that the dis-integration of aspects of awareness takes place in non-distressing and non-pathological ways all the time, both outside and within Euro-American contexts. For this reason, we don't see any limitation on a potential therapeutic use of trance. Intervening on the dis-integration and re-integration of functions, trance

and dissociative states can be used for an optimization of the overall health of the persona through the regulation of awareness—for example of pain or other sensations. Such regulation can lead to shifts in response and modulation or even reshaping of neuro-physiological pathways underpinning FND.

> “ Intervening on the dis-integration and re-integration of functions, trance and dissociative states can be used to for an optimization of the overall health of the persona through the regulation of awareness—for example of pain or other sensations. ”

You argued that, in the case of Alice, her symptoms could arise from an enhanced sensitivity to her bodily signals along with a poor perceptual accuracy, explaining how benign bodily sensations can be amplified and misperceived as signs of the cancer spread (Canna & Seligman, 2020). To account for this phenomenon, you coined the notion of “interoceptive affordance” describing how “cultural models and exposures create encultured bodies, influencing not only the meanings of bodily symptoms but the very way in which bodily sensations are themselves perceived” (Canna & Seligman, p. 3). You propose to operationalize the study of interoceptive affordance by:

> i) characterizing the meaning associated with somatic sensations as expressed through metaphors referring to the bodily experiences
>
> ii) measuring the modifications of interoceptive abilities, *e.g.*, the sensitivity and accuracy of heart-beat detection
>
> iii) investigating the role of social factors such as gender in shaping the subjective and objective features of mind-body relationships

I would like to make the case for this approach by examining the case of anxiety. It has been established that anxiety is associated with altered interoceptive abilities (Paulus & Stein, 2010). On one hand, it is characterized by an enhanced interoceptive sensitivity, measured at the subjective level by a better heart-beat detection and at the neural level by a stronger heart-

evoked potential, the cerebral response to heart-beats (Domschke et al., 2010). Moreover, anxiety is more prevalent in women than men, in accordance with the clinical picture that 80% of FND patients are women, suggesting the role of social factors (Pigott, 1999; Canna & Seligman, 2020). Do you think that the concept of "interoceptive affordance" is helpful in understanding some aspects of anxiety? Is there a systematic link between anxiety and FND and what would be then the nature of this link?

You further refer to Ian Hacking's (1995) concept of "biolooping" to capture the way that social meanings not only affect peoples' behaviors and how they conceptualize themselves, but also how such meanings affect their own bodily states (Hacking, 1995; Seligman, 2018; Canna & Seligman, 2020). For example, anxiety is not just linked to an increased sensitivity to interoceptive signals, but it also actively alters bodily states since fear from panic attack can lead to an increased heart-beat and ultimately trigger panic attack itself. Such kinds of circular inferential mechanisms have been described in other types of conscious states such as schizophrenia, whereby delusions are created by selective sampling, amplification and reinterpretation of evidence at hand results not just in the misperception of the external world, but also the creation of an alternate worldview (Leptourgos et al., 2017). The notion of inference has been extended to interoception (Seth, 2013). Would you endorse the view that FND could rely on a similar type of circular interoceptive inference?

Importantly, schizophrenia is a condition which is differently appraised across cultures (Lin & Kleinman, 1988). This notably results in considering the apparition of hallucinations either as being symptomatic or not, and to vary in frequency and content depending on cultural contexts (Larøi et al., 2014). How do you expect FND and its symptomatology to vary across cultures?

We do think culture acts at the level of appraisal—and re-appraisal—in shaping and reinforcing loops of interoceptive inferences. For example, a sensation can be appraised as a symptom and trigger cascades of pathogenic reactions because of the negative meaning associated (Hay 2010, Canna and Seligman 2020). We learn to be afraid of some internal cues, and this red flag associated with specific sensations triggers emotional and physiological reactions, leading to it being experienced as disruptive. The parallel with schizophrenia is interesting. As studied by Luhrmann et al. (2012), some mental events like hearing voices (or auditory hallucination, from a

pathologizing perspective) can be associated with different moral meanings across cultures. Voice-hearing can be appraised differently, from a stigmatizing sign of "being crazy" in the US, to a positive help received from gods or dead ancestors in other contexts (Ghana and India) (Luhrmann et al. 2015). Processes of socially shaped appraisal (also called cultural scaffolding, or social kindling) are not only a cultural gloss, or a superficial layer of experience, but they are at the very core of how an event is experienced and integrated in individual lives. In this sense, we expect that culture impacts on all key aspects of FND experience, namely the three broad axes that we identified as (a) interiorized cultural models of illness, (b) social stressors, (c) and stigma (Canna and Seligman, 2020).

Anxiety plays a key role in FND, even though it is indispensable to avoid the risk of conflation. People with FND have been burdened by medical dismissal for a long time, a dismissal that often came with the implicit moralizing accusation of "paying too much attention" to the symptoms or being overly anxious. Even the current DSM definition of Somatic Symptom Disorder reports the ambiguous criterion of "excessive thinking or worrying about a symptom". A notion of "excessive worries" paves the way for further medical dismissal and the reproduction of the trite stereotype that "It is all in their heads", implicitly entailing a moral responsibility in the reproduction of the symptom. We take a strong stance against the tendency to conflate FND with a by-product of anxiety. If anxiety often plays a role in FND, it is not its necessary nor sufficient cause, nor can it be modeled as functioning in the exact same way.

That said, if we go back to the idea that appraisal is a key, socially scaffolded or kindled aspect of interoceptive inference, then negative appraisals of

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sensations can reinforce interoceptive attention to particular cues as well as increasing anxiety. We refer to the subsequent loops as "bio-looping" because the mechanisms are not only cognitive and affective but can also entail physiological responses that become activated or reinforced through such loops—for example stress hormones and inflammatory processes. In light of such processes, it would be especially productive to consider how gender-specific forms of anxiety—for example the hyper-focus on the control of feminine bodies common in Euro-American societies—may concentrate patterns of sensitization among specific pockets of the population and contribute to the huge gender disparity in FND.

You introduce the notion of "self-scape" to describe the set of possibilities that a given society offers to individuals to realize themselves. This allows us to explain how personal history as well as cultural factors such as gender or race shape the models available to FND patients to express and cope with their disorder. Notably, you describe psychogenic non-epileptic seizures (PNES), a form of symptom occurring during FND, "as a complex form of communication, which is not merely a constellation of symptoms distributed across the mind-body divide, but also a complex language for soliciting interactional collaboration in coping" (Canna & Seligman, 2020, p4). What do you think PNES can tell us about the cultural models available to FND patients to express their symptoms? How do you think gender and race shape not only predispositions but also the way FND patients might express or relate to their bodily symptoms?

During the course of our study, we decided to abandon the notion of PNES, for a more neutral NES, in order to avoid the implicit assumption that these seizures are mostly psychogenic. We do think that psychological factors are at play in all FND, but not as the only cause, and not more than in any other health condition. We strongly endorse a non-binary model of mind and body, hence reducing a condition to psychogenic-only or physical-only etiology would be theoretically and pragmatically problematic. Because of this co-constitutive nature of mental and physical aspects of health, the main intersectional variables of sex/gender and race/ethnicity are always at play.

Concerning gender, we discussed the issue of the hyper-focalization on the control of feminine bodies in the previous answer. We expect that this and other gender constructions, such as gendered models of caregiving, will play important roles in FND. Men may also interiorize gendered models, such as the model of the "tough guy" typical of many masculinities where vulnerability and dependency are morally despised, and this model may interfere with their coping mechanisms and increase risk of FND (Canna, preliminary evidence 2021). Also, race and ethnicity work at multiple levels. In our preliminary study we analyze a case where institutional racism in the US made a FND patient feel treated like a "crackhead" by the healthcare providers because of her skin color (Canna and Seligman, 2020). Medical mistrust generated by structural racism aggravates patterns of dysfunctional interoception that, in turn, may reinforce FND. When we are talking about cultural difference, we should at least disentangle between two main axes:

> i) cultural diversity as the availability of multiple models to appraise and reappraise symptoms, a process that can be negative, positive or neutral. For example, in Brazilian Candomblé individuals who experience loss of control over their bodies and consciousness learn to reappraise and shape the experience as opportunities to connect with gods (Canna and Seligman, 2020).
>
> ii) racial and ethnic variables as different positional identities in a single society, often entailing power differentials. In the US, where we are conducting our study, a long history of medical mistrust affects in particular Latinx and African American populations (Sewell, 2015) and this is just one among the manifold variables that count in the modulation of FND.

> "We strongly endorse a non-binary model of mind and body, hence reducing a condition to psychogenic-only or physical-only etiology would be theoretically and pragmatically problematic."

You argued that "although the three dimensions that we presented—the embodiment of cultural meaning, the conversion of chronic stress and the impact of stigma—are particularly evident in PNES, (...) the range of their applicability can be extended to other Functional Neurological Disorders, and other Somatic Symptom Disorders as well" (Canna and Seligman, 2020, p.7). In FND, the conversion of cultural models into symptoms is rendered clear-cut from the fact that the physiological state by definition does not match the symptoms expressed.

Do you think these dimensions play a role in a larger spectrum of diseases in which psychological factors play a role in the apparition and expression of somatic symptoms, such as psychosomatic disorders? What features of the patient and environment might be important to measure to study the interactions between somatic symptoms and cultural variables?

Coming back to trance, there are cases in which people are possessed and their experience is attributed to the presence of some external force controlling their body and mind. Do you know about any reports of changes in interoceptive abilities in this case? More generally, the contribution of mind-body relationship to consciousness is drawing more and more interest, inasmuch as the integration of the visceral signals into cognitive activity has been proposed as a foundation for the subjective component of conscious experience (Nikolova et al., 2021; Park & Tallon-Baudry, 2014). How do you think that the study of interoception and its cultural shaping can be a promising avenue of research for the study of the diversity of conscious states?

The cultural shaping of interoception is without any doubt a promising avenue for further research not only on FND, but on all the somatic dimensions of any other condition. As mentioned previously, we endorse a strongly non-binary model of health and human experience. What we call "mind" and "body" in Western societies are not separated entities in many other cultures. Hence, we don't see any structural reason—beyond conventional disciplinary boundaries—to consider the physical and the mental as two separate realms. One of the main reasons for our interest in FND is that it is a compelling illustration of the artificiality of the mind/body divide. In the case of FND, the mind/body divide comes to its most nefarious consequences: inadequate healthcare and a long history of mistreatment. Theoretically, this stems from an incapability to conceive of health in holistic

terms, by taking into account the multiple entanglements of different physiological and psychological processes. Through a cross-cultural perspective, we can question the artificiality of this divide and aim at offering a more encompassing—and humanized—vision of treatment and care.

A great illustration of this is our work on trance and possession, in which mind, body and self can be seen to influence one another in powerful ways. In Rebecca Seligman's work on spirit possession, she found that certain interoceptive cues signaled the onset of trance, therefore spirit mediums were particularly tuned into these sensations and typically shifted consciousness away from self-awareness and bodiliness, to a different state. In Maddalena Canna's work a comparable tuning happens when the possession is deemed dangerous—or demonic in spiritual terms. Complex sets of interoceptive cues signal the onset of a state of consciousness where the reconfiguration of perceptive, cognitive and bodily processes is experienced as disruptive (Seligman 2014, 2018; Canna 2017, 2021). Something similar is likely to be happening in FND, but within an entirely different context of meaning—one in which the connection between mind, body, and self is not embraced. Thus, different contexts of meaning can radically shift interoception and the experience of somatic symptoms.

These ideas are supported by some interesting recent neuroscience research on the "Material Me" (Seth 2013), which suggests that interoceptive functions—or interoceptive affordances, as we call them—can be at the origin of the most primary sense of self. By closely monitoring this process—in collaboration with the patients as active participants in our investigation—we hope to pave the way not only for a better understanding of FND, but most broadly for a more encompassing model of human health.

“ Through a cross-cultural perspective, we can question the artificiality of this divide and aim at offering a more encompassing—and humanized—vision of treatment and care ”

The stigma surrounding mental diseases and its internalization by patients plays a primary role in the severity of symptoms, adherence to treatment and the outcome of the disease (Livingston & Boyd, 2010). In line with this consideration, you argue that "effective treatments of FND must act as "moral laboratories" where individuals' selves are reshaped through innovative social experiments that serve to modify moral appraisals of their symptoms. In the current context of the quality-of-care crisis, effective therapies must be based on the co-construction of a common ground of meaning between patient and therapist." (Canna & Seligman, 2020, p.5).

More generally, I would like to frame this type of approach as part of a bigger movement of "action research", where scientific research is thought as integrated within and accompanying social action. How do you think anthropological research can be incorporated into medical contexts to integrate medical treatments skillfully and appropriately with morality, bioethics, and personal preferences?

Anthropological research *is* action, at many levels. First of all, ethnography, which is the staple of anthropological methodology, is a method based on establishing a qualitative, in-depth exchange with our participants. Maddalena Canna likes to say that, as anthropologists, we don't study people, we study *with* people. When we conduct our usual 2-3-hour long sessions of dialogue with the participants (also called the one-on-one in-depth interviews) many things happen. Some participants may experience their symptoms, e.g., functional paralysis and blindness, during the interview, monitor them with the researcher in real time, and sometimes identify meaningful connections to what is being discussed in the interview.

This is just an example of how qualitative methodology is generative by itself. This verbal *and somatic* dialogue not only fosters self-reflexivity in the participants, but also offers the empathy and participatory care that many patients can't find in the current healthcare system. In this sense, we aim at offering a first, immediate response to the current quality-of-care-crisis described by many patients, who feel that the healthcare system is more and more compartmentalized and dehumanized (Marcum 2008, Oldani 2014, Eck 2020). Providing the participant with a context for expressing their distress in their own words and being recognized for the specificity of their

> “ Anthropological research *is* action, (…) we don’t study people, we study *with* people. ”

experience can impact on further coping, if not healing. During her ethnography of seizures related to demonic possession in Nicaragua, Maddalena Canna used drawing as a means to establish a non-verbal dialogue with sufferers. Many of them experienced the processes of drawing their demons as a healthy expulsion of pathogenic meanings, a form of assisted self-healing practice (Canna 2017). Even if we won’t go as far as considering ethnographic dialogue as a healing process in and of itself, we do consider that the process of recognition intrinsic in qualitative research is likely to have a positive impact on the overall wellbeing of the participants.

Also, our methodology includes a practice of self-journaling, providing each participant with a digital platform to monitor symptoms and comment on them in real-time through a phone application (mEMA, mobile Ecological Momentary Assessment). This provides an additional occasion for a participatory analysis of what daily living with FND entails. Our participants are extremely well-informed and aware of the scientific literature, as well as aware of the social representations and misrepresentations circulating on FND. FND are still a mostly unknown and frequently misrecognized condition. Participants/patients are eager to work on furthering awareness and global education about FND, by contributing not as objects, but as active participants of our study. In the long term, trends are emerging in the treatment of FND towards a multi-disciplinary approach, bringing together not only psychologists and neurologists, but also social scientists and workers, towards increasingly integrated care (Bael and al., in press).

Our project is a pioneer in this direction, as it is the first federal project on FND lead by social scientists in the US. In addition, we strongly believe that anthropological knowledge can be translational, allowing it to be applied in different kinds of practice. While translation can be challenging, one of things that we excel at in anthropology is understanding the different stakes

and stakeholders, social and political dynamics in different contexts. This kind of insight can help us translate the findings of this work on FND in terms that will be meaningful to clinicians. In so doing, we hope to pave the way for a more multi-faceted, multi-disciplinary approach to treatment and care for people living with FND.

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Indian philosophy and the value of transformative experiences

An interview with Monima Chadha

by Edvard Avilés and Matthieu Koroma

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Abstract

In this interview, we engage in a cross-cultural discussion about the diversity of consciousness. Indian philosophy can seem quite cryptic and difficult to follow because it is a primary oral tradition. However, Monima Chadha has developed a series of work aiming at introducing the rich insights of Indian philosophy of mind into the western literature. Key aspects of metaphysical debates such as the nature of consciousness and the notion of no-self are framed in Indian philosophy as primarily guided by the aim to achieve enlightenment or liberation. Altered states of consciousness are considered as transformative experiences and meditation is highlighted as an additional resource in the Indian tradition to gain insight into the nature of consciousness.

keywords: *Indian philosophy*, *consciousness*, *meditation*, *transformative experiences*, *psychedelics*, *no-self*

You are an Associate Professor in Philosophy at Monash University (Melbourne, Australia). In your research, you discuss contemporary debates of philosophy of mind, including consciousness, through the lens of Buddhist and Hinduist philosophy. Would you say that your interest for Indian philosophy led you to your interest for the philosophy of mind or the reverse? Is there something in particular in the Indian philosophical corpus that sparkled your interest?

I have always been intrigued by issues in philosophy of mind and language, so in a sense it was philosophy of mind that came first. My interest in Indian philosophy was sparked by the Buddhist no-self doctrine. Some Buddhists, *Abhidharma* philosophers in the northern Indian tradition, in particular, claim that the work of the self can be transferred to the mind. The self is an ontological dangler that does not do any causal work. I became interested in investigating this claim.

An important concern for a lot of traditions in Indian philosophy (both *Astika* and *Nastika* systems) has been the nature of consciousness. However, Indian philosophy has been totally overlooked in the standard curricula of the philosophy of mind despite the fact that a lot of the contemporary discussions are about consciousness. In fact, a typical course starts with Descartes and ends with discussions about Chalmers' philosophical zombies ignoring more than 4000 years of Indian reflections about consciousness. Do you have a diagnostic of why this is the case? How could Indian philosophy contribute in your opinion to our understanding of the mind and do you have any suggestions of Indian texts or readings to implement in the philosophy of mind curricula to overcome this gap?

I hesitate to recommend texts because the Indian tradition is primarily an oral tradition. So, the texts are quite cryptic and difficult to follow. For example, the famous *Nyaya* proof for the existence of the self in *Nyāya-sūtra* 1.1.10 states that "Desire, aversion, effort, pleasure, pain etc. are the inferential signs of the self". Then there is the whole corpus of the *Nyaya* commentaries on this sutra which itself contain many sophisticated arguments for the existence of the self. The other problem is that good translations of the primary texts have been few and far between. The situation is changing now. Books I would recommend readily for undergraduate curricula.

1.The *Nyāya-sūtra*: Selections with Early Commentaries trans. by Matthew Dasti and Stephen Phillips.

2. The Concealed Art of the Soul, by Jonardon Ganeri

3. Buddhism as Philosophy by Mark Siderits.

> “ I hesitate to recommend texts because the Indian tradition is primarily an oral tradition. ”

Since the 90's there has been a rising interest in the neuroscience of consciousness. In the field, neurobiologists and psychologists usually operate with a cognitive concept of consciousness: consciousness is cognitive access (roughly: awareness). Some philosophers have objected to this framework that a cognitive concept of consciousness isn't enough, to solve the hard problem we need to target what's like to be in a certain state (roughly: experience) (Chalmers, 2007). Are there different conceptions of consciousness in the Indian tradition?

Our pre-theoretical concept of consciousness is a mongrel concept which calls for refinement if it is to do useful work for a theory of consciousness. Just like Block and Chalmers in the contemporary scene, the Indian philosophers also suggested many refinements and distinctions to be made within the concept of consciousness. But I don’t think we can map them directly onto distinctions drawn in contemporary philosophy. This requires careful comparative work which is yet to be done. That said, I do think there are echoes of the phenomenal/cognitive distinction in the *Abhidharma* tradition in that the notions of feeling (*vedana*) and perceptual discrimination (*saṃjñā*) as components of consciousness, but I do not think this clearly maps onto the phenomenal/cognitive distinction.

A lot of people would agree with the claim that phenomenology makes life worth living. A good life is about -among other things- having good experiences. Similarly, prolonged experiences of suffering can undermine the value of our life. So, there seems to be an important connection between consciousness and value. One explanation of this connection is that experiences themselves have an intrinsic valenced dimension (experiences feel good, bad, pleasant, unpleasant, etc). Furthermore, both consciousness and suffering played an important role in some Indian doctrines, for example, the doctrine of *samsara* in the Upanishads and *duhka* in the first noble truth of Buddhism. However, with few exceptions (Kriegel, 2019) in contemporary philosophy of perception, the study of consciousness is focused on the sensory features of experience ignoring its valenced aspects.

What do Indian traditions have to say about the relationship between consciousness and value?

A primary concern that motivated most philosophers in ancient India was to find the best way forward in an individual person 's quest for liberation from suffering. All living beings are trapped in the cycle of birth and rebirth (*saṃsāra*) which according to most classical Indian philosophers, is characterised by suffering. The highest goal of life is liberation (*mokṣa* or *nirvāṇa*). Except the *Cārvāka* materialists who believed that death is the end and there is nothing like rebirth or liberation, all other philosophical schools believed in the possibility of liberation in this life or in future lifetimes. The ultimate aim of the classical Indian philosophy teachings is thus to help individual persons attain liberation or at least a better life in this life and future lifetimes. Most classical Indian philosophers agreed that our ignorance about "who we really are" is the source and the means to bringing an end to suffering. Thus, metaphysical debates about the nature of consciousness and the universe and our place in it are central to the classical Indian philosophical traditions, but only insofar as they suggest a route to liberation.

Current debates on consciousness tackle the possibility that consciousness is an illusion (Frankish, 2016). The notion of illusion has been deeply anchored in the Indian philosophical tradition, such as the concept of maya, the idea that the phenomenal world is illusory, being central for the Hinduist *Advaita* school. Do you see a way by which discussions in Indian philosophy on consciousness echo and differ from contemporary debates about the nature of consciousness?

You are right the notion of illusion gets much airtime in the *Advaita* Hindu tradition, but it has an equally important role in all other Indian traditions as well. This should come as no surprise, philosophers in all traditions have been interested in illusions in the discussions of perception, consciousness and ontology. The discussions in Indian philosophy differ because the primary aim guiding Indian philosophers is how to achieve enlightenment or

> "The discussions in Indian philosophy differ because the primary aim guiding Indian philosophers is how to achieve enlightenment or liberation."

liberation. This concern gives the Indian discussion of consciousness a different flavour, but in the end, this concern cannot be divorced from the nature of human beings and what they are capable of. So, the Indian philosophers are indirectly led to metaphysical and epistemological questions about the nature of the world and human beings within it. Keeping this primary aim in mind, we should consider what the Indian philosophers have to say about the mind and we will see many of the same questions being discussed in the classical Indian debates.

One of the most important doctrines in the Upanishads and the *Advaita Vedanta* is the identity between *Brahman* and *Atman* (self). A tendentious reading of this claim is that fundamental reality involves consciousness. Similar claims are found in unorthodox systems, like *Abhidharma* Buddhism. Furthermore, in the contemporary metaphysics of mind, Russellian Monists have championed the idea that fundamental reality involves consciousness (or proto-phenomenal properties) in a widespread manner (Goff, 2017). What are the main differences between *Vedanta*'s panpsychism and *Abhidharma* panpsychism? Do any of these views have something to say about the combination problem for contemporary panpsychism?

Vedanta panpsychism is rooted in their monism: consciousness is the only reality. *Abhidharma* Buddhism accepts physical and mental atoms as part of the basic furniture of the universe. This, I think, is the most important difference. I am not sure what Vedantins have to say about the combination problem, but there is a new special volume of the *Monist* coming out in January 2022 which addresses Cosmopsychism (the holistic counterpart of panpsychism) and Indian philosophy might have more thoughtful responses to this issue. I have a paper forthcoming in that volume which suggests that the *Abhidharma* philosophers have various resources that they may use to respond to the group of problems that are called combination problems: the subject combination problem, the quality combination problem, etc.

You recently explained how *Abhidharma* Buddhism had a panprotopsychist account of reality based on the notion of *dharma* (Chadha, 2019). *Dharmas* can be described as particular qualities of existence and they can be aggregated into subjective experiences under the combined action of mental processes. Our attention has been brought on the suggestion that differences in metaphysical conception about consciousness may depend on practices, as you say:

"If we think that conscious states supervene on collections of present mental *dharmas* which are best thought of as proto-conscious or proto-intentional features as the result of logical analysis, then we favor the panprotopsychist option. Alternatively, if we hold that mental *dharmas* are potentially phenomenologically available as they can be discerned as such by experts who have mastered the art of mindfulness meditation, then we favour the panpsychist option." (p.31).
Could you elaborate on how Buddhists have conceptualized the interrelation between understanding consciousness and experiencing conscious states? How can the experience of conscious states such as meditation change our ideas about the nature of consciousness?

This is a difficult question to answer because there is not one Buddhist view. There are many different Buddhist traditions, and they have different views about conscious states. I think that it is worth emphasising is that there is nothing like mind or consciousness, all there is, is a collection of mental states and conscious experiences. And again, there is not one kind of meditation but different meditation practices depending on the tradition. To take an example, in Vasubandhu's seminal text the *Abhidharmakośabhasya*, mindfulness meditation is explained carefully as a stepwise progression. Mindfulness meditation has the aim of curbing thoughts that proliferate naturally because of the variety of external objects and karmic imprints. This aim is achieved by controlling the mind by focusing attention on breathing to eliminate mind-wandering. The initial aim of mindfulness meditation is to train the mind to fix attention on the complex phenomenon of breathing in order to analyze or break down the phenomenon into its most basic constituents (*dharmas*), so that the meditator discerns the real nature of conscious experiences. The process of meditation, however, reveals that the realization of the real nature of ultimate *dharmas* (impermanence, suffering, emptiness, and being not-self) results in an attitudinal and behavioural change. The knowledge of real nature of self and other objects leads to the cessation of all emotional attachments and desires.

Both neuroscientists and philosophers recognize the role of introspection and first-person data for a science of consciousness. What's the role of introspection and first-person data to understand consciousness in the Indian traditions? Does the Indian philosophical legacy have something to contribute to the prospects of a scientific understanding of consciousness?

> “ Indian philosophers have an additional resource in first-person data available in meditative experiences. ”

Philosophers cannot afford to ignore first-person data and introspection if they want to understand the nature of consciousness. Indian philosophers have an additional resource in first-person data available in meditative experiences. The “special access” to one’s own conscious states available in conscious experiences is amenable to be investigated by third-person methods in neuroscience of consciousness. This has the potential to offer additional insights that might contribute to a scientific understanding of consciousness. But it needs a deeper understanding of the particular Indian tradition in question and the role that meditation practices are supposed to lead to intellectual and spiritual progress.

The practice of meditation (*dhyana*) is pervasive among the Indian philosophical tradition. Through meditation, altered states of consciousness can be attained through which fundamental insight about the nature of reality can be attained. In some traditions, this is known as '*samadhi*'. The very idea of *nirvana* also suggests something similarly. On the other hand, it is well-known that psychedelic drugs can induce states of *depersonalization* and more radically, *ego-dissolution*, in about 7% of trip reports of high-dosage intakes of *Psilocybe* mushrooms, LSD, Salvia, DMT, 5-MeO-DMT, ayahuasca and ketamine (Millière, 2017). Despite being rare, these experiences have been interpreted in relation to the Buddhist concept of no-self (*anatman*) by some early advocates of the use of psychedelics such as Timothy Leary or Aldous Huxley (Huxley, 1999; Leary et al., 1964). What role do altered states of consciousness play in Indian meditative practices? Do you think that we can interpret the lack of self in conscious experiences under psychedelics in the light of Buddhist philosophy?

I think it is better to describe the altered states of consciousness as transformative experiences. These experiences, at least in the Buddhist tradition are brought about by a variety of spiritual exercises. In keeping with the general Buddhist tradition Vasubandhu in the *Abhidharmakośabhasya* notes that the spiritual path is an integrated system of *śīla* (moral conduct)-*samādhi* (meditation)-*prajñā* (wisdom or internalization of philosophical

> “ I think it is better to describe the altered states of consciousness as transformative experiences. ”

insights of the Abhidharma tradition). In the commentary that follows, Vasubandhu writes that whoever desires to see the truths should first of all guard morality (*śīla*), then they read the teachings on which the insight into the truths depends, and listen to their meaning, having listened they reflect on the teachings, and having reflected, they devote themselves to the cultivation of meditation. You can interpret the lack of self in conscious experiences under psychedelics in the light of Buddhist philosophy, but I think that would be unfair to the tradition. The experience of no self in meditation is not an isolated phenomenon, it is embedded within the spiritual exercises considered as a whole, including knowledge of Buddhist philosophical insights.

> “ The experience of no self in meditation is not an isolated phenomenon, it is embedded within the spiritual exercises considered as a whole, including knowledge of Buddhist philosophical insights. ”

In the Buddhist traditions, the notion of no-self has both metaphysical and practical aspects, as holding the self as a substance is considered not only as a false view about the reality but also as a source of suffering. How do Buddhist traditions explain the therapeutic effects that can be attributed to a change in our views about the self? Would you think that some aspects of Buddhist philosophy could be useful to anchor therapeutic effects of psychedelics by offering an understanding of the mental states being experienced and their significance?

Belief in a continuing self is the basis of our special concern for our own future self. We do put away money in superannuation rather than giving to charity? Because we care more about our future self than contemporary others, some of whom are suffering. The Buddhists do recognize that it is built-in precondition of our form of life that we have self-concern and special concern for our loved ones. That is why the Buddhists do not recommend

giving up on this self-concern or special concern for our loved ones. Rather they recommend extending similar concern to others. And they do not think that such an extension comes easy to us given our human nature: it has to be inculcated by extensive meditation practices. As Parfit puts it, the discovery of no self is liberating and consoling! Given what I've said in response to the last question, I don't think we can better understand the therapeutic effects of psychedelics by turning to Buddhist philosophy.

The *Abhidharma*-Buddhist metaphysics of persons has some important similarities to a 4D ontology of temporal parts (Sider, 2001), in particular, to a 'stage-theory' in which persons are momentary beings that strictly speaking don't persist through time (impermanence). The stage theory has important theoretical advantages in dealing with classical puzzles of the metaphysics of material objects. However, when the stage theory is applied to persons (Olson, 2007), it faces an immediate objection: diachronic features seem rather crucial in personal identity. Even if not for metaphysical reasons, some practical affairs seem essentially diachronic (*e.g.*, norms of rationality, responsibility, and regret, etc). How do you think the *Abhidharma* theory of persons can deal with this problem?

The central normative goal of Buddhism is to ameliorate suffering and that guides its revision of descriptive metaphysics. The no-self and no-person metaphysics aims to produce a better structure that is motivated by the normative goal of eliminating, or at least reducing, suffering. Buddhist revisionary metaphysics is not aimed at capturing the structure the world really has, and a justification of our ordinary person-related practices. Rather it aims at providing a structure that aims to reduce suffering. The revised structure, in turn, entails a major reconsideration of our ordinary everyday person-related concerns and practices and interpersonal attitudes, such as moral responsibility, praise and blame, compensation, and social treatment.

ALIUS is most interested in the diversity of consciousness. This involves both discussing the diversity of conscious states and the diversity of disciplines or cultural outlooks that can inform a scientific understanding of the nature of consciousness. What are the challenges according to you in developing a cross-cultural discussion about consciousness and the mind? What is your approach to overcome these challenges?

One of the most important challenges is to draw the attention of mainstream

philosophers of mind and consciousness to pay serious attention to the classical Indian tradition and what it has to offer. There is not just the language barrier but also the misconception that Indian philosophy is mostly mystical mumbo-jumbo. Correcting that misconception is a hard task. So my approach has been trying to publish in mainstream journals rather than specialist Indian philosophy journals so that these materials have a chance of broader uptake. It is hard, but I think it is worth doing.

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Are the Subjective Effects of Psychedelics Necessary for Their Enduring Therapeutic Effects?

A conversation with David E. Olson and David B. Yaden

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Abstract

ALIUS recently invited Dr. David E. Olson and Dr. David B. Yaden to discuss whether or not the subjective effects of psychedelics are necessary for their enduring therapeutic benefit in an interactive online discussion. The aim of this discussion is to examine their most recent back-to-back publication wherein Yaden & Griffiths (2021) emphasized the subjective effects of psychedelics, such as mystical experiences, in relation to their long-lasting therapeutic effects, whereas Olson (2021) emphasized that there are certain therapeutic benefits related to the psychoplastogenic properties of these substances that are unrelated to their subjective effects. We invited the authors to clarify the fine points of their arguments and to tease out any point of disagreement between these two perspectives. What follows is an edited transcript of their discussion.

keywords: *psychedelics*, *psychoplastogens*, *subjective effects*, *therapeutics benefits*, *treatment ethics*

Although you are addressing two sides of the same coin, your back-to-back publications are primarily aimed at questioning whether the subjective effects play a causal role within the therapeutic process, or whether it can be regarded as an epiphenomenon that accompanies therapeutic outcomes, but not a principal mechanism.

The first question is related to the subject-matter of dualism, and whether the comparison between neuroplasticity alone versus neuroplasticity plus subjective experience implies that there is a dichotomous relationship between subjectivity and the neurobiological substrate. How do you define the subjective experience, in terms of its biological function and embeddedness within a neurobiological substrate? What is its relationship to neuroplasticity? Are these pitted against each other within your scientific framework in a manner that implicitly endorses dualism?

D.B. Yaden: I would like to take this one first. If you don't mind David, I think both of us agree on so much and this particular topic of dualism was definitely something that we agreed on from the get-go. My co-author Roland Griffiths and I talked quite a bit about whether to include a discussion of dualism or not at the beginning of our article. We were constrained by word limits, but also we just thought it was so screamingly obvious that we weren't promoting any kind of dualistic notion of consciousness in our viewpoint that it didn't seem like we really needed to cover this point in depth. But several of our colleagues have been worried that people might take away the misconception that we are promoting a kind of mind-matter dualism with our argument, and I think that that's just absolutely not the case.

Basically, the question of the nature of consciousness, what it actually consists of is referred to as the "hard problem of consciousness" and it's unclear at this point what any kind of scientific explanation of the nature and origin of consciousness might be. So I think it is best to take that topic and set it aside and leave that for more of a philosophical discussion, at least in my view.

When we are talking about subjective effects we are talking about drug effects on what is referred to sometimes as phenomenal consciousness, the "what it feels like" quality of being—as in, we are all looking at a screen, we are all in rooms, we are all listening to my voice at the moment. And this is what we mean by subjective effects, we are absolutely not referring to any kind of sense of consciousness beyond something that is tractable, at least theoretically, in terms of neurobiology.

D.E. Olson: I actually think maybe it's the other way around, where the plasticity effects are an epiphenomenon arising from subjective experience. I think that the production of the subjective effects will inherently lead to the plasticity effects, but the question of whether or not you can decouple those two is one we are actively pursuing.

[When I'm talking about the subjective effects of the drug] I lean on experts like David Yaden and the questionnaires that they have developed, such as the Mystical Experiences Questionnaire.

> “ D.E. Olson: I actually think maybe it's the other way around, where the plasticity effects are an epiphenomenon arising from subjective experience. ”

Would you treat these two phenomena of 'the subjective' and 'the neurobiological' according to a micro-level and a macro-level explanation of their causal role? On the one hand, neuroplasticity seems to be specific to events that take place on the level of cells and receptors, whereas subjective experiences seem to describe events that take place on the level of brain states and their corresponding external correlates. Would you argue that there is any privileged level of causation when it comes to investigating what should be regarded as the principal mechanism of therapeutic effects?

D.B. Yaden: I want to address at least part of your question, which still seems to take issue with misconceptions around dualism. As we know from the work of Paul Bloom and others, people are intuitive dualists, they think of mind and brain as two separate things. This is also reflected in the way our language is structured. People say things like *"my brain is thinking"*, and it's difficult for people to imagine that their thoughts and feelings have a neurobiological substrate.

This is also the kind of thing that psychologists and neuroscientists will take for granted when they are talking, but the vast majority of neuroscientists

believe that even very abstract mental states are ultimately reducible to neurobiological changes. Even if we do not specifically know the complex array of brain changes at a really granular level that instantiate complex feelings, such as the sense of space, time or connectedness—these are all still brain changes.

I agree with David Olson about the psychoplastogenic effects of psychedelics and that there would likely be some therapeutic benefit with or without the subjective effects. We also agree that the subjective effects probably are necessary for *full and enduring* therapeutic effects. Cognitive and affective processes seem to be what is conveying beneficial effects for four months or more, and it is amazing that we see positive effects persisting for so long. That is what makes these compounds so interesting from a clinical standpoint.

> “ **D.B. Yaden:** Even if we do not specifically know the complex array of brain changes at a really granular level that instantiate complex feelings, such as the sense of space, time or connectedness—these are all still brain changes. ”

D.E. Olson: I agree with all of the above and share the opinion that brain states are essentially the emergent properties of circuits, built up on cells, built up on proteins, built up on ligands, etc. More importantly, I want to emphasize that my argument is *not* that the subjective effects are unimportant for the therapeutic response.

In fact, the subjective effects of compounds like psilocybin are probably really important for their maximal effects. But they may not be necessary for certain types of therapeutic responses, and whether or not that leads to maximal efficacy is an entirely different question. I still think that it's possible to get enduring effects, but maybe they do not last quite as long. We just don't know yet, as this is still an open question.

> **D.B. Yaden:** I agree with David Olson about the psychoplastogenic effects of psychedelics and that there would likely be some therapeutic benefit with or without the subjective effects. We also agree that the subjective effects probably are necessary for *full and enduring* therapeutic effects.

> **D.E. Olson**: my argument is *not* that the subjective effects are unimportant for the therapeutic response. In fact, the subjective effects of compounds like psilocybin are probably really important for their maximal effects.

One aspect of the article that many people in the psychedelic community appraised critically was the statement that:

"the intense subjective effects of these drugs make it unlikely that they will ever become widespread treatments for disorders such as depression." (Olson, 2020).

However, it seems that you agree on nearly every aspect of each other's perspectives. Are there any points of disagreement?

D.B. Yaden: I am also wondering whether this portrayal of the subjective experience is intended to depict it as overall challenging and inherently risky. While our psychometric data show that the acute stage after ingesting psychedelics can be quite difficult and challenging, the experiences are overall overwhelmingly positive, reaching a degree of meaning that we rarely see in other contexts. The empirical data from these clinical trials show that these experiences are often among the most meaningful experiences that one can possibly have. But I can imagine there are people who have contraindications, such as some kinds of mental disorders like psychotic disorders or certain family histories, where the psychedelic experience would be inappropriate. Of course, there's risk in any kind of treatment. Therefore, I am also curious to know David Olson's thoughts on this matter.

> **D.B. Yaden:** While our psychometric data show that the acute stage after ingesting psychedelics can be quite difficult and challenging, the experiences are overall overwhelmingly positive, reaching a degree of meaning that we rarely see in other contexts.

> **D.E. Olson:** My statement also did not mean to convey that substances such as psilocybin only produce challenging experiences that are going to be problematic for people.

D.E. Olson: I am sorry if it came across this way since it was not my intention to portray the subjective experience as inherently challenging. My statement also did not mean to convey that substances such as psilocybin only produce challenging experiences that are going to be problematic for people. I am certain that psilocybin will ultimately be approved by the Food and Drug Administration (FDA) for some kind of indication, and I have a lot of hope for the patients who are going to benefit from this type of therapy. When I say that it will not be a widespread medication, that has to do with two factors.

The first one has to do with the fact that the subjective effects of psilocybin make it hard to administer outside of the confines of a clinical setting. I think that these drugs will always be administered under the care of a physician, and it is not going to be the type of medicine you can take home and put in your medicine cabinet like a Selective Serotonin Reuptake Inhibitor (SSRI).

The other reason is related to the healthcare costs associated with that type of model right now. People have to undergo fairly long preparation and integration sessions with the clinicians, which requires a lot of time spent in the presence of a healthcare provider. I think that it is going to be challenging

to treat a large number of patients, and approximately 20% of the population suffer from some type of neuropsychiatric disorder.

I do think that some people, especially those with treatment-resistant depression, are going to benefit greatly from things like psilocybin, and so it will become a regular part of the psychiatrist's arsenal. I just do not think they will become as widespread as SSRIs.

From a clinical standpoint, there are certainly some patients for whom the subjective effects of psychedelics may not be appropriate and may thus benefit more from the psychoplastogenic effects. But do you think the goal of decoupling the subjective and the psychoplastogenic effects is scientifically feasible?

There are several studies showing that neuroplasticity is also enhanced through exposure to enriched environments, a process that is commonly mediated through the neurotrophic factor BDNF (Cowansage, LeDoux, & Monfils, 2010). This type of neuroplasticity is also elicited by 5-HT2A agonists and selectively blocked via ketanserin (Vaidya, Marek, Aghajanian, & Duman, 1997). The natural coupling between plasticity and enriched environments may serve a crucial function in facilitating social adaptation and learning. Do you think there is any inherent risk in disrupting the coupling between the neuroplasticity and the subjective experience of psychedelics?

D.E. Olson: One thing I want to emphasize is that pretty much every treatment for depression, from classical antidepressants, exercise, or acute sleep deprivation, to next generation therapeutics like ketamine or transcranial magnetic stimulation—they all seem to promote neuronal growth, particularly in the prefrontal cortex. Psychedelics just seem to be particularly good at this. I take it that this question is asking how the experience is involved in plasticity. People often ask what happens if you are promoting plasticity in a negative context and whether this will have a negative effect on the subjects.

Plasticity can mean a lot of different things to different people, and what I am referring to is the ability of psychoplastogenic drugs to promote the

growth of particular neurons. Our line of work was inspired by research on extinction learning, where the idea is to promote plasticity in order to enhance the extinction of a fearful memory. You might expect that if you promote plasticity, before you do fear conditioning, this might enhance the formation of fear memory. Originally, we thought that might happen, but this turned out to be false, at least in rodents. We would administer psychedelics to rodents in an attempt to enhance fear memory that was formed by conditioning a tone to the expectation of a mild foot shock. But psychedelics did not enhance this fear memory, but instead enhanced the safety memory, or fear extinction memory.

The reason we think this is the case is because the specific circuits involved are different. Circuits that mediate the safety memory involve neurons in the prefrontal cortex that tend to grow in response to psychedelic drugs. So when we started, we thought that psychedelic-induced plasticity would amplify all of the subjective effects, but we surprisingly found that it only had antidepressant and anxiolytic properties, regardless of whether the subjective experience was good or bad, in rodents.

Do you think that psychedelics should be implemented as a first-line treatment for depression, or should patients first attempt a treatment option that does not carry the risks related to the subjective effects?

D.E. Olson: I do not necessarily think that psychedelics should be a first line treatment, like SSRIs currently are. I think that they should rather be used for treatment-resistant populations after something that can be administered more easily, fails, and only then moves on to the psychedelics. But I also think that we need to do everything that we can to just make sure patients are being treated with what they need. Another thing to consider is that psychedelic assisted psychotherapy is contraindicated for people with psychotic illnesses or a history of mental disorders. Psychiatric disorders have a lot of overlap and comorbidity, so there will probably be a subset of patients who will not be able to use these treatments safely. In these particular cases, the non-hallucinogenic version of the drug might have some advantages.

> **D.E. Olson:** I do not necessarily think that psychedelics should be a first-line treatment like SSRIs currently are. I think that they should rather be used for treatment-resistant populations after something that can be administered more easily fails, and only then moves on to the psychedelics.

D.B. Yaden: I think we both agree that for some people, the treatment without subjective effects would be important for contraindications and other safety reasons. On the other hand, we are mostly talking about the ethical concerns around the risks of psychedelics without factoring in the potential benefits. I think the attention to risk is extremely important, since many people are not aware of them in seeking treatment for depression. But in terms of implementing psychedelics as a treatment option, I think the burden of proof lies on the proponents for non-subjective psychedelics, in terms of both risks and benefits.

There is a high socioeconomic burden for society from the many people who suffer from a mental illness in addition to the personal suffering. So there is an argument to be made that we don't invest enough in treatments that we know work. Psilocybin appears to be a treatment that works, though more research is still needed, but the cost-benefit analysis may easily show that there is an obligation to provide people with the most effective treatment. Maybe this is a philosophical question, but if you can provide an experience that many people report as being the most meaningful of their entire lives, is it unethical to withhold it from them?

There are real risks, but there are also tremendous benefits. I am open to the possibility that psychedelics may actually be a more effective first line treatment than then getting on SSRIs, but I do not think this question can be resolved based on the current state of evidence. Either way, I am open to both possibilities until more research is available.

> **D.B. Yaden:** We don't invest enough in treatments that we know work. Psilocybin appears to be a treatment that works, though more research is still needed, but the cost-benefit analysis may easily show that there is an obligation to provide people with the most effective treatment.

A major criticism regarding the therapeutic benefits attributed to the subjective experience is that the data are largely correlational. Do you have any suggestions for improvements, from a methodological standpoint?

D.B. Yaden: The first thing you learn in any statistics class is that correlation does not equal causation. But actually, correlation can *imply* causation, in the sense that it indicates there is a possibility of causation. Correlation is often a first step along that path of determining causation, and there are certain features of the subjective experience that do seem to predict therapeutic responses weeks or even months later. In my opinion, this indicates that psychedelics elicit affective or cognitive processes that could potentially go on to have ripple effects.

In terms of testing this, it's very difficult. Our article Yaden & Griffiths (2021) discusses the possibility of administering psychedelics under general anesthesia, where people have little to no awareness or memory of the subjective experience, to see whether there are persisting therapeutic effects. This raises a lot of ethical issues, it is a bit of a risky, and fairly difficult to do practically. But it is a basic science question, so I am actually surprised why there has not been rodent research conducted on this topic yet.

I think this study needs to be done, and I'm very curious about the results. My strong suspicion would be that being awake will result in much larger and more enduring therapeutic effects than being heavily sedated. Of course, you have to worry about drug interactions between the kind of anesthetic that's used and the psychedelic.

D.E. Olson: In order to experimentally determine what causes the most enduring therapeutic effects, I think you either need to find a way to block the subjective effects, while leaving the plasticity promoting effects intact, or vice versa: block the plasticity promoting effects and leave the subjective effects intact. There are a couple of ways to do this, depending on whether you consider ketamine as a psychedelic.

The first is to administer psychedelic compounds under anesthesia, and one way to get around the ethical issue is to look at patient populations who are going into surgery anyway. If you count ketamine as a psychedelic, then there are at least three studies where people were given low doses of ketamine while they were under anesthesia. Although this patient population was not being treated for severe depression, they reported long-lasting, profound elevations in mood. Future studies should look into this with treatment resistant patient populations as well.

The other thing to consider is the difference between R- and S-Ketamine enantiomers. As you may know, these are left-handed and right-handed versions of the same molecule, and the left-handed S-enantiomer is FDA approved for treatment-resistant depression under the brand name Spravato by Janssen. My understanding is that this version was chosen because it has a higher affinity to the NMDA-receptor and produces stronger subjective effects. So it was assumed that it was going to produce greater antidepressant effects. But it turns out that in rodents that is not the case, and in fact the R-enantiomer which produce fewer subjective effects has a greater antidepressant efficacy.

There are actually companies now who are dedicated to using R-ketamine as the better version. Even in clinics, you have anecdotal reports that the racemic combination of the two enantiomers works better than Spravato. This might indicate that some of the subjective effects are less important than the other neurobiological effects, since the R-enantiomer is also a stronger psychoplastogen. These are also just correlations, so in addition to putting people under anesthesia to block out the subjective effects, you can produce

psychoplastogens without any subjective effects, which is what my lab is currently doing.

If we want to understand the importance of plasticity effects relative to the subjective effects, we should also find substances that produce mystical-type experiences in the absence of enhancing neuroplasticity. It would be awesome to find a drug like this, but as we discussed earlier, I believe that plasticity might always result after a mystical type experience, so it is probably difficult to decouple them in this manner. One thing that is potentially doable, is to block growth pathways downstream of the mystical experiences, and our research group is currently also pursuing this.

> **D.E. Olson:** There are at least three studies where people were given low doses of ketamine while they were under anesthesia. Although this patient population was not being treated for severe depression, they reported long-lasting, profound elevations in mood.

It is also interesting to note that the antidepressant efficacy of ketamine has a very different temporal profile compared to serotonergic tryptamines. Ketamine is fast-acting, but its antidepressant effects often wear off after 1 to 2 weeks. Is there a particular reason why serotonergic tryptamines work longer?

D.E. Olson: I have a student in my group who has a hypothesis, which he calls "the shitty fast acting antidepressant hypothesis". The hypothesis is that slow acting antidepressants like SSRIs, are really bad at turning on the same pathways that are triggered by substances such as ketamine. The idea is that ketamine activates these pathways for the duration of one or two weeks, whereas psychedelics seem to activate these pathways for even longer. We found that even if we do a short stimulation with these compounds, it activates an autoregulatory circuit that keeps neuronal growth going for a period of time.

There is also some interesting work with animal models being done by Alex Kwan at Yale around this topic (Phoumthipphavong et al., 2016). Their group found that in rodents, ketamine exposure increases spine density for about a week, which correlates nicely with the antidepressant effects. By comparison, the effects of psilocybin on dendritic spine density lasts for at least a month, which correlates nicely with the fact that the antidepressant effects are also much longer (Shao et al., 2021).

D.B. Yaden: Before I studied psychedelics, I studied mystical type experiences and altered states of consciousness caused by non-pharmacological triggers. So I am also curious to know how much more psychoplastogenic psychedelic substances are compared to other psychological experiences. Are these just slight differences or orders of magnitude? Can you give us a sense of the effect size and their scale? [questions directed toward David Olson]

D.E. Olson: I would say the difference is orders of magnitude compared to other substances, like traditional SSRIs. You will see the same types of changes in brain structure with an SSRI, but you need to administer them chronically over the course of weeks to months before you start seeing those types of changes.

In terms of subjective experiences, I do not have a way to comment on that because research is lacking a way to measure this. We have been focusing on animal models for now, but there are some exciting advances that might open future studies with a new radiotracer that labels pre-synaptic vesicles. That might be a way to "label" synapses in the brain to look for increased synaptogenesis in response to particular experiences or pharmacological interventions.

D.B. Yaden: But even in the rodent literature, are there any significant life events, like birth or changing the environment, which produce similar levels of plasticity as psychedelics? [question directed toward David Olson]

D.E. Olson: Enriched environments, i.e. filling their cages with a bunch of toys for them to play with, produces lots of neuronal growth in the cortex. So does exercise—if you expose mice to a running wheel, this also produces neuronal growth. Nobody has done a head to head analysis on whether these psychoplastogenic effects are comparable in degree to ketamine or psilocybin, but they both produce robust antidepressant effects for the rodents.

Psychedelics strongly rely on what has been termed the meaning response (Hartogsohn, 2018), which depends on the whole set and setting in which psychedelic action takes place (Hartogsohn, 2016). There is a recent paper showing psychedelic experience can be induced by placebo effects that strongly rely on contextual factors, prior expectations, and beliefs (Olson et al., 2020). What is your take on this?

D.B. Yaden: Based on placebo research, particularly the God-helmet experiment (Maij et al., 2019), it does not surprise me that you could convince someone that they received a psychedelic and see them report all kinds of vivid, subjective experiences in response.I think the study by Roland Griffiths (2006) bears well on this issue, because it compared the effects of psilocybin with high dose methylphenidate among psychedelic naive participants.
With a high dose of methylphenidate, you do feel substantially altered, so I think that it is a pretty decent active placebo control for psychedelic naive participants. I hope there will be more studies that use active placebo controls. But this standard might be difficult to achieve for experienced psychedelic users. Something like a high dose of THC might help control these expectancy effects.

D.E. Olson: I think the idea of using high dose THC is intriguing because it is unlikely to induce any type of plasticity, in fact it may even have the opposite effect. It would be very interesting to use it as a placebo control, and this is actually something that the FDA would be really interested in, because it might help control for some of the expectations.

Do you think that microdosing, i.e., using psychedelics on an intermittent schedule within a sub-hallucinogenic dose range, has a therapeutic effect?

D.E. Olson: I think that using a sub-hallucinogenic dose is a good way to control for the placebo effect, because it can also trigger the plasticity without inducing subjective effects. We investigated microdosing in rodents (Cameron et al., 2019) and it seemed to produce a similar type of antidepressant and anxiolytic response as a single dose.

But it is very unclear whether this is also the case for people because there are no placebo-controlled double-blind clinical trials on psychedelic microdosing to suggest that it is effective. I think the microdosing paradigm is actually more dangerous than a single dose paradigm, because a lot of these drugs engage the 5-HT2B receptor, which can lead to cardiovascular valvopathy if you are using these drugs on a chronic intermittent basis (*editor's note: this topic is discussed in detail by Kuypers et al. (2019)*).

The other thing to keep in mind is that chronically stimulating these growth pathways can actually lead to something that resembles excitotoxicity. The brain has a very set level of excitation that it likes, so if you are constantly exciting its pathways, you will actually see a retraction of dendritic spines in order to lower the input to these neurons. In our study within female rodents, we saw that a single dose of DMT causes a big growth of dendritic spines, whereas if you administer DMT every third day for a month, you actually see retraction of the dendritic spines. It is important to keep this in mind.

D.B. Yaden: I also think that the cardiac risks of microdosing are an important issue to raise and wanted to emphasize that we intentionally decided not to cover this topic in our paper because there is just no evidence as of yet to suggest that there's substantial clinical efficacy, or really any efficacy at all. It does appear that a certain dose is required in order to get remarkable clinical effects.

> **D.B. Yaden:** I also think that the cardiac risks of microdosing are an important issue to raise (...) and there is just no evidence as of yet to suggest that there's substantial clinical efficacy, or really any efficacy at all.

Thank you very much for your time. Do you have any concluding remarks?

D.B. Yaden: Well, I just want to thank you for inviting us and thank you, David, for inviting Roland Griffiths and me to write this companion article it was really a lot of fun to think about this topic and fun to discuss it.

My closing thought is that I think there is a lot of creativity that is required in this space, as well as a lot of rigorous testing. And so the kind of work on creating these new compounds that David Olson and his lab are doing is really inspiring and absolutely necessary.

There will be individuals who cannot have subjective experiences for various reasons, but I think by and large, we need to remember that the evidence so far has been on psychedelics that do produce subjective effects and that these experiences can be among the most meaningful in one's entire life. So we want to be careful about removing these for reasons such as cost.

> **D.B. Yaden:** I think by and large, we need to remember that the evidence so far has been on psychedelics that do produce subjective effects and that these experiences can be among the most meaningful in one's entire life. So we want to be careful about removing these for reasons such as cost.

D.E. Olson: I would also like to thank you all for the discussion and emphasize that it was a lot of fun writing this with David Yaden and Roland Griffiths.

What I really want to emphasize is the uniqueness of the community that really cares about psychedelics. We have a lot of really smart, thoughtful people trying to work on this problem, which I think is really critical. And while our two papers might seem like they are at odds with one another, after this conversation it should be clear that we mostly agree on everything.

The thing that we definitely all agree on is that we need to do everything in our power to treat as many patients as we can. Neuropsychiatric disorders affect an enormous number of people and are some of the leading causes of disability worldwide. I think we are all aligned on trying to do whatever we can to bring relief to patients. That is why we do this work. So hopefully, there are going to be a lot more of these interesting conversations where we can figure out the best way to make the world a better place.

> “ **D.E. Olson**: Neuropsychiatric disorders affect an enormous number of people and are some of the leading causes of disability worldwide. I think we are all aligned on trying to do whatever we can to bring relief to patients. That is why we do this work. ”

I want to thank both of the speakers for discussing this on-going debate and hopefully we will have more data to address this issue soon. A reminder that interested readers can read the initial exchange here:

i) 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

ii) Yaden, D. B., & Griffiths, R. R. (2021). The Subjective Effects of Psychedelics Are Necessary for Their Enduring Therapeutic Effects. *ACS Pharmacology & Translational Science*, *4*(2), 568-572. https://doi.org/10.1021/acsptsci.0c00194

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Yaden, D. B., & Griffiths, R. R. (2021). The Subjective Effects of Psychedelics Are Necessary for Their Enduring Therapeutic Effects. *ACS Pharmacology & Translational Science*, *4*(2), 568-572. https://doi.org/10.1021/acsptsci.0c00194

Phenomenoconnectomics and the Neural Correlates of Altered Consciousness

An interview with Timo Torsten Schmidt

By George Fejer

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Abstract

In this interview, Timo Torsten Schmidt provides details about his efforts to compile a comprehensive database of all psychometric measures gathered from controlled experiments investigating altered states of consciousness (ASCs) induced by pharmacological and non-pharmacological methods. He also introduces the paradigm of Phenomenoconnectomics which aims to systematically investigate the phenomenology and functional connectivity of ASCs to identify commonalities and differences, to ultimately identify the necessary neuronal correlates of specific experiences as they occur during ASCs. He explains some key findings of his own neuroscientific research on the neural correlates of consciousness under the influence of non-pharmacological manipulations, such as Ganzfeld exposure and flicker light stimulation-induced visual illusory percepts. Finally, we touch upon the current limitations of psychometric methods in their ability to capture the full diversity of the phenomenal space and future plans to overcome these caveats through Open Science initiatives that support harm reduction efforts.

keywords: *Altered States of Consciousness*, *non-pharmacologic induction methods*, *flicker light stimulation*, *Ganzfeld*, *psychedelics*, *psilocybin*

The Altered States Database (Schmidt & Berkemeyer, 2018, http://www.asdb.info/) is by far the most ambitious attempt to systematically catalog psychometric data on both pharmacologically and non-pharmacologically induced altered states of consciousness, up to date. How did you become interested in Altered States of Consciousness (ASC) and what was your motivation to embark on this project?

I am passionate about contributing to the empirical work investigating the neural correlates of human consciousness (NCC). The idea of compiling the database was born at a time when I discovered the existing literature about the diverse methods of inducing ASCs and their effects. I felt that it might have been a missed chance in the history of science, that after their discovery psychedelics were not used further to elucidate the relevant neuronal mechanisms that correlate with their effects on consciousness. I felt such drugs would be a great experimental tool for consciousness research.

This is because they allow induction of a substantial deviation from normal conscious functioning for a short amount of time in healthy people and their use was reported to be mostly safe under controlled laboratory conditions. I, therefore, thought that such induced deviations from average conscious experiences could be used as experimental tools with multiple advantages over studying ASCs that occur in psychopathologies.

Let's take the example of hallucinations. Such phenomena typically do not occur spontaneously in healthy study participants. Therefore, it is not possible to directly compare a normal (non-hallucinating) state with a hallucinating state. Of course, there are some patients who suffer from hallucinations, such as during psychosis. However, it is very challenging to study the neuronal correlates of hallucinations in such patient groups, as their brains might have already undergone substantial long-term changes, including structural alterations. An on-off within-subject design rendered possible with the experimental induction of ASCs has much more power to reveal the relevant neural correlates of hallucinations.

With this motivation in mind, I was curious what type of effects could be induced with different methods and which of these methods could be safely used in scientific experiments. I did find some resources on this subject, such as erowid.org and other web platforms where people share subjective reports about their drug experiences. However, upon reading them, it was clear that there is a major bias in these reports, as people tend to report either the most challenging or the particularly meaningful experiences, but little in between these two extremes. Unfortunately, I did not find a systematic collection of scientific data that covers the whole spectrum in an unbiased manner.

> “there is a major bias in these [first-person] reports, as people tend to report either the most challenging or the particularly meaningful experiences, but little in between these two extremes.”

Thus, the idea was born to create a database to unify all data that was acquired via standardized measures.

At the same time, I am a neuroscientist and not a drug researcher. I was interested in the neural correlates of consciousness alterations, and not in the drug effects per se. Nor was I majorly interested in potential therapeutic applications. In my research, I was moving to work with human fMRI—so I was thinking of how to conduct meaningful experiments with fMRI in combination with psychedelics to identify NCCs. There are multiple methodological challenges when combining fMRI with pharmacological interventions, which makes it very hard to develop meaningful task-based fMRI studies.

Currently, it appears that resting-state fMRI is a method well suited to characterize brain states in terms of network properties, *e.g.*, functional brain connectivity. I am convinced that the systematic study of brain connectivity across diversely induced ASCs can reveal correlates of specific subjective experiences. Across studies, different features of experiences will be more or less pronounced depending on the applied induction methods.

> “There are multiple methodological challenges when combining fMRI with pharmacological interventions, which makes it very hard to develop meaningful task-based fMRI studies. Currently, it appears that resting-state fMRI is a method well suited to characterize brain states in terms of network properties, *e.g.*, functional brain connectivity.”

This will allow researchers to establish correlations between specific ASC phenomena and accompanying brain connectivity patterns (*e.g.*, the pattern of connectivity increases and decreases that accompany an out-of-body experience). Ultimately, the identification of such connectivity patterns might contribute to the formulation of NCCs of specific subjective experiences.

It must have been a lot of effort to compile this database! Are you still actively updating it?

Indeed, it was a lot of work to build the database, and I have not done this work alone—it was a group of students at the University of Osnabrück who were working with me on the Altered States Database. I was very happy that students were interested in supporting the vision to have a database that allows us to compare the types of experiences that people have when using diverse methods to induce ASCs. I am also happy that this project still attracts students to work with me, and currently, we are upgrading the Database to conform to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards for systematic literature reviews. A preprint will be online in the upcoming weeks.

Befitting of the lengthy effort, you designated this paradigm with the lengthy title of "Phenomenoconnectomics", which aims to jointly investigate the correlations between brain connectivity and phenomenology. What are the aims of this framework?

I thought it is fun to introduce a complicated term such as "Phenomenoconnectomics" that people will at least remember the challenge to pronounce it. With this term, I want to refer to the joint study of the phenomenology of ASC experiences and changes in resting-state connectivity, which co-occur during these experiences. This is my research goal up to this day. I want to contribute to the systematic study of what type of subjective experiences occur under what conditions. To promote this goal, I make data on the phenomenology of ASC accessible, and I acquire fMRI data on changes in functional connectivity that accompany ASC experiences. However, contrary to my initial fascination for psychedelic substances, I have turned my focus to the non-pharmacological methods of inducing ASCs.

What are the main advantages of using pharmacological versus non-pharmacological methods? Is there any non-pharmacological method that has been understudied?

Pharmacologic human studies are very demanding to be carried out. This is for good reasons, as we all want that participants in studies can rely on the highest degree of safety and researchers stick to good scientific practice. Such research is therefore enormously expensive and takes a lot of resources. I want to emphasize that this is not due to any "discrimination" to research on psychedelics—as some people suspected—it is simply the case that experimental basic research needs to stick to the same safety rules as the pharmaceutical industry. When exploring the safety and efficacy of new substances, one wants to make sure that the principle of safety-first is applied.

Furthermore, there are always some remaining risks that come with pharmacological studies inducing ASCs, and plenty of considerations that have to be made. But beyond all that, there are also limitations in the interpretation of the data. If you have a pharmacologic agent in the system, it will typically not only act on the brain. Complex physiological reactions take place—simply consider changes in blood pressure, heartbeat, and changes in neurovascular coupling as potential confounders for fMRI studies.

Given the possibility to induce similar effects with non-pharmacologic methods, this might be preferred as a much safer option that produces data that is less confounded by such factors. One advantage is that typically you can terminate a non-pharmacologically induced ASC within seconds or at least minutes, which is not easily possible for many pharmacologically induced ASCs. Also, several physiologic confounders will not apply,

“ If you have a pharmacologic agent in the system, it will typically not only act on the brain. Complex physiological reactions play a role—simply consider changes in blood pressure, heartbeat, and potential changes in neurovascular coupling as potential confounders for fMRI studies. ”

and it will be much more straightforward to implement well-controlled on-off within-subject designs.

Stroboscopic light in different forms of presentation has been used in various ways, *e.g.*, with so-called "Dream machines" (Ter Meulen et al., 2009) to induce deep relaxing, immersed, "hypnagogic" states. The first time people sit with closed eyes in front of a stroboscopic white light, most of them are surprised how colorful, dynamic, and immersive the visual effects are. At the moment, I am working with flicker light stimulation as a method with which one can induce very fascinating visual effects, which are often called Flicker-induced Hallucinations (Bartossek et al. 2020).

We show that the visual effects are reported to reach an intensity that can otherwise only be reached with psychedelics. I think it is an important step for research to see what neural mechanisms are shared between psychedelic-induced and flicker-induced hallucinations. In particular, Cortico-Thalamo-Cortical interactions seem to play a role here.

It is interesting to experimentally test on what hierarchical level of processing there is a divergence from normal everyday perceptual processing. In particular, it has to be investigated where bottom-up (perceptual stimulation) and top-down effects (brain's internally generated signals/expectations) mismatch. As an effect of this mismatch, multimodal integration failures are produced, which come with altered subjective experiences.

For the future, I also find it fascinating to systematically explore how multimodal stimulation can influence those aspects of conscious experiences and compare it to the effects of hallucinogenic drugs. I find this type of comparison very interesting because some drugs can produce ASC effects, but some of these effects can also be induced by non-pharmacological methods. The mechanisms that lead to subjective experiences are fundamentally different, although there are also some similarities. I think this is exactly what we need in research to identify the necessary NCC for subjective experiences.

From what we know by now, I think it is fair to say that it is not the stimulation of a specific receptor type (*e.g.*, the stimulation of 5-HT2A receptors), which is the necessary NCC of the effects of psychedelics on consciousness. I think it makes more sense to look at the downstream effects of such a receptor stimulation. One possibility for this is to look at changes in network interactions as a consequence of drug intake. But most importantly, we require more studies on non-pharmacological methods that can induce ASCs. Such techniques are much easier to apply, typically safer, and will ultimately contribute important data which reveals what needs to happen in the brain in order to experience a specific phenomenon.

Your previous work investigated ASCs via the Ganzfeld induction method (Schmidt et al., 2020). This is a relatively simple procedure, whereby the visual field is masked by halved ping-pong balls and exposed to red light, which generates unstructured homogenous input, while participants listen to white noise via headphones.

The fMRI results indicated decreased thalamo-cortical coupling and an increase of Default Mode Network centrality in relation to the hypnagogic state induced by this procedure. By contrast, psychedelic states exhibit an opposite trend, with increased thalamo-cortical coupling (Preller et al., 2019) and decreased connectivity of the Default Mode Network (Carhart-Harris et al., 2016).

According to the relaxed beliefs under psychedelics (REBUS) model by Carhart-Harris and Friston (2019), psychedelic substances relax top-down expectations and liberate the flow of bottom-up information. But your data suggests that similar experiences can also be elicited by depriving bottom-up input of sensory structure, and this has the opposite effect on the Default Mode Network compared to psychedelics. Do you think this discrepancy reflects differences between the phenomenology of these different states of consciousness?

Indeed, there are relevant differences in the phenomenology of Ganzfeld-induced hallucinations and hallucinations that are experienced under psychedelics, not to mention those experienced during psychosis. In the end, it might be that the neural mechanisms from which hallucinations result are also distinct. This is exactly what I am interested in: looking at different

induction methods that lead to somewhat similar phenomena. The next step will be to stringently characterize the differences and elucidate what neuronal mechanisms relate to the differences and what neuronal mechanisms are shared.

The REBUS model focuses on predictive cortical processing. In this context, I can also recommend the formulation of predictive mechanisms that contribute to the emergence of ASCs in the context of psychosis by Phillip Corlett (2009, 2019), which also contains links to pharmacological and non-pharmacological induction methods of such phenomena. He is speculating about how bottom-up and top-down influences could be imbalanced in different ways so that they ultimately converge to similar phenomenology.

What I like in his suggestion is that it considers different modulations of predictive processes on different levels of the cortical hierarchy. The REBUS model is rather formulated in the context of psychedelics, where effects on all levels of cortical hierarchical processing are assumed, while overall I consider the model as somewhat too simplistic and too much focused on cortical processing, neglecting important subcortical circuitries.

I think our work formulates the demand to focus on thalamo-cortical interactions as an important mechanism that contributes to ASC experiences. In my view, the REBUS model does not emphasize the potential contributions of the Cortico-Striato-Thalamo-Cortical feedback mechanisms enough. I think particularly our work with non-pharmacological methods emphasizes that future research should not forget about subcortical mechanisms as potential NCCs of ASC experiences.

“ the REBUS model does not emphasize the potential contributions of the Cortico-Striato-Thalamo-Cortical feedback mechanisms enough. I think particularly our work with non-pharmacological methods emphasizes that future work should not forget about subcortical mechanisms as potential NCCs of ASC experiences. ”

From a conceptual standpoint, what do you think about the construct validity of psychometric tools that are currently at our disposal? Most of the data represented in the ASC database stems from studies that used the 5D/11-Altered States of Consciousness questionnaire (Dittrich et al., 2010; Studerus et al., 2010), the Mystical Experience Questionnaire (MacLean et al., 2012), and the Hallucinogen Rating Scale (Riba et al., 2001). Whereas the Mystical Experience Questionnaire and the Hallucinogen Rating Scale seem to be designed for measuring specific types of experience, the ASC questionnaire seems to cover a wider spectrum of experience. Do you think this questionnaire captures the full diversity of experience, or do you see some room for improvement?

Adolf Dittrich, who developed the 5D-ASC questionnaire, pursued the goal that this questionnaire allows the comparison of the subjective effects induced by pharmacological and non-pharmacological methods. He described the goal to identify etiology-invariant structures of consciousness alterations. This is a big vision, and it basically aims to map the entire space of possible consciousness states that people can experience. Even though this is a big vision, I like it and share his ambitions.

Dittrich's questionnaire, however, had a focus on those effects that people experience after the intake of psychedelics. As of now, it is still the best tool to achieve comparability between studies, as it is the most widely used questionnaire. But this does not mean that the questionnaire would provide a full description of the subjective experiences. It certainly does not.

There is a lot of work ahead of us to find proper questionnaire items and psychological constructs that capture the whole phenomenal state space. For now, I would consider these questionnaires suitable for comparing data collected in clinical studies. The comparison of any new clinical datasets with the existing ones allows us to detect if for any reason participants had majorly different experiences. However, the development and application of additional measures are important for future research.

> “There is lots of work ahead of us to find proper questionnaire items and psychological constructs that capture the whole phenomenal state space.”

In our studies on non-pharmacological induction methods for ASCs, we use these standardized questionnaires to characterize the phenomenology of the experience in order to allow a comparison between experiences induced by pharmacological means. However, the questionnaires mainly provide a quantitative approximation of the intensity of such phenomena, and they do not provide a detailed description of the experiences as such.

I think it is important to put more effort into research within this domain and obtain more detailed descriptions of experiences—qualitative work is of importance here as well. Unfortunately, I am not an expert on that, but I am curious about the work of others in this research. One major challenge is that much of the vocabulary used in the description of experiences is very metaphoric, as it is designed to capture specific qualities of experiences that are very difficult to put into words. There are experiences that are beyond the previously experienced epistemic range, and there may be no appropriate vocabulary to describe them at the moment. I am curious about what qualitative research might contribute to this challenge in future work.

A key assumption of your approach (as well as Dittrich's) is that ASCs have certain invariant attributes that can be measured via psychometric tools. Your most recent meta-analysis (Hirschfeld & Schmidt, 2021) utilized the altered states database to examine the dose-response relationship of psilocybin-induced subjective experiences. Based on the regression analyses, all of the above questionnaires (MEQ, HRS, ASC) exhibited a fairly robust and linear dose-response relationship for most of their factors and subscales. This seems to confirm that there are indeed invariant features of psychedelic experiences and that their intensity can be quantified in a dose-dependent manner.

However, other studies implicate that contextual factors and prior expectations play a significant role in how people score on these reports. For instance, Olson et al. (2020) demonstrated that certain individuals will even report stronger alterations of consciousness under the influence of a convincing placebo manipulation than others under the influence of psilocybin (Studerus et al., 2011). This also raises concern for controlled clinical trials, where it is difficult (if not impossible) to maintain placebo-blinding, and the effect sizes of subjective measures are likely to be overestimated (Muthukumaraswamy et al., 2021). Do you see this as a major caveat in

comparing the intensity of different experiences to each other across different samples and environmental conditions?

This is indeed an important point. The dose-response relationships that we present ignore other factors that contribute to the ASC experience, except for the dosage. Also, the data we used, mainly stems from well-controlled laboratory studies. It would not be appropriate to directly generalize these data to recreational drug consumption. Strong effects of set and setting, which are not systematically reported in the literature, are known and could have huge influences.

I believe our analysis is helpful to determine the dosage for studies carried out under laboratory settings. Alternatively, our results can be used as a reference when carrying out a field study and comparing if the observed effects are stronger or weaker than under laboratory conditions. The given data can show a specific profile of experiences. It can inform researchers if a specific drug or non-pharmacological method produces specific effects, *e.g.*, hallucinations or out-of-body experiences, or anxiety. With more available standardized data, it will become increasingly feasible to compare the experiences across different induction methods.

In controlled clinical trials, one can control for such placebo effects very well. Other research, in which there is no control condition for placebo effects (many field studies) might overestimate the effects or suffer from a huge variability in the data. I was involved in online surveys where we wanted to investigate the subjective effects induced by Kambô, the skin secretions of frog species (Schmidt et al., 2020; Majić et al., 2021). The relationship between pharmacology and subjective experiences is far from clear.

> “The dose-response relationships that we present [from well-controlled laboratory studies] ignore factors that contribute to the ASC experience, except for the dosage. (...) It would not be appropriate to directly generalize these data to recreational drug consumption.”

We were interested in how people score on the standardized questionnaires, and whether this would provide supporting evidence alluding to potential psychoactive effects of Kambô. But as you pointed out, in the end, it is not possible to separate which of the reported effects emerge from psychoactive properties, and which effects are related to other mechanisms of action. One clue for this could be the variability you see in the data—the less variability, the more of a causal pharmacologic effect on subjective experiences should be present. To nail these down, we need more data and innovative research approaches.

The utility of the database also seems dependent on the amount of data covering the spectrum of the phenomenal space that can currently be measured via pharmacological and non-pharmacological methods. It seems that the currently available data still does not reach this order of magnitude, and this puts certain limitations on what kind of insights can be generated. Do you have any suggestions on addressing this issue?

In order to address such shortcomings of the current data, as well as to improve the amount of available data, we plan to develop the ASDB into an Open Science Citizen Science platform. The idea would be that everyone can report their experiences and compare them with the experiences of thousands of other people. At the same time, one could collect anonymous data on potential factors that influence the experiences and potentially also long-term effects. The basic idea is to collect Big Data. Something that is not possible in laboratory experiments, where each study is limited to a few participants. A website or app where you can compare your experience with the experiences of thousands of other users would make it possible to collect hundreds of thousands of data points from users around the world.

However, Citizen Science also has its very own limitations. When doing Citizen Science one needs to think about the user experience—the users need to have fun with such an app and see their own benefit from using it. Therefore, you can not apply long and detailed questionnaires, but only short sets of questions. On the other hand, one can obtain bigger amounts of data, if you involve a whole community of users. Big data will solve multiple problems in the validation of questionnaires, but also comes with new

challenges. I have high hopes that it will be an important step to address some of the biases in the literature, which I mentioned earlier. I am confident that acting transparent and according to the highest standards of Open Science will also motivate users to contribute to such a project.

In this light, my motivation to further develop the Altered States Database is twofold. On the one hand, the ASDB provides a reference for the subjective experiences that can be expected when performing neurophysiologic experiments and enables a direct comparison of new datasets. It allows researchers to ask under what conditions a specific experience does or does not occur. I believe that this knowledge in combination with human neuroimaging studies can contribute to real advances in the identification of the relevant neural correlates of specific subjective experiences.

My second motivation is that the ASDB could be developed to contribute to the identification of predictors for specific experiences. In other words, it could be extended to incorporate measures of special biophysical or personality factors that might predict what is going to be experienced if somebody takes a drug or applies a non-pharmacological method to induce an ASC.

I also hope that the transparent presentation and the summarizing and sharing of scientific data, in the sense of Open Science, can contribute to harm reduction. Currently, there is a huge enthusiasm for the potential positive effects of psychedelics. Often, enthusiasm comes with some neglect of risks. I feel it is important that within the research community there is more discussion and research on the identification of risk factors. I hope that further development of my database can also contribute to this.

Could you reflect on some of the negative risks of psychedelics and why the current era of research has shifted towards a one-sided positive reporting of their effects?

All clinical studies are highly selective with regard to the included participants. This is of course for very good reasons—it would be terrible if a clinical study harmed a patient—as said before: safety-first. At the same time,

this produces a bias in the literature. One mostly hears about positive/helpful/beneficial effects of psychedelics because negative side effects seem to rarely occur in controlled studies.

There are diverse potential side effects that can result from the consumption of psychedelics, however, by now only a few predictors for such have been identified. It seems that most side effects are relatively rare. But it is obviously a problem if one does not have good knowledge about their predictors. It seems to me that there is not enough attention being paid to these questions in current research.

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