### Mechanisms Underlying the Therapeutic Effects of Psychedelic States of Awareness

## A Paradigm-Shifting Revolution in Psychiatry

Recent controlled studies on psychedelics at major medical centers including Johns Hopkins, NYU, and UCLA have reported groundbreaking results for the treatment of psychiatric disorders. In studies using psilocybin for treatment-resistant depression, improvement and remission rates are double or triple those of SSRI medications after just one treatment session. Because these are unprecedented improvements over currently available therapies, the FDA recently moved research on psilocybin for treatment-resistant depression into final Phase 3 stages, labelling the treatment with a rare "Breakthrough Therapy" designation. Psilocybin is also being tested for the treatment of addiction and cancer-related depression and anxiety.

Although psychedelics can also produce a range of negative experiences including anxiety, controlled studies have shown that psilocybin occasions experiences similar to spontaneously occurring mystical experiences in the majority of patients, with corresponding improvements in personality that may be permanent. Michael Pollan, in his recent New York Times Bestseller How to Change Your Mind, has written about the potential of psychedelics for transformation and transcendence.

What are the therapeutic mechanisms underlying the effects of psychedelics that can result in mystical-type experiences in the majority of patients? The dramatic therapeutic effects of psychedelics\_can be understood from recent research in three related areas of affective neuroscience: the default mode network and the ego, the core affective self, and the neurobiology of psychedelic states of awareness.

#### The Default Mode Network (DMN) and the Ego

The DMN is a core brain network that is active in the conscious resting brain. It exhibits persistent and vigorous brain activity that deactivates when the brain is directed toward a task or goal. The DMN represents the default baseline state of the awake brain when the eyes are closed and individuals are engaged in internally focused tasks like autobiographical memory retrieval, envisioning the future, and conceiving the perspectives of others. These tasks cause the DMN to consume a high amount of the brain's energy during its default resting state. Reading or other routine tasks require minimal additional energy over what is already consumed by the DMN. Because the DMN receives more blood flow and consumes more energy than other brain regions, and is a center of dense connectivity, it serves as an important "connector hub" for information integration and routing in the brain.

The DMN is thought to deal with introspection, memory and other "inner" processes, in contrast to other regions responding to the environment and what happens in it. The DMN allows individuals to simulate the past and future and reflect on the mental states of others. Instead of being psychologically constrained to the here-and-now, humans have the unique ability to disengage from the external world and turn our thoughts inwards to construct mental simulations of hypothetical scenarios to help us anticipate and evaluate future events before they happen. Through mental simulation of our past, future, and the minds of others, we travel far beyond the observable.

The DMN's metacognitive processes include the internal monologue, mind wandering and day-dreaming, autobiographical memory, mental time travel into the past and future, imagining hypothetical events and scenarios, theory of mind (the ability to know what others are thinking), and the generation of narratives about ourselves that help create a stable sense of self over time. Because the DMN is primarily responsible for internally focused, self-reflective processes, it is the neurobiological orchestrator of the conscious self, or what psychologists and Eastern traditions call the ego.

The DMN also edits and filters sensory stimuli impinging upon the brain. Because the brain is continually bombarded by a significant number of external stimuli such as vision and sound, and internal stimuli such as emotions and thoughts, we would be overwhelmed unless the brain had a filtering mechanism to determine what reaches conscious awareness or stays unconscious. The filter is a function of selective inhibition by the DMN that is energy-demanding. This inhibition, which is reflected in the highly active resting baseline default state of the brain, occurs at the level of cortex by the DMN's top-down control. The DMN also exerts its inhibitory filtering influence at the level of the thalamus and reticular formation,

two lower brain areas that play a central role in alertness, attention, and consciousness. Central to the DMN's thalamic/reticular filtering process is habituation, in which the brain learns to consciously ignore safe, repetitive stimuli while remaining sensitive to more important, novel stimuli. Through this mechanism of reduction and restriction, the DMN controls the gates of awareness by deciding what reaches conscious awareness or is inhibited and repressed into the unconscious.

The DMN may have come online as recently as 40,000 years ago, when we see the first widespread evidence of self-conscious, symbolic thinking and mental time travel in the cave art of Cro-Magnon man. It was here that we emerged from the primary affective consciousness that we shared with animals and become truly modern humans: problem solvers, artists, inventors of ritual and technologies, possessors of an aesthetic consciousness, and creatures of intelligence and complexity.

As the DMN's psychological coordinator of the conscious self, the ego edits and limits our personal awareness by regulating the DMN's filtering process. Chief among the ego's editing functions is to maintain the boundary between the conscious and unconscious realms of the mind, as well as the boundary between self and other objects. Experience cannot enter awareness unless it can bypass this filter. The filter is constructed, selective, and socially conditioned based on society and culture, language, and science. It is constructed in light of our past experience, needs and desires, biases, wishes and fears, likes and dislikes, and expectations. It is characterized by active control and manipulation of the environment, sequence and order, rationalism and materialism, causes and effects, and beginnings and ends. The ego creates a relatively stable personal reality through this selective awareness and attention.

The hallmark of the ego is the subject-object relationship in which differences are seen by categorizing the world as either "I" or as objects separate from "I". All objects are a thing to be analyzed, evaluated, explained, and compared by categorizing as known or unknown, useful or irrelevant. This helps create our social definition of self-identity and the stories we tell ourselves about who we are: our jobs, how much we earn and own, our roles at work and at home, and how attractive and successful we are. Coveting, possessing, having, acquiring, status, material possessions, and power are all products of the ego's subject-object dichotomy.

The ego may have come online as recently as 10,000 years ago, coincident with the development of agriculture, as a subject-object interface for a world view that involved control over nature. Although the natural and social worlds were previously integrated into one world that included humans, animals, plants, and objects that formed a living nature, we began to see the world in terms of the subject-object relationship, causes and effects, beginnings and ends, and the importance of an explanatory nature of events and the self. Through writing, philosophy and the beginnings of science, we rapidly progressed to the age of reason, the industrial age, and finally to the computer age as the ego and science became our sole arbiters of reality.

Eastern traditions teach that the ego reduces and restricts information from conscious awareness and blocks perception of a more comprehensive awareness of ourselves, others, and the world. Instead of hearing and seeing what truly exists, we see things through the ego's distorting thought-based filter. We are not our ego identity or social role, and awareness of our self as a separate entity from objects increases our sense of existential isolation.

#### The Core Affective Self

Whereas the DMN and ego are the hub of the conscious, rational self, the core of our emotional life lies in more ancient, unconscious brain regions. These neural territories below the cortex are the primordial affective systems that are shared by all mammalian brains. The original form of consciousness was affective, and the primal state of mammals and infants is intrinsically affective. It is from these ancient affective systems that we inherit emotions as evolutionary, unconscious tools for living. Emotions are built into the brain by evolution as archetypal memories that are encoded in our genes as the evolutionary wisdom of our collective ancestral past that helped us play the game of survival and reproduction. Emotions allow us to unconsciously and quickly deal with matters of importance that affect our well-being in ways that have been repeatedly successful throughout our individual past and our ancestors' distant

evolutionary past. They represent an innate, biologically based form of knowing and a non-reflective, primary process type of consciousness that precedes our cognitive understanding of the world.

Although higher cognitive forms of self-consciousness emerged in the neocortex, they were built upon an evolutionary foundation of ancient brain regions and their affective consciousness. Because emotions lie at the core of our beings, the affective mechanisms that generate such emotions may constitute an essential foundation for the evolution of higher, more rational forms of consciousness.

Converging neuroscientific evidence involving emotional processes in ancient brain regions supports the concept of a core affective self as the neural foundation for all affective experience. Jaak Panksepp, a research pioneer in affective neuroscience, postulated that a primordial self and its pure form of affective consciousness interacts with higher rational cognitive processes to form the neural foundation for all emotional experience. The core affective self is preserved through species rather than being unique to humans. However, once the DMN and the ego came online, they inhibited and repressed the core affective self and its affective consciousness into the unconscious.

Brain networks that produce innate emotional responses also generate feelings that are experienced consciously by the core affective self as an ancient form of consciousness. Although not self-conscious, the core affective self is an innate intelligence that has an internally felt unified presence in the world. It provides the capacity for pure experience without the capacity to reflect on the experience. It is an underlying dimension that represents a unitary reality and a non-reflective consciousness. Because it evolved long before the recent emergence of the DMN and the ego, it does not see itself as the subject with all other objects as separate and to be acted upon.

Panksepp postulated that the periaqueductal grey (PAG), as the brain's emotional control center, is the locus of the core affective self for all animals. The PAG is the most ancient and highly concentrated emotional convergence zone in the brain and is located in the upper brainstem. It is the grand central station of emotion because it is involved in all emotions, not just fear like the amygdala. It also has the most massive convergence of brain systems and can induce the most powerful emotional changes in the brain. Damage to it causes greater impairment in consciousness than any other areas of the brain, suggesting that it is crucial for consciousness. The thalamus and reticular formation, which play a key role in the filtering mechanism for the DMN, lie adjacent to the PAG.

Carl Jung thought the organizing system of the self is predominantly affective and archetypal, and must lie subcortically in the brain stem. He conjectured that such a subcortical system might somehow reflect a symbolic, pre-verbal archetypal form of the unconscious that is contained in the brain of all individuals as the collective unconscious. It holds the totality of all human experience back to its remotest beginnings and contains the whole spiritual heritage of man's evolution. The collective unconscious is identical in all individuals throughout history and cultures and is inherited and independent of the individual, i.e., a universal mind that may be synonymous with the core affective self.

# The Neurobiology of Psychedelic States of Awareness

Psychedelics are associated with increased networking between otherwise disconnected areas of the brain, particularly ancient levels of the brain. They also reduce connectivity between areas of the brain that comprise the DMN, thus suppressing and disabling it. This inhibition of the DMN and its normal top-down and thalamic/reticular filtering process produces several profound effects on awareness that result in an altered state of consciousness.

A common and extraordinary effect on awareness is the inhibition of the ego's habitual, automated filtering of perception. This is experienced as a more direct, immediate, intuitive state of awareness that "mirrors" sensory stimuli rather than filtering and distorting it so that we "see" and "hear" rather than think and filter, and we perceive without interpreting and analyzing. The senses and perceptions are keener and richer, and the world looks new and vivid. There is an intuitive sense of realness and ineffability. Acquired beliefs are stripped and the world is seen with an innocent eye in a state of child-like wonder. The horizon of awareness is perceived as greatly expanded, as if a veil was pulled aside, and one is often left with the unmistakable feeling that one has perceived the true essence of things.

Another common and profound effect on awareness is a breakdown of subject-object boundaries as the ego becomes less real or disappears. Instead of separating and analyzing objects in terms of use and purpose, there is no separation between self and object. Because time is based on the ego's constructed sense of past and future, time does not exist and awareness profoundly merges with the present. Objects are seen for the first time without the distortions of needs, wishes, use, or purpose, and there is a profound realization that we are more than our ego identity. An integral connection with the environment is experienced so that inanimate objects are perceived as alive and personal, and mystery and divinity are perceived in ordinary phenomenon. Objects are typically perceived as a part of a connected, unified whole as the ego is swept away by a vaster, deeper Self. The ego's anxieties and fears, needs and desires, likes and dislikes and sense of isolation are replaced with openness, trust, confidence, and feelings of compassion and empathy toward one's self and others.

As the ego recedes and its filtering process disabled, unconscious emotional stimuli are disinhibited from ancient brain systems and flood conscious awareness. These emotional stimuli significantly affect our conscious perceptions and behaviors in daily life despite being outside of conscious awareness. By gaining awareness to emotional stimuli that have been suppressed in the unconscious, including memories, worries, fears, and conflicts, the stimuli can be re-appraised consciously in a calm, accepting, compassionate, ego-free state.

These dramatic changes in awareness, which would be considered miraculous in psychotherapy, constitute the core affective experience that commonly underlies psychedelic states of awareness.

#### The Core Affective Self and Transcendence

When psychedelics occasion a mystical-type experience, it is consistent with a disinhibition of the core affective self from ancient brain regions that allows it to flood conscious awareness. This primordial territory of awareness precedes language and the ego and exists in the unconscious as a genetic memory. It represents an archetypal, collective affective consciousness that is available as a universal dimension of human awareness but is rarely accessed because it has been inhibited and repressed into the unconscious. The core affective self is imbued with an ancestral sense of timelessness and oneness and is perceived as a deeply familiar innate, intuitive intelligence.

The disinhibition and conscious experience of the core affective self often produces ineffable feelings of illumination and insight not previously experienced by the ego, and the unmistakable sense of authority and durability of objective truth that is beyond explanation, yet comprehensible. Eastern traditions consider this state of awareness the highest, most direct state of consciousness because it transcends the ego. It is perceived to be a collective unity shared by all that allows the individual to see the true essence of the Self.

The initial anxiety of the ego dissolving is typically followed by feelings of being transported into a new reality of self-transcendence as the boundaries of the self greatly expand and the core affective self becomes conscious. The hallmark descriptions of this experience are awe, joy, oneness, grace, and bliss. So transcendent is this experience that it is described as a sacred, miraculous, unfathomable reality that is hidden from everyday sight. Feelings of emotional communion, oneness, and a spiritual epiphany are commonly reported. The experience is often described as being re-awakened and touched by one's higher Self and, universally across psychedelics, cultures, and time as a feeling of cosmic union, reverence, humility, grandeur, or rapture that mirror reports of mystical experiences in the major religions and annals of history. Known as the awakening of the Self in mystical traditions, the exact time and place of this rebirth are commonly remembered for the rest of life as the moment the ego surrendered to a higher, sacred truth.

This transcendent experience becomes a landmark emotional memory of what lies below the surface of everyday awareness. It promotes a deep assurance of meaning and divinity that alters perception of one's self, others and the world in a new way that produces permanent\_improvements in personality and well-being. The result is a\_more integrated mind that strikes a greater balance between affective and rational consciousness, ego and core affective self.