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Psychedelics and the future evolution of humanity

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ABSTRACT

This paper examines possible future evolution through knowledge of how past human evolution constrains possibilities for the future. Uniquely human evolution—brain, ultrasociality, and cultural niche development—are examined to see what these suggest about future adaptations. Rapid brain evolution involves neuroplasticity, a re-use and rewiring of neural networks. Psychedelics are extraordinary plastogens stimulating neuroplasticity. This makes consideration of clinical evidence regarding their effects pertinent to inferences about their possible future roles through their ability to: enhance brain neuroplasticity and neurogenesis providing new networks; stimulate serotonin-mediated active stress adaptation strategy and its innovative problem-solving; induction of openness, extroversion, and positive social relations; dissolution of self-boundaries permitting broader identifications; and increasing cognitive novelty and integration. The paper reviews interdisciplinary knowledge to situate psychedelics in futures inquiry and assess their implications for enhancing adaptation to the future. Evolutionary sciences illustrate psychedelics likely can enhance our adaptations for more harmonious futures in which humanity can overcome challenges posed by social differences. This psychedelic instrumentalization can facilitate human self-transformations needed for future adaptations by enhancing major trends of human transformation through augmentation, symbiosis and transcendence. Psychedelics' strong set and setting influences illustrate their risks and the need for carefully guided efforts to assure their positive contributions to human transformations.

KEYWORDS

drug instrumentalization, creative futures, ultrasociality, neuroplasticity, transhumanism

INTRODUCTION

How can we know what the future evolution of humans will be like? [Carbonell and Hortolà \(2020\)](#) propose that we can “explore alternative futures an insight into how knowledge of past human evolution might contribute to shaping the way we think about the future and the relationship that humankind has to its future . . . [through] a potential new paradigm of social evolution by exploring possibilities arising from the forms of past social behavior and future self-understanding” (p. 4). A scientific approach to human futures involves examining how we evolved in the past, both the trends from past changes that illustrate our trajectory into the future and the processes through which we changed. Understanding past evolution is key to projecting future evolution because natural selection must act on variation within existing biogenetic structures and functions. The conservative nature of evolution means that the same dynamics and processes that enabled change in the past will be the basis for future change, as well the limitations on future evolution. If we want to fly, we cannot evolve wings from our biological capacities, but we can use our biological capacities to invent winged machines and use them to fly.

This paper expands Carbonell & Hortolà's approach by examining major aspects of uniquely human evolution—the brain, ultrasociality, and cultural niche development—to see what these potentials suggest about our future evolution of adaptive social behaviors. These ideas are integrated with a novel proposal about future evolution based on evidence from the ongoing “Psychedelic Renaissance” of clinical applications of psychedelics to resistant diseases (see [Winkelman & Sessa, 2019](#)) and the increasing recognition of the central role of sociality in the

effects of these enigmatic substances (see Roseman, Preller, Fotiou, & Winkelman, 2022). The clinical and laboratory research into the transdiagnostic potentials of psychedelics not only gives hope for diverse future medical and psychological treatments, but also robust evidence regarding what were the likely adaptive effects of psychedelic ingestion in our past. Clinical evidence regarding effects of psychedelics on stress management, psychological well-being, and social relations suggests they had effects on past adaptations and can contribute to future evolution as well through effects on: enhanced neuroplasticity and neurogenesis; serotonin-mediated stress adaptation and problem solving; disintegration of self-boundaries producing broader identifications; and enhanced openness, extroversion, and cognitive integration (for reviews of primary literature see below and Winkelman, Attila, & Frecska, 2023; Arce and Winkelman 2021).

The paper reviews interdisciplinary evidence for situating psychedelic substances in futures inquiry. Interdisciplinary knowledge about past evolutionary trends combined with assessment of current challenges and research about the effects of psychedelic substances shows they have significant implications for enhancing humanity's future adaptations to pressing problems. Integration of knowledge from evolutionary sciences, anthropology, and clinical studies illustrates how the effects of psychedelics likely enhanced our adaptations in the past. Psychedelics can also enhance our adaptations in the present in ways that will create more harmonious futures in which humanity can have a better chance at overcoming its major challenges created by the barriers of social differences. The use of psychedelic substances in indigenous traditions indicate that they had, and still have, central roles in developing foresight, providing diagnosis, and engaging in scenario planning and horizon scanning through their central roles in divination. The healing is of more than just the person's illness or disease, but addresses a wide range of personal, interpersonal, and even community problems. Psychedelic therapies address spiritual conditions, fears, and traumas, resolving imbalances created by stressful social relations, conflicts, and overwork. They serve a range of social functions in personal, familial, communal and even inter-community conflict resolution (see Winkelman, 2025a).

An interdisciplinary integration of knowledge across scientific fields provides perspectives about psychedelic-facilitated human augmentation that is consistent with our past, appropriate for addressing current challenges, and a likely positive force for our futures if used wisely. This integration is also consistent with cutting-edge scientific discoveries about psychedelics that see them as significant resources for the future of medicine because of their transdiagnostic applications and potentials. This proposal for the deliberate instrumentalization of psychedelics to enhance future adaptations emphasizes the major trends of future human transformation through augmentation, symbiosis, and transcendence (Anderson, 2003).

How did humans evolve?

A long-term view of human evolution indicates several principal aspects of our past evolution that are likely areas

for future developments. The broad changes that made us human involved: 1) hominization—a series of primate enhancements in sociality spanning many millions of years; and 2) humanization—processes involved in the uniquely human adaptations (Carbonell & Hortolà, 2020; also see Rappaport & Corbally, 2021). This distinction of hominization involving changes also seen in other hominid species shows the emergence of complex social behavior in various hominid species over millions of years and long before emergence of hominins and human uniqueness such as big brains and culture. Hominization built upon a long process of enhanced primate sociality through reduction of aggression and increases in the complexity of social relations, essentially the beginnings of society.

Human separation from our hominid ancestry is associated with several principal advancements: brain growth; sociality; and cognitive and cultural niches, our uniquely human mental capacities and their use to develop cultural systems for mediation with the environment. The three-fold increase in the brain over the last 2 million years stands out as the central change that led to the apex of humanization. Ultrasociality is another extraordinary human quality, the ability to function in large, organized groups, a feature even more startling given the lack of high levels of sociality in most of the other hominid species. This ultrasociality is what led to the development of human culture. And it is culture which is a defining adaptation of our species and a pinnacle achievement that almost exclusively separates humans from other species. These biological, social, and cultural dynamics of past evolution are examined below to illustrate their potentials, especially through their interactions with psychedelic agents as environmental factors affecting neurotransmission, social behavior, and evolutionary adaptations.

BIOLOGICAL DYNAMICS OF BRAIN EVOLUTION

Our enormous brains are clearly a central factor in our evolution, but can further evolution of our brain provide new potentials for future human adaptations to address the pressing problems facing humanity today? The change in brain size from the beginning of the *Homo* genus almost 2 million years ago to the appearance of anatomically modern *Homo sapiens* around 200,000 years ago spans more than 1.5 million years (Dunbar, 2014). This is an enormous period that belies any notion that we can expect brain evolution to be a significant aspect of our adaptation in the foreseeable future. The doubling in brain size from 760cc of *Homo ergaster* to the 1,170 cc of *Homo heidelbergensis* spanned more than a million years, and the subsequent 17 % increase in brain size to 1,370 cc in early anatomically *Homo sapiens* took an additional 300,000 years (Dunbar, 2014). These changes are relatively rapid in evolutionary terms. Such time spans for significant changes in brain size and function make it clear that we cannot expect macro brain evolution to play a significant role in our foreseeable future.

But our evolution of greater skills is not solely dependent on the macroevolution of our brains. Rappaport and

Corbally (2021) illustrate this in an examination of a new paradigm of “cultural neural reuse” where human activity uses pre-existing brain networks for new functions. This notion of neural reuse replaces the traditional notions of evolution through selection for new structures or functions with the emergence of increasingly higher-level social and cognitive capacities through re-purposing existing brain architecture for new adaptations.

These new uses of prior adaptations (exaptations) can exercise a selective influence for additional capacities that support these reuses. Through the processes of neural reuse, humans become agents of their own evolution because of the roles of our volition, choices, preferences, and behaviors in modifying the selection processes. Rappaport and Corbally (2021) propose that since such choices shape the social environments, they can exercise a selective influence on the genome for features that further enable the new purposes for which these existing structures are re-deployed, including new higher-level cognitive processes. Repetitive collective engagement with these new cognitive processes changed our genome through the cumulative influences embodied in culture, which exerted selective pressures for neural features supporting higher cognitive processes. An interaction between cultural and biological evolution (gene-culture evolution) gradually changed the genome to enhance human features of ultrasociality and enabled our most important adaptation, cultural niche exploitation. This selection exploits existing biological capacities (neural networks), as well as our extreme neuroplasticity, which is enhanced by environmental sources of neurotransmitter analogues such as psychedelics.

Rewiring of the brain through neuroplasticity and neurogenesis

Neuroplasticity (also referred to as cortical re-mapping) refers to nervous system changes involving modifications in its structural connections. The brain’s natural ability to form new connections across levels of neural networks has an essential role in enhancing the brain’s capacities for adaptive behavior and adjusting to the environment (De Gregorio, Aguilar-Valles, et al., 2021). Neuroplasticity involves reorganizing neuronal activity, including the physical structures of neural networks, their functions, and their interconnections. Neuroplastic responses can occur “from signal transduction, to gene expression, to synaptic, neuronal, network, and whole-brain adaptation” (De Gregorio, Aguilar-Valles, et al., 2021, p. 10; also see Raval et al., 2021).

Plasticity in the central nervous system involves multiple processes of reorganization including axonal sprouting and stimulation of precursor cell division and survival of daughter cells. This neurogenesis also involves promoting cellular processes underlying the growth of the dendrites and axons for synaptic formation and long-term potentiation of plasticity-related genomic responses. These effects and processes, individually and combined, can produce an adaptive rewiring of the brain’s neurocircuitry through (paraphrased from Aleksandrov & Phillips, 2021, pp. 2–4):

- *Synaptic plasticity* produced by enhancing the efficacy of glutamatergic synaptic transmission manifested in long-term potentiation of cellular substrates for learning and memory; and
- *Structural plasticity* involving modifications of axonal/dendritic branches, spine morphology, and increased synaptic numbers that mediate sustained adaptations to the environment such as synaptogenesis and synaptic atrophy.

These types of increased neuroplasticity can further support behavioral plasticity. In particular, they can support learning new responses to changing environmental conditions, which can positively impact coping and overall well-being (Aleksandrov & Phillips, 2021). Similarly, new experiences can result in changes in neural networks, strengthening the connections within their organizational networks, and even increasing functions by adding new nerve cells and interconnecting glial cells.

Psychedelics as plastogens

Psychedelics can enhance the processes of rewiring the brain through their functions as plastogens, substances with the capacity to stimulate rapid neuroplasticity with sustained positive effects on neurogenesis and the structure and function of neural networks (see Calder & Hasler, 2023; De Vos, Mason, & Kuypers, 2021; Inserra, De Gregorio, & Gobbi, 2021; Lukasiewicz, Baker, Zuo, & Lu, 2021; Ly, Greb, Cameron, et al., 2018; Vargas, Meyer, Avanes, Rus, & Olson, 2021). Psychedelics have rapid plastogenic effects on cognitive processes, learning, and memory (Garcia-Romeu, Darcy, Jackson, White, & Rosenberg, 2022).

Neuroplasticity is a mechanism of 5-HT_{2A} psychedelics (psilocybin, lysergic acid diethylamide [LSD], and N, N-dimethyltryptamine [DMT]) through their action on serotonin receptors via their targeted action on 5-HT_{2A} pyramidal neurons in the prefrontal cortex, where they induce synaptic, structural, and functional changes (Aleksandrov & Phillips, 2021, p. 2). The effects of 5-HT_{2A} psychedelics on glutamatergic transmission stimulates neural network remodeling by facilitating plasticity at synaptic, structural and behavioral levels. Aleksandrov and Phillips (2021) and Garcia-Romeu et al. (2022) review evidence for multiple pathways for producing these psychoplastogenic effects via psychedelic stimulation of 5-HT_{2A} receptor system. These multiple mechanisms, through which psychedelics stimulate neuroplasticity and plastogenesis, make it apparent that psychedelics could have been powerful agents for our past adaptations, as well as for current and future physical, psychological and social adaptations. Contemporary neuroscience on psychedelics illustrates their abilities to promote neuroplasticity, neurogenesis and neural cell growth that can powerfully enhance the creation of new neural networks and their use for novel models. Psychedelics’ action as psychoplastogens producing structural and functional plasticity in key neural circuits has made them promising new treatments for degenerative brain diseases (Vargas et al., 2021; Winkelman, Szabo, & Frecska, 2023).

The 5-HT_{2A} psychedelics are among the most effective plastogens, stimulating neurotrophic pathways, increasing neurogenesis and neuroplasticity, promoting cognitive flexibility, and generating changes in behavior (Garcia-Romeu et al., 2022).

Long before entheogenic healing practices were incorporated into human culture and coping responses, psilocybin effects likely played a crucial role in human evolutionary development through enhancing plasticity and adaptability during extreme stress conditions. The 5-HT_{2A} psychedelics (e.g., psilocybin) activate a coping strategy that is mediated by 5-HT_{2A} receptor signaling which provides an enhanced capacity for stress management through change. Psychedelics are serotonin analogues that preferentially activate the 5-HT_{2A} receptor subtype that stimulates the enhanced stress-adaptation mechanism. Since serotonin moderates anxiety and stress, promotes patience and coping, and under conditions of increased environmental volatility, increased neural plasticity, Carhart-Harris and Nutt (2017) have shown how 5-HT_{2A} receptor signaling played an important role in the evolution of active stress responses. Psychedelics may have contributed to that adaptive response. This serotonergic system, aided by 5-HT_{2A} psychedelics, evolved to confer enhanced adaptability to address conditions of extreme adversity, stimulating an active coping strategy that induces a plastic state of enhanced cognitive flexibility and associative learning processes.

Across humans' evolutionary trajectory, the incidental consumption of psilocybin mushrooms would have enhanced serotonergic neural signaling, and countered depressed mood, stress and cognitive inflexibility by stimulating the adaptive stress-response system that evolved to mediate rapid and deep learning when faced with environmental changes that demanded action be taken. Ancient psilocybin use would have enhanced fitness by supporting the capacity to actively address sources of stress via major changes in perspectives and/or behavior involving enhanced sociality and cultural niche construction. These changes in stress management are proposed to have played a central role in the evolution of ritual healing practices (Brouwer, Winkelman, & Raison, 2023) through the stimulation of high levels of stress mediated neurotransmitter responses (Winkelman, 2017) caused by intense ritual activities (also see Winkelman, 2010).

ULTRASOCIALITY AND GENE-CULTURE EVOLUTION

The evolution of humanity's altruistic, moral, other-oriented, inclusive, and empathetic behaviors—sociality—has a past stretching across millions of years to behaviors still manifested in our hominid relatives today. Frequent, intense, and highly affective interactions with others is a widespread primate pattern that attests to the deep evolutionary origins of human sociality. This primate capacity for intense sociality emerged as long as 48 million years ago,

creating a basis for adaptations involving a shared social life (Rappaport & Corbally, 2021). Significant evolution of sociality occurred long before the evolution of hominins, the uniquely human ancestors. Increased sociality is present in our more ancient hominid ancestors who already achieved features enhancing group life such as reduction of aggression, increased social tolerance, greater emotional sensitivity, and enhanced social coordination. Our ability to function in larger groups was a survival mechanism, a safety in numbers approach, that became even more important when the most dangerous predators in the environment were other groups of humans. Sociality enhances survival through the better ability of larger groups to deter predators, defend against attacks by enemies, and increase reproductive success.

Human ultrasociality is a more remarkable extension of these capacities to live in coordinated groups of millions of others. Ultrasociality is the social dynamic that clearly sets us apart from our hominid relatives, primates, and other mammals whose loyalty and preferences are primarily kin-based. The adaptive forces selecting for a broader concern with the well-being of others of our species has been a longstanding aspect of the environment of evolutionary adaptiveness. The human propensity to adopt others' infants, even the children of enemies, and care for them as if they were their own biological descendants, is an adaptive tendency in our species that dramatically demarks humans from all other species. Evolution enhanced the dynamic functioning of hominin social systems and their members through selection for features facilitating cooperation, as illustrated in the trait of elective affinity, an inherent desire of wanting to be in association with others (Carbonell & Hortolà, 2020). The adaptive consequences of cooperation and the subsequent forms of complex symbiosis explain why affinity is a seminal process necessary for humanness. Elective affinity drives a desire for social interaction and building interpersonal and group social relationships to help us meet our individual and collective objectives. Across millions of years of evolution, our genome was selected for those tendencies at inclusiveness that enabled our ancestors to bolster the size of their groups with acquired and learned mechanisms to assure the maintenance of a minimal breeding populations and optimal size groups for both sustenance and coalitions for defense.

These social adaptations may have also been enhanced through exploiting the effects of psilocybin. Studies show psychedelics have sociality enhancing effects on emotions, psychosocial dynamics, and personality. There are overall psychedelic-induced changes in socially-oriented aspects of personality manifested in increases in measures of Extraversion, Conscientiousness, and Openness (Bouso, dos Santos, Alcazar-Corcoles, & Hallak, 2018; Erritzoe et al., 2018; MacLean, Johnson, & Griffiths, 2011). Clinical studies also show that 5-HT_{2A} psychedelics can produce acute significant interpersonal and social effects in enhancement social behaviors (De Gregorio, Popic, et al., 2021) and feelings of emotional empathy, happiness, trust, and sense of closeness and desire to be with others (Dolder, Schmid, Müller, Borgwardt, & Liechti, 2016). Psychedelics can

enhance positive social-emotional states as illustrated in higher measures of euphoria and exuberance, and happiness ranging from playfulness, involuntary grinning, and giddiness to uncontrollable laughter (Preller et al., 2016). Psilocybin enhances the expression of positive mood states (De Gregorio, Enns, Nuñez, Posa, & Gobbi, 2018) and increases behavior towards positive cues (Kometer et al., 2012). Psilocybin has effects of enhancing connection of the self with others and the outside world (Watts, Day, Krzanowski, & Carhart-Harris, 2017), increased amygdala sensitivity to emotional faces (Roseman, Demetriou, Wall, Nutt, & Carhart-Harris, 2017), and reduced threat perception and reactions (Kraehenmann, Schmidt, & Friston, 2016). These factors and others, such as increased altruism (Griffiths et al., 2018), would have enhanced our capacity for construction of cultural systems, the key mechanism sustaining ultrasociality.

Cognitive and cultural niches

What has made humans the most dominant species is our interactions with the natural and social environments through shared cognitive and cultural niches—the capacity to conceptualize the world through the tools of culture; and the specific models of the environment that mediate our relationships with the physical, social and cultural worlds we inhabit. There are profound implications of the mediation of human experience and behavior not only through the cognitive niche (our generic biologically based cognitive capacities) but also the specific cultural niche of the society. Culture has exerted selective influences on the genome for brain and cognitive evolution and even self-domestication to enhance our ability to function within cultural niches. This gene-culture interaction increased the transition from survival primarily through biological adaptations to foundational adaptive strategies based on cultural learning. This trend towards dependence of socially learned models began before hominins, illustrated by the presence of rudimentary elements of cultural behavior in chimpanzees. The latent cognitive capacities of hominids are illustrated in chimpanzees' abilities to learn complex cognitive systems, such as sign language, that they could never invent. This latent capacity was exploited by our hominin ancestors to create culture, a shared pattern of behavior that produces a sense of social inclusion that intensifies the sentiments of group belonging.

Cultural models played central roles in adaptations and evolution by contributing to survival through the selective influences they exerted for genetic features that enhance overall functioning within a cultural system. The cognitive niche abilities of humans resulted from co-evolutionary processes in which the genetic changes that permitted increases in certain mental capacities also generated selection pressures for other mental and social capacities that supported the capacity for engaging in cultural developments. This "gene-culture coevolution" (Richerson & Christiansen, 2013) emphasizes the processes of cultural selection acting on biology. This involves natural selection acting on cultural

memes, and through social inheritance, interacting with and influencing genetic inheritance. Consequently, the resulting cognitive niche and cultural niche exerted mutually reinforcing selective influences enhancing biological capacities for culture.

Since humans evolved through culture, with culture shaping our biological evolution to extend its optimal functioning supporting cultural behavior, the socially constructed environmental conditions also generated selective pressures on genes. The cultural niche approach emphasizes that the driving force in human evolution involves culturally transmitted information (Morgan, 2016), an unfolding evolutionary process which changes as the organisms' behaviors alter the developmental conditions which constitute selection pressures on both physical and social environments. It was these reinforcing relationships among biological and cultural forces that created humans' unique survival mode, the processes of cultural niche construction.

The cultural niche is not merely a mental model but depends on social relations based in a cooperative lifeway involving group-mindedness and mental intermingling. This socially infused form of thinking gives humans their unique cognitive skills involving a reliance on shared cognitive models derived from inferring others' thoughts and intentions and internalizing those models to enhance collaboration with others. Incorporation of the mind and even the self-models of social others produced cognitive capacities that enabled a shared cultural model and cooperation among non-kin that was mediated through social learning and eventually language.

The socially interdependent lifestyle that drove human cognitive evolution was based on the ability to learn complex information from others, exemplified in "mind-reading," a capacity for mental inference of the mind states of others to determine their intentions. It is this cognitive capacity to understand others' minds that enables the social relations that support the willingness to act in egalitarian, empathic and altruistic ways beyond kin. This capacity for "mind reading" is unique to humans and is also the basis of another of humanity's unique features, namely the development of spiritual beliefs and religion.

Our dependence on religion as a model of the world reflects our dependence upon a cultural niche and intense affinity for accommodating the beliefs and intentions of others, human and extra-human. These desires for shared understandings rely on a mime-like ability to grasp and share both individual and social representations, a drive so fundamental to being human they spread across cultural and language populations, exemplified in globalized religious traditions. What was the spark that started this interactive relationship between biological and social evolution that enabled and eventually required spiritual beliefs for social participation? The centrality of religious beliefs in national politics and international relations show that they are influences so deeply engrained in our evolved psychology that even in our post-modern, highly rational era we have not been able to escape these ancient, evolved tendencies. This cultural capacity for religious membership as a criterion for

social inclusion is also a two-edge sword in that it also creates the mechanism for exclusion of the culturally different other, a major impediment to positive world futures.

Where did these enhanced capacities for such knowing, thinking and acting originate? How did they lead to a dependence on imagined realities exemplified in the spirit beliefs that underlie religions which have guided tens of thousands of generations of humans to achieve collective goals? How did we acquire a total dependence on the systems of beliefs such as religion that are arguably false for our very survival? The answers to these questions also can guide our future adaptations in enhancing ultrasociality.

BIOCULTURAL EVOLUTIONARY ADAPTATIONS IN THE CULTURAL NICHE

Psychedelic instrumentalization

The drug instrumentalization paradigm (Müller, 2020) shows drug use can be adaptive, as environmental sources of psychoactive substances had effects on human evolution as adaptogens (Doyle, 2011; Kennedy, 2014). Arce and Winkelman (2021) review evidence that the effects of psilocybin could have significantly contributed to the evolution of sociality, cultural niches and religion through “psychedelic instrumentalization,” the deliberate use of psychedelics for their instrumental effects. While our large cranial capacity was a central part of our evolution, there are additional features that appear so crucial that without their presence it is hard to imagine how we could have evolved our human uniqueness. These include our opposable thumb and its precision grasp, our upright posture, as well as our behavioral capacities for hunting, fire, language, as well as cultural traditions. Arce and Winkelman contend that psychedelics might also be included in this list of indispensable agents of human evolution.

Psilocybin effects could have contributed to the articulation of sociality in group life and development of the socio-cognitive niche through their enhancement of the social dynamics necessary for engaging in cooperative lifeways, enhancing visualization and cognitive processes supporting formation of novel cultural models. Psychedelics’ effects on psychosocial dynamics and personality such as extraversion and positive interpersonal and social relations, including empathy, trust, and other positive emotional states, would have enhanced connection with others and enhanced our capacity for sociality. The ability of psychedelics to enhance novel cognitive processes is renowned in their ability to induce imagery (de Araujo et al., 2012) and enhance meaning (Hartogsohn, 2018). These symbolic forms of visual cognition provide novel templates for information integration through presentational symbolism (Winkelman, 2010, 2017). Psychedelic states are information enriched states (Lord et al., 2019) characterized by enhanced cognitive flexibility (Carhart-Harris Kaelen et al., 2016), heightened creativity (Mason, Kuypers, Reckweg, Müller, Tse, et al.,

2021; Mason, Mischler, Uthaug, & Kuypers, 2019), and increased insightfulness (Kometer, Pokorny, Seifritz, & Volleinweider, 2015).

The sociality-amplifying effects of psilocybin and their ability to enhance novel representations could have acted on individual and population differences in the abilities of ancestral hominin populations to respond to these effects, providing selection pressures for those with the capacities for sociality and cognition that were stimulated by psilocybin and necessary for participation in the cognitive niche.

Psilocybin ingestion would have provided further enabling influences in hominization, especially as deliberate human activities involving psilocybin exploitation contributed to the existing ritual dynamic of hominin life derived from the hominid collective ritual complex (Winkelman, 2009, 2019b). The effects of psilocybin utilization on emotional and social behavior and cognitive states and models illustrated in the visionary and entheogenic experiences intrinsic to psilocybin would have also generated spiritual experiences and religious tendencies. These effects contributed directly to the development of the primordial practices of shamanism, arguably the first religion (Winkelman, 2010, 2013).

Religion and social evolution

The principal tool through which past groups institutionalized psychedelics to enhance sociality was religion. Not only were psychedelics widely encountered in the foraging and simple agricultural societies, but they also persisted in religions of complex societies (Guerra, 2006), and even in historical roots of most world religions of today (Winkelman, 2019a).

Anthropological models of social evolution emphasize the determinant roles of the material mode of production, the basic ways in which we acquire our food. Major social transformations of the past were produced by changes in food production, and these subsistence changes were accompanied by new spiritual beliefs and religious practices (Winkelman, 2021b). These changes produced powerful influences on the ideological frameworks for conceptualizing self and our groups, shifting us from familial and tribal structures, to chiefdoms, states and universal religious ideologies.

A multifamily band structure characterized most of humanity’s evolution. Some 30–50 people living together in day-to-day life was augmented though a larger group of approximately 150 relatives encountered occasionally, particularly in special ritual events. The core of ritual practices, spiritual experiences, and community life involved a shamanic complex that guided human societies for millennium in foraging lifestyles that reflected our ties to nature and animals, exemplified in the animal powers of the shaman (Winkelman, 2010). Psychedelics were core aspects of many shamanic practices, particularly training, although they were not always necessary for shamanic ritual.

With the advent of simple agriculture, new religious practices arose that glorified the fertility of crops and kinship

descent groups (lineages) that expanded their kin based social systems into ancestor worship, exemplified in the political concept of a tribe (see Dunbar, 2022; Winkelman, 2021b). These social organizations based on an extended clan hierarchy became the next level of human collective identity, a vast social group of the living and the deceased all traced back to a common ancestor glorified in group ancestor worship symbolically identified by the totem animal. Psychedelic ritual practices are also reported for simple agricultural societies, often playing a central role in the cults of the deceased (i.e., Fernandez, 1982; also see Fitzpatrick, 2018).

In a span of a few thousand years the Neolithic Revolution, and then later the Agricultural Revolution, rapidly transformed human society from a multimillion-year dynamic of small-scale foraging societies adapted to nature's bounty and limitations. This was eventually overtaken by the complex state societies that have controlled regional and even global developments over the past 3,000 years. There monotheistic gods help stabilize moral systems in this new level of sociality integrating hundreds of thousands guided by kings and their gods. State level religions tend to suppress psychedelic spiritual practices, sadly exemplified in the tortuous treatment of Native American healers during the Spanish colonization and Inquisition. But some evidence suggests entheogenic practices persisted even in the priestly traditions of complex societies (Winkelman, 2019a), but as an elite practice rather than a popular activity.

Modern and post-modern religion

The primary forces of macrosocial integration of the pre-modern world were religion, whether the shamanic animal powers protecting the band, the totemic ancestral deities protecting the clan, the god-given rights of chiefs and nobility guiding chiefdoms, or the monotheistic gods of states. These religious beliefs and practices mediated cultures' environmental and societal relations across millennium of stability, an exemplification of sociality, with new forms of religion mediating the adaptations to increasing societal complexity.

But the emergence of Reformation and the Industrial Revolution thrust humanity into a global world system that has swept away the religious power of thousands of cultures and lifestyles in the creation of the nationalistic ethnicities of modern nation states. This trajectory has taken us beyond family-band-clan-ethnic-national-religious identities but has yet to form a system for global human identity. So, today's world is this fragmented system of pervasive identity oppositions, the West vs. East, Capitalism vs. Socialism, Democracy vs. Totalitarianism, Christianity vs. the Islamic World, etc. that supersedes the identities of nation-state systems but does not replace them.

But notably these are identities of division and separation, not global integration. What awaits our collective future identity as a globalized humanity? We have traveled from band level family-based morality to tribal identities,

and moved on to ethnic and national identities, and now have begun to supersede them in the religious and political identities that characterize the current world system. What will lead to our next stage of evolution from these various oppositional identities into a global human identity? What will it take to move us from the remaining bastions of prejudice and exclusion, to finally supersede the in-group versus out-group dynamic that so viciously stimulates endless generations of mortal conflict? Can we achieve such a unifying sense of collective planetary identity and responsibility beyond the shallow parochial religious missionization and capitalist-aid programs?

While post-modernity has often been characterized as an evolution beyond the religious superstitions of the past, the reality of the post-modern world is that religion still holds enormous sway over peoples' lives, even national and international politics. Despite our enormous technological and even political evolution, we are still at heart religious creatures, a cultural practice that paradoxically both unites groups and separates them from others.

Does this history suggest that some form of religious belief will be a mechanism for future human evolution, or is religion an ancient crutch that now hobbles our progress toward more inclusive human futures? Is there a paradigm for religion of the future that overcomes our parochial religiosity and its limitations??

THE FUTURE OF RELIGIOUS EVOLUTION?

Limitations on our capacity for sociality are clearly a key feature for future global development, as social demarcations still constitute a major impediment to intergroup harmony at all levels of social complexity (i.e., neighborhoods to international actors). Evolutionary psychologists contend that religion involved a suite of adaptations that better enabled humans to work together in cooperative groups, substituting selfish gene motivations for a prosocial altruism that enhances group survival. Yet these prosocial adaptations of religion are better known today for their intransigent tendency to divide the in-group from the out-group, to reinforce group think and insider preferences to the exclusion of outsiders. Given that religions are divisive, norms for separating the in-group from the out-group, how do we keep our most important adaptations from getting in the way of everybody getting along?

This out-group exclusion and even demonization of others characteristic of religion is in stark contrast with the effects of spirituality and mystical experiences in encouraging acceptance of others and tendencies to inclusiveness and universalism that are renown. Can our spiritual impulses be more inclusive than our religious tendencies, moving beyond parochial divisions toward a sense of a common humanity? Can spirituality provide a sense of planetary identification superseding the dichotomies of us vs. other? If our personal and societal evolution and a common planetary identity can be achieved through a spiritual transcendence, what is its best source?

Entheogenic spirituality

In the past, ritual use of psychedelics were key tools that were instrumentalized to create group integration, contributing intrinsic biological effects that enhance such relationships. Although they are not guarantees of mystical experiences, psychedelics are the most reliable technologies we have to induce these paradigm shattering experiences. These transformations from religious identification to spirituality is a broad trend in contemporary Western society, one that fits squarely with the influences of psychedelics on spirituality (Johnstad, 2018, 2020; Roberts, 2020), effects which have already begun a psychedelic-transformation within Christianity (Winkelman et al., 2024).

Our hopes for a spiritual solution to humanity's divisions can only be achieved by a radical shift in perspective, one that moves from culturally determined concepts of religion and the sacred to concepts of human spiritual universality reflected in concepts of entheogenic spirituality. Psychedelics appear to offer the best tool we have to make these dramatic changes as individuals, groups and a species.

Humans' interdependence requires further decentering of the self to consider others' perspectives. Such psychological and cognitive changes can be induced by psilocybin and other 5-HT_{2A} psychedelics known for their ability to induce ego-loss, reduced defensiveness, enhanced extraversion, increased interpersonal connectedness, and to facilitate cognitive states that support cooperation (Roberts, 2020). Psychedelics also produce an animistic and entheogenic mind set, where the natural world is personalized and socialized with human traits (sentience, relationality, intentionality, cooperation, intelligence) (Winkelman, 2013). Recent clinical applications of psychedelics spotlight something known to psychology more than half a century ago. These substances have neurological potentials that reliably stimulate mystical experiences, a range of specific experiences that are indistinguishable from what are considered genuine non-drug mystical experiences and often their most significant life-time spiritual experiences (Barrett & Griffiths, 2018; Griffiths, Richards, Johnson, McCann, & Jesse, 2008, 2011, 2018; Johnstad, 2018, 2020).

Clinical research based on double blind controls show the objective ability of psychedelics to produce the common core of mystical experiences, namely: experiences of intuitive knowledge and unity, transcendence of time and space, sacredness, ineffability and positive mood (see Richards, 2015 for reviews). The similarities of psychedelic and mystical experiences indicates that they represent something intrinsic to human nature rather than the product of cultural expectations, a biological basis for common mystical experiences available to people across cultures and time. Mystical traditions extol the superiority of these forms of perception, considering them to provide access to universal truths and perspectives far exceeding the comprehensions of reality rendered by ordinary culture-bound consciousness. Winkelman (2024) has characterized these mystical changes in consciousness in terms of epistemological shifts that enable the acquisition of perspectives based in neurognostic

systems by suspending culturally-mediated conceptual frameworks. The effects that such experiences have on people's subsequent beliefs, attitudes and behaviors are also a significant factor in understanding the potential roles and significance of these substances in human evolution. Psychedelics have the potential to rapidly and radically change existing personal and cultural templates and instill new world views and personal and emotional orientations to others and the environment. However, Johnstad (2020) presents evidence that non-clinical psychedelic use typically produces experiences different from the classic mystical features reported in the John Hopkins studies. Most psychedelic users typically experience positive feelings and improved connections rather than the classic mystical dynamics of ego dissolution, unity, and ineffability. Typical entheogenic experiences were not immediately transformative life-changing but did provide insight, connectedness with others and nature, and positive emotions of joy, love, and peace from a sense of having returned to an aspect of one's true nature.

These biological views of spirituality induced by entheogens provide new vantage points from which to address our cultural divides based in a sense of commonality derived from neurological perspectives on spirituality as an innate set of capacities related to specific extreme activations of our neurotransmitter systems. These kinds of experiences are also associated with enhanced altruism and prosocial tendencies, speaking volumes to their potentials for enhancing future evolution of our species. The psychedelic potentials for future transnational sociality are exemplified in the transpersonal experiences they induce that expand identity beyond the individual, ego, personal identity, even one's culture, provoking a sense of connection with others, even unity with other life forms (Grof, 2000; Roberts & Winkelman, 2013; Winkelman, 2025b). Psychedelics can stimulate personal transformations of engaging one's higher potentials through their powerful tendency to induce spiritual experiences, exemplified in their synonym entheogen—referring to their capacity to produce an awareness of and relationships with indwelling spiritual presences. The ability of psychedelics to transform deep seated international and inter-religious tensions with psychedelics (Israeli-Palestinian) has been explored (Roseman & Karkabi, 2021), offering hope for the future.

These powerful psychotropic substances that so reliably induce spiritual experiences can be directed for the future of humanity and our need for a transcendent identification and connection with nature (Terhaar, 2009). Irvine, Luke, Harrild, Gandy, and Watts (2023) report on a psychedelically induced biophilia, an enhanced connection with nature among people who did not have established relations with nature, helping them experiencing a bonding with the natural world. These experiences of 'interconnectedness' were mediated by transpersonal experiences and resulted in changes in attitudes and behaviours about nature, leading people who were not previously nature oriented to be more passionate and protective about nature.

Evans (2023) provides a review of Western cultures' dominant frameworks for psychedelics, noting a persistent tradition of evolutionary spirituality going back more than a century that proposes psychedelics be used to guide us towards self-improvement. This historical tradition of evolutionary spirituality has ethical limitations in an often Darwinian and narcissistic illiberal utopian program, but Evans notes this can be overcome. This integration of spirituality with evolutionary theory proposes psychedelics can contribute to engaging the unfinished projects of human evolution in gene-cultural interactions that exemplifies the plasticity of our species and psychedelics.

Psychedelic evolutionary spirituality can move beyond its basis in personal testimony and belief with the current clinical sciences supporting psychedelics transdiagnostic efficacy, extensive sociability enhancing effects, and lab science establishing their diverse plastogenic mechanisms. Psychedelics have the potential to influence future human evolution through positive changes in psychological functioning, especially prosocial attitudes and behaviors (Griffiths et al., 2018). Psilocybin may augment empathy and prosocial behavior by inducing a positive feedback loop between them (Bhatt & Weissman, 2024). That possibility has been championed by leading figures of the psychedelic movement who proposed a psychedelic-induced higher state of consciousness could form the basis of a global psychedelic religion of people who advance human evolution. Such uses of psychedelics for enhancing humanity's future adaptations reflects Gordon's (2022) proposal that psychedelics might be used to facilitate moral enhancement as adjuncts to moral development through facilitating trusting relationships. Roberts (2013, 2019, 2020) has explored these psychedelic applications to the future development of the spirituality, religion, mind and morals. Psychedelics clearly have moral implications (Langlitz, Dyck, Scheidegger, & Repantis, 2021) and require careful assessment of their most beneficial applications.

Future evolution

The unprecedented conditions currently confronting humanity present challenges to traditional forms of sociability, but can our future types of collectivities be substantially different than our evolutionary history of intergenerational ties of kinship that we have been dependent on for millions of years? Carbonell & Hortolà propose that we are active agents in a great self-experiment of nature where it is now culture that provides the potentials for creating new evolutionary responses mediated by our emerging conceptions of who we are individually and collectively. "Becoming human is also the awareness that we have about our own evolution . . . We can take a leap towards a type of knowledge and consciousness that we have not known until now . . . To become human . . . depends on us, on our will and on our ability to know, think and act with the critical conscience of a species" (Carbonell & Hortolà, p. 16, 17).

Carbonell & Hortolà propose we are headed to a new social paradigm in which the collectivization of energy leads

to a dynamic in which individual self-identity is strongly bound to a specific identity community. These dynamics of collective individuality present a challenge to how we form these group identities without reinforcing dynamics of opposition so characteristic of religions. Human sociability depends not on biological kinship but on cultural factors that allow us to fictionalize those ties, extending categories of kinship to unrelated significant others.

But our intergroup dispositions are wired into our brains during early development, the prejudices embedded in our habitus before we ever become conscious of them or learn to think about them. The need for a rapid re-adjustment to radically changing dynamics suggests that only neuroplasticity provides a brain capacity for such rapid changes, and these are a central mechanism of psychedelic effects. These mechanisms can advance our brain's functionality, particularly our capacity for inclusive social relations, through the ability to rewire them through neurogenesis and neuroplasticity.

Carbonell & Hortolà propose that the current needs of our species are to strategically incorporate the concept of complementarity to engage a determination of why we have not substantially exploited our inherent properties to increase our sociability and restructure the sourcing and allocation of resources and energies in a more effective way to confront the crises confronting humanity. Complementarity is about a mode of interdependence and guides social behavior in a systemic dynamic that generates and reinforces social bonds. Complementarity is based in connections that produce an inter-complementarity among members of populations.

We cannot evolve quickly enough through biology to solve our current and future social and ecological problems. Our evolution as a species was driven not by just overall brain growth but also by our expanded ability to reuse old capacities for new adaptive functions. This is seen in the role of the serotonergic and dopaminergic neuromodulatory systems in human evolution. These serotonergic and dopaminergic systems are widespread in the animal kingdoms, and also significantly expanded in human evolution as the most important neuromodulatory systems supporting a range of uniquely human capacities. When we look for the factors that stimulated enhancement of these neurotransmitter systems in the environment of evolutionary adaptation and provided environment factors for selection for such enhanced neural capacities, psilocybin stands out as the only significant factor. We evolved the capacities to transform plant toxins into significant sources of vital neurotransmitters (Rockman et al., 2005) and used them to enhance our evolutionary potentials. Some of these enhance our capacities for positive social relations and cooperative cognitive models that provide the basis of our uniquely human lifeways (Arce & Winkelman, 2021). The stimulation of these neuromodulatory systems, especially by natural products that serve as exogenous neurotransmitter analogues (i.e., 5-HT_{2A} psychedelics), also elicits a capacity to produce genuine spiritual and mystical experiences.

So, if we want rapid changes in the capacity of our brains, especially their capacity to change, what we can do is to focus on agents and processes that enhance neural plasticity, the ability of our brains to rewire themselves in new adaptive ways, particularly with positive emotional and social effects. The concept of *plastogens*—substances that produce structural and functional neuroplasticity and neurogenesis—are key to understanding our immediate possibilities for brain evolution, as well as personal, social and cultural adaptations to rapidly changing circumstances.

The neuroplastic changes that are induced are activity- and experience dependent, making the context of these intense psychedelic-enhanced experiences the determinant factors in their effects of the neuroplasticity. The window for psychedelic induced neuroplastic effects begins during the intense subjective experiences, meaning their effects are implanted into the brain during this highly plastic period (Calder & Hasler, 2023). These intense experiences under highly plastic brain conditions makes these experiences more powerful influences on neural circuitry than influences from everyday occurrences. Psychedelic influences are known to be powerfully shaped by the set and setting, making a safe and supportive setting essential for the positive effects of psychedelic drugs and the therapeutic and transformative experiences they can induce.

Baker (2005) reviews the traditional use of psychedelic sacraments which illustrates that they were strongly shaped by rituals and cultural traditions and were used to help maintain society, providing a context for teaching about basic cultural beliefs and values. They enhanced processes for social identity formation and engagement with the cultural realities and priorities. The post-modern world lacks these traditions for psychedelic use, and indeed if they are to be used to engage planning for novel futures, tradition might seem to be irrelevant.

Given that the cultural model of the world is what is basic to our adaptation and survival, what models do we need for the future to produce reliable alternatives to the present and for the future? The cross-cultural patterns of entheogenic healing practices (see Winkelman, 2025a) reveal the underlying evolved psychology of entheogenic and ritual healing (Winkelman, 2021a, 2025c) that provide biogenetic models for engaging these substances in ways that optimize their use for therapeutic and transformative effects.

ADDRESSING THE RISKS OF PSYCHEDELIC-ENHANCED FUTURES

Despite the promising evidence of benefits from psychedelics for the present and future, there is a broad perception that they are dangerous, and indeed, evidence regarding the risks of their uses and abuse should raise concern. Despite real risks from unprepared and unsupervised use and inadequate support for and integration of psychedelic-induced experiences, the knowledge of how to help ensure beneficial psychedelic experiences is well developed (i.e., see Johnson, Richards, & Griffiths, 2008).

However, the expanded institutional instrumentalized use of psychedelics should not be approached with just a simple, blissful attitude about their inherent potential to bring enhanced well-being. The 60's hippie attitude about psychedelics inducing love, acceptance, and harmony may have some merit, but there is also a potentially dark side to psychedelic effects that requires careful consideration. Psychedelics were administered by the covert agencies of the US government in studies of their potential as a mind control tool. The potential of psychedelics to induce a group think is also a powerful risk in addition to a potential benefit that might be acquired from increased group cohesion.

Even in the pre-modern context, psychedelics were used in horrifying rituals, exemplified in the human sacrifices performed by the Aztec priests who consumed psilocybin mushrooms and mescaline in preparation for the public rituals of sacred murder of captives and enslaved people (Hansen, 2024). The Jivaro of the northwest Amazon region were known for their consumption of ayahuasca as preparation for nighttime collective head-hunting raids, using the psychedelic to increase stamina and nighttime vision as they went to kill and decapitate their enemies for war trophies (Karsten, 1935). Pace and Devenot (2021) document the contemporary use of psychedelics for enhancing group bonding among members of right-wing authoritarian political movements, including several neo-Nazi organizations. Such uses make clear that the intrinsic effects of psychedelics do not assure that they will be used for broad humanitarian goals.

The primary determinants of psychedelic effects have been long recognized as set and setting, making consideration of these factors central to addressing concerns about the outcomes of psychedelic experiences. In pre-modern cultures, these concerns were largely addressed by their incorporation into a collective ritual setting, even into organized societal festivals and religions (see Fitzpatrick, 2018; Guerra-Doce, 2006). The cultural, psychological, and social settings provided by historical and contemporary traditions certainly constituted a principal barrier against diverse risks and, furthermore, strongly shaped the outcome of the experiences. Contemporary societies are notably lacking in such frameworks for the construction of the psychedelic experience, posing risks to users and possibly others. The various levels of risk — pharmacological, emotional, behavioral, and social — are briefly addressed to establish the existence of knowledge that informs best practices. Set and setting are the most important issues to be addressed to ensure safe use and experiences.

The expanded use of psychedelics also poses risks to the natural substances when they are naturally sourced (i.e., the toad venom of *Incilius alvarius*, native growth of the ingredient plants of ayahuasca, and peyote and iboga, etc.). Reliance on cultivated psilocybin and laboratory-produced substances eliminates that problem and will be the focus of the assessments here.

Risks from psychedelics

The question of the safety of broad psychedelic use must begin with a consideration of the various forms of risks that

psychedelics can pose, from physiological drug interactions to psychological and emotional reactions, social responses, and behavioral risks of physical harm. Despite a broad cultural view of psychedelics as high risk, reinforced by their FDA classification as Schedule 1 (meaning no recognized medical uses and high abuse potential), the psychedelics are, by medical criteria, some of the safest of all categories of drugs (Dodd et al., 2023; Family et al., 2020). This is not to discount negative psychedelic experiences, but as the following review will show, the risks come mainly from the context (set and setting) rather than pharmacology.

Toxicity and safety. Schlag, Aday, Salam, Neill, and Nutt's (2022) assessment of the medical evidence base for psychedelic-induced psychological and psychiatric risks and medical harms, including toxicity, found that the claims for these harms are largely anecdotal and do not stand up to scientific scrutiny. Their review concludes that medical risks are minimal, that there is a lack of scientific support for the negative perceptions of psychological risks, and that adverse effects are not reported when use occurs in a regulated context. Contemporary research shows that the classic psychedelics do not cause organ or neurocognitive damage, even at high doses and with repeated use. Psychedelics are well established as having a high degree of physiological safety, even being 'one of the safest known classes of CNS drugs' (Nichols, 2016: 275). From a physiological perspective, LSD is non-toxic and even medically safe at standard dosages (50–200 µg) (Nichols & Grob, 2018). Dodd et al. (2023) review the evidence for the low potential for acute toxicity associated with psilocybin and psilocin, especially given their high therapeutic index (also see Studerus, Kometer, Hasler, & Vollenweider, 2011). Since a lethal dose is estimated to be 500 times greater than a therapeutic dose, they concluded that it is almost impossible to achieve a lethal dose by consuming psilocybin-containing mushrooms. MacCallum, Lo, Pistawka, and Deol (2022) note the very large therapeutic index (1:1000) associated with psilocybin and propose that, consequently, a lethal dose is virtually unattainable, giving psilocybin an exceptional safety profile. Consequently, "The primary risk for psilocybin is psychological safety, not physiological safety."

MacCallum et al. (2022) outline practical safety considerations for psychedelic therapy for safe dosing and monitoring and management of considerations for adverse events and problematic drug interactions. Minimizing the risks for psychological harm requires appropriate preparation and monitoring of patients to reduce risks for psychological distress. Tested practical guidelines for psychedelic-assisted psychotherapy have been well developed (i.e., Horton, Morrison, & Schmidt, 2021; Johnson et al., 2008; Phelps, 2017; Penn, Phelps, Rosa, & Watson, 2021).

Contra-indications and adverse drug interactions. MacCallum et al.'s (2022) review indicates that the principal contraindications for psychedelic therapy involve the rare possibility of adverse psychotic reactions, making it poorly advised for patients with prior diagnoses of schizophrenia or

bipolar and borderline personality disorders. However, despite these traditional contraindications for psychedelic therapy, there is a lack of systematic observational data or controlled assessments of actual risk-benefits for these populations. Other contra-indicated populations are pregnant or lactating women, but there is a lack of sufficient scientific evidence for evaluation of those risks to infants (and the use of small quantities of peyote and ayahuasca by pregnant women is permitted in entheogenic traditions).

Although screening for clinical trials generally excludes people with a personal (or even familial) history of diagnoses of psychosis, schizophrenia, and mood disorders, there is no strong evidence of a heightened risk of adverse effects despite a notable case where a person with such prior conditions have committed homicide following use. Even among these psychedelic users with prior at-risk diagnoses, La Torre, Gallo, Mahammadli, Zalewa, and Williams (2024) found that most of them reported the psychedelic experience as positive and promoting personal growth, as well as symptomatic improvements, improved insight, and positive feelings such as love and appreciation.

A specific form of post-psychedelic disturbance is the Hallucinogen Persisting Perceptual Disorder (HPPD) (Irvine & Luke, 2022), where psychedelic-induced visual disturbances persist long after the pharmacological effects have ended. Individual differences in assessing the significance of these experiences play a role in the problematic effects of HPPD, particularly whether the persistent visual symptoms induce increased concern and anxiety. Irvine & Luke's study shows that those who have negative experiences of HPPD are characterized by prior conditions (pre-existing trait anxiety) and set and setting factors (lack of adequate preparation and prior knowledge) that increase the potential for precipitating a negative experience.

Medicine interaction risks. Interaction problems may be posed by concurrent use of psychedelics with antidepressants and antipsychotics because these medications often act through serotonergic modulation as well, posing the potential for pharmacodynamic drug interactions that may cause problems. A well-recognized risk is the serotonin syndrome, where adverse events may result from interactions between psychedelics and other serotonergic drugs. The serotonin syndrome is rare but can result in excessive serotonin signaling that can potentially be life-threatening. Consequently, clinical trial protocols generally recommend a cessation of such medications, beginning with a period of tapering off and washout of such medications to eliminate the risk of provoking the serotonin syndrome. MacCallum et al. note, however, a lack of verified serotonin toxicity cases and, in contrast, findings from a recent psilocybin study that included patients who were concurrently using SSRIs. The study reported no safety concerns related to the serotonin syndrome and no indication of a reduction in efficacy or positive mood.

Negative physical experiences. Bouso et al.'s (2022) Global Ayahuasca Survey found the lifetime incidence of

people requiring subsequent medical attention was low (2.3%). Although more than half of respondents reported adverse mental health effects experiences in the following weeks or months, almost all (88%) considered these adverse experiences as making a positive contribution to the long-term process of personal growth. Although as many as 12% sought professional medical assistance for persistent effects, there are clear risk factors for such adverse experiences, including: prior diagnosis of mental or physical health problems, especially substance use disorders; consumption in contexts without supervision, particularly non-religious settings; first use at older age; and higher overall ayahuasca use. But even among those who reported high levels of adverse effects and challenging experiences, most found benefits in the ayahuasca use and continued to attend ceremonies, illustrating the principle that adverse experiences can nonetheless contribute to positive changes in well-being.

Psychological risks

Psychedelics are known for posing risks of disturbing and distressful psychological experiences, often referred to as “bad trips.” These negative psychedelic experiences are typically transient (Calder & Hasler, 2023) and manageable with appropriate therapeutic support to ameliorate the distressing symptoms. Furthermore, such experiences are generally part of the therapeutic process, and the appropriate integration of these experiences is usually a key part of the healing process. These typically acute psychedelic experiences normally do not provoke prolonged decreases in well-being (Studerus, Komater, & Hasler, et al., 2011; Carbonaro et al., 2016) and with appropriate set and setting their appropriate resolution can turn the “bad trip” into a psychological growth experience.

While psilocybin and other 5HT_{2A} psychedelics are well-known for inducing symptoms similar to those of psychosis and schizophrenia, their resolution with immediate and follow-up counseling is the norm, rather than prolonged mental disturbances. Dodd et al. (2023) note the relatively mild “adverse effects for psilocybin, psilocin or psilocybe mushrooms include: tachycardia, anxiety, nausea, vomiting, diarrhea, emotional lability, delusions, feelings of impending doom and confusion, dysphoria, derealisation, depersonalization, and mydriasis.” Another concern is a rare hallucinogen persisting perception disorder (HPPD), a condition where hallucinogenic symptoms often called “flashbacks” persist for prolonged periods after cessation of use. But even among people with a high level of lifetime hallucinogen use, the syndrome is rare. The risk that psychoanalytic therapy produces major complications such as suicide attempts or prolonged psychotic reactions is no higher than in conventional psychotherapy, indicating relative safety in an admittedly significant risk area for unsupervised psychedelic use (Passie, Guss, & Krähenmann, 2022).

Emotional distress. Although highly distressing psychedelic experiences with post-session persistence are relatively rare,

even when such distressing psychedelic-induced experiences occur, the primary problems include acute anxiety and even panic attacks that usually subside post-session with appropriate peer and family support (Robinson, Evans, McAlpine, Argyri, & Luke, 2025). Reducing and resolving such problems requires prioritizing multifaceted support systems that integrate assessment and screening, prior educational orientation, professional supervision, and diverse community resources, including non-professional healers, such as peer and family support for implementation of effective coping strategies.

Nordin, Hlynsson, Håkansson, and Carlbring (2024) identified the short-term adverse effects of psilocybin in clinical interventions as involving therapeutic processes and relationships, as well as difficult self-experiences that needed to be resolved. These difficult long-term negative experiences included self-destabilization and difficulties in re-adaptation to life following the realizations that occurred during treatment. Such difficulties can be viewed as normal aspects of therapeutic processes and emphasize the importance of pre-treatment assessment, treatment orientation, and the development of therapeutic relationships, as well as support for post-intervention integration.

Lutkajtis and Evans (2023) assessed difficult post-experience integration experiences and found that “mood fluctuations, ‘post-ecstatic blues,’ disconnection from community, re-experiencing symptoms, spiritual bypass, and perceived lack of support” were generally transient immediately following the psilocybin retreat. These were not only resolved in a short time with integration support but were also correlated with positive outcomes, including long-term remission of precipitating concerns. The experiences often referred to as ‘spiritual emergencies’ illustrate that what might appear as psychedelic-induced problems are better understood as difficult challenges provoked by the psychedelic experiences that can provide the impetus for the unfolding of transformative processes with effective integration.

DISCUSSION

Historical representations of psychedelics going back to the colonial era depicted them as sources of the Devil’s power, emphasizing negative evaluations of the experiences they produce. In contrast, the physiological risks of psychedelics are negligible, and the psychological risks are very low with appropriate set, setting, and follow-up. In an about-face to the traditional prejudices against psychedelics, recent media and even journal articles have expressed claims about the potential of psychedelics to improve society by leading to increased concern about the environment and others. Such statements may be overly optimistic. Such shifts in beliefs are not intrinsic to psychedelics, as Pace and Devenot (2021) point to historical and contemporary cases of people whose authoritarian views persisted following psychedelic experiences or even led them to become further polarized and

radicalized to conservative views. Psychedelic experiences can challenge worldviews and precipitate changes in fundamental orientations, but the direction of change, including political beliefs, will likely be a function of set and setting, the contextual effects, rather than the intrinsic physiological effects of psychedelics.

The concern with safe psychedelic use is primarily about the appropriate set and setting to provide the context for safe use, appropriate supervision for the prevention of self-harm, and sufficient protection for people in vulnerable psychological and emotional conditions. Studies that make assessments of adverse outcomes typically find that the retrospective predictors of difficult psychedelic experiences reflect a failure to assess, prepare for, or address central factors such as: screening for high-risk or psychological vulnerability; lack of an experienced and organized support team; unsafe or adverse environmental conditions; use of large quantities or polydrug use; and lack of psychological counseling and integration following the experience.

The review study of [Aday, Mitzkovitz, Bloesch, Davoli, and Davis \(2020\)](#) that integrated results from 34 follow-up clinical studies with classic psychedelics found enduring effects that bode well for their positive impact on human futures. Enhanced personality dynamics and attitudes, connectedness with others, emotional breakthroughs and a sense of well-being, meditative practices, and spirituality were complemented with reductions in anxiety, depression, and substance abuse. However, achieving these long-term improvements in psychological functioning depend on providing the proper set and setting through adequate education and preparation, appropriate supervision and support, and post-session integration. [Calder and Hasler \(2023\)](#) note that the enhanced neuroplasticity produced by psychedelics should enhance responsiveness to various forms of interventions. This enhanced neuroplasticity, achieved through a safe setting and supportive psychotherapy, should generate synergistic interactions that facilitate diverse transformations.

Ultimately, the maximizing of psychedelic use must recognize and incorporate the essential roles of rituals linked to broader social and cultural institutions as resources for creating the set and setting of the psychedelic experience ([Winkelman, 2025a](#)). [Blainey \(2025\)](#) highlights the importance of drawing on the experiences, guidelines, and practices of existing psychedelic religions, such as Santo Daime, which has an established history of almost 100 years. Incorporating of psychedelic sacraments into existing Western religious organizations is already a reality, as exemplified in a recent consideration of Psychedelic Christianity ([McCarthy & Priest, 2024](#) with Commentary [Winkelman et al., 2024](#)).

In focusing on possible psychedelic-induced transformations of humanity, a narrow focus on individual problems is insufficient for the broad vision required. Psychedelic-induced experiences such as derealization and depersonalization are not merely personal problems to resolve but also conditions that require social transformations to provide relief. [Noorani and Liebert \(2024\)](#)

offer a positive assessment of the potential of psychedelics to function as agents of not only personal change but also social transformation. [Noorani and Liebert \(2024\)](#) base their 'transformative paradigm' on social justice perspectives and the incorporation of 'marginalized expertise' from grassroots sources. This transformative paradigm involves more than acceptance of the medicalized approaches of clinical studies. Instead, it engages perspectives of social transformation that address concerns with changing mental health institutions and broader social systems to achieve social justice goals that reduce the wider institutional conditions that constitute structural features that produce personal mental health difficulties.

CONCLUSIONS

Psychedelics can play a direct role in the central future trends of human self-transformation of augmentation, symbiosis, and transcendence, as noted by [Anderson \(1996, 1997, 2003\)](#). Psychedelics enhance operation of some cognitive abilities beyond normal parameters, stimulating exceptional performance levels. This is exemplified in the extraordinary visionary experiences they produce, which do occur without drugs such as in meditation experiences, but which are rare, sometimes once in a lifetime experience. These experiences are far more reliably produced by psychedelics. This is a result of a symbiosis between the human organism and the exogenous neurotransmitter source that allows the organism to transcendence its ordinary capacities, even identity boundaries, producing an experience of a merging of the self with a larger entity/framework. These effects of psychedelics exemplify the types of "future self" examined by [Anderson \(1997\)](#). These are exemplified in the transformation to a multicentric identity and personality, a recognition of the self as a socially constructed form rather than a permanent, individual entity. This reflects the multiple dimensions of the ongoing 'stream of consciousness' that alters people's experience of their personal boundaries and selfhood to go beyond present identity, so that they feel that they are part of a global or universal identity.

The effects of psychedelics on cognition, sociality, and ecological relations exemplify the effects on the pluralization of the self that must be a part of humanity's successful adaptation to the challenges of a global multiculturalism and the threats of global ecocide unprecedented in humanity's evolutionary history. These kinds of changes in the self would serve well for increasing social tolerance in a world confronted by the boundaries created by differences and social inequalities that are confronting humankind. The kinds of transformative changes that are possible through the extrovertive and neuroplastic effects of psychedelic substances can be a key to producing the social tolerance and cognitive shifts necessary for successful transnational culturally pluralistic selves and innovation responses to produce more optimistic futures for the planet and its many forms of life. Their established effects show that psychedelics can contribute to shaping people to be more tolerant of

difference, have a greater desire for ecologically and socially just futures, and the creativity and innovation to envision such alternate realities.

Costa (2022) provides an integrative literature review of psychometric studies on the effects of psychedelics on creativity, a long-alleged capacity of these substances that is supported by evidence that suggests that during post-acute phases convergent thinking may increase. Gandy, Bonnelle, Jacobs, and Luke (2022) review evidence of the role of psychedelics in enhancing creativity. Psychedelic states engage cognitive processes, induce hyperconnectivity, and enhance meta-cognitive awareness that enable them to contribute to scientific insights and creativity. Campo and Yali (2024) review evidence that these and other psychedelic effects may be mediated through enhancements in psychological flexibility. The increased awareness of thoughts and behavior permit the simultaneous perception of multiple explanations or solutions for life events that result from ego-dissolution and other decentering experiences, indicating the broad applicability of psychedelics for preparing people for radically different futures.

Psychedelics' sociality-enhancing effects (Roseman, Winkelman, Preller, & Fotiou, 2022) provide a pluralization of worldviews and perspectives, shifting the paradigm from that of hallucinogens and dangerous drugs to one that recognizes the transdiagnostic applications of these substances as medicines, and especially the power of their sacred and social potentials. This evidence is promissory for future improvement of some of humanity's most intractable problems by addressing limiting behaviors and beliefs. These psychedelic-inspired anticipatory practices have a modern history of more than 100 years of forward-looking perspectives on human enhancement (Evans, 2023), and a prehistory that stretches back millennia (Arce Rodriguez & Winkelman, 2021). It would serve humanity well to have these practices brought to contemporary futures planning, policy, and decision-making.

Given that psychedelics have a long history and prehistory as central cultural institutions in the pre-modern world (Fitzpatrick, 2018; Guerra-Doce, 2006, 2015; Labate & Goulart, 2005; Räscher, 2005; Samorini, 2019; Schultes, Hofmann, & Räscher, 1998; Winkelman, 2019a), the current paper is intended to animate professional interest in addressing novel ways the instrumentalization of psychedelics might enhance future adaptations through their use in enhancing self-transformations and discovery of future possibilities. Integrating psychedelics into responsible approaches to futures education and analysis can contribute original insights and novel approaches to determining how to better address the positive futures of all people on the planet in a just manner. Such uses of psychedelics for orienting us to the future could offer novel ideas for consideration and implementation into planning and policy settings. Central uses could be to explore how to guide personal transformations to enable people to be more tolerant of differences and more willing to engage with new paradigms of thought and behavior to address the changes we need to achieve as a species.

Just how psychedelic uses will be instrumentalized for possible roles in creating novel futures remains to be determined, but appropriate set and setting factors are recognized as essential to optimizing the effects of psychedelics (Hartogsohn, 2017). Orientation for these crucial set and setting factors can be provided by knowledge regarding the commonalities among contemporary indigenous entheogenic healing traditions (Winkelman, 2025a) and the relationship of these shared traditions to humans' evolved psychology of ritual healing (Winkelman, 2021a, 2025c).

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