

Neurobiological Mechanisms Underlying the Therapeutic Effects of Psychedelics

A Paradigm-Shifting Revolution in Psychiatry

Recent controlled studies from psychedelic medicine centers at Johns Hopkins, Duke, Berkeley, Harvard, NYU, Michigan, and UCLA have reported groundbreaking results for the treatment of psychiatric disorders. In studies using psilocybin for treatment-resistant depression and major depressive disorder, 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 has designated Psilocybin for treatment-resistant depression and major depressive disorder as a rare "Breakthrough Therapy". 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.

The dramatic therapeutic effects of psychedelics may be understood, in part, from research in affective neuroscience on the default mode network and the core affective self.

The Default Mode Network

The Default Mode Network (DMN) is a recently identified core brain network that is active in the conscious resting brain. It represents the default baseline state of the awake brain when the eyes are closed and individuals are engaged in internally focused tasks like memories of one's personal history, 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 and other inner processes in contrast to other brain regions that respond to what happens in the external environment. The DMN allows individuals to mentally simulate the past and future and infer the mental states of others. Instead of being psychologically constrained to the here-and-now, the DMN allows us the unique ability to disengage from the external world and turn our thoughts inwards to construct mental simulations of hypothetical scenarios that anticipate and evaluate future events. Through this mental simulation of our past, future, and the minds of others, we travel far beyond the observable. Consequently, we spend a lot of time thinking about what happened in the past, might happen in the future, or may never happen at all instead of the here-and-now.

The DMN's metacognitive processes include the internal monologue ("the voice in our head"); mind wandering and day-dreaming; mental time travel into the past and future; imagining hypothetical events and scenarios; theory of mind (the ability to infer what others are feeling or 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 foundation of the ego.

The DMN also 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, the brain has a filtering mechanism to determine what reaches conscious awareness. The filter is a function of selective inhibition by the DMN that is energy-demanding. This inhibition, which is partly 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 subcortical brain areas that play a central role in alertness, attention, and consciousness. Central to the DMN's thalamic/reticular filtering is habituation,

the process by which the brain learns to consciously ignore safe, repetitive stimuli while attending to more important, novel stimuli. Through this mechanism of selective restriction and reduction, the DMN controls the gates of awareness by determining what reaches conscious awareness or remains 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 self-aware humans: problem solvers, artists, inventors of ritual and technologies, possessors of an aesthetic consciousness, and creatures of intelligence and complexity.

As our conscious self, the ego edits and limits our personal awareness by regulating the DMN's filtering process. Chief among the ego's filtering functions is to maintain the boundary between the conscious and unconscious mind, as well as the boundary between self and other objects. Experience cannot enter awareness unless it bypasses this filter, which is selective and socially conditioned by language, culture, and science. The ego's filter is constructed in terms of our needs and desires, wishes and fears, likes and dislikes, and biases 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 maintains a relatively stable personal reality and sense of self 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 things to be analyzed, evaluated, explained, and compared to create our self-identity and the stories we tell ourselves about who we are, how much we earn and own, how attractive and successful we are, and the roles we play at work and home. Resentment, possessing, 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 began to involve control over nature and ownership of plants and animals. Although the natural and social worlds were previously integrated into a cyclical, rhythmic world that included humans, animals, plants, and objects to form an animistic, living nature, we began to see the world in terms of the subject-object relationship and the importance of an explanatory nature of events. This separated and detached us from the world, and we began to experience the world rationally and impersonally. Through writing, philosophy, and the beginnings of science, we rapidly progressed to the age of reason, the industrial age and the invention of clock time, and finally to the computer age. The ego and science have become 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 explanatory filter. We are not our ego identity or social role, and awareness of our self as a separate entity from objects is the source of our sense of existential isolation.

The Core Affective Self

While the DMN and ego form the hub of our conscious, rational self, the core of our affective self lies in more ancient, unconscious brain regions. These neural territories below the cortex are the primordial affective systems shared by all mammalian brains. From these systems, we inherit the wisdom of emotions as evolutionary, unconscious tools for living that form the affective foundations of our mind. Emotions are built into the brain by evolution as archetypal genetic memories held in common of our collective ancestral past.

Converging neuroscientific evidence involving emotional processes in ancient brain regions supports the concept of a core affective self (CAS) as an innate, primordial self. Jaak Panksepp, a pioneer in affective neuroscience, postulated that the CAS and its pure form of affective consciousness interact with higher rational cognitive processes to form the neural foundation for all emotional experience. 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, they may constitute an essential foundation for the evolution of higher, more rational forms of consciousness.

According to Panksepp, the CAS is a highly evolved element of the mammalian brain that is preserved through species rather than being unique to humans, yielding a trans-species concept of self. Because animals have the neurobiological substrates of conscious states, humans are not unique in possessing substrates that generate consciousness. All mammals and birds, and many other creatures including octopuses, possess these neurological substrates, and many animals exhibit self-awareness (i.e., the mirror recognition test).

As a primordial affective consciousness, the CAS has the power to feel, and because feelings may have been the first sources of consciously felt experience in the brain, the CAS may have been the first form of consciousness that evolved on earth. The CAS has the capacity for pure conscious experience, without the capacity to reflect on the experience. Although not self-conscious, the CAS is an innate intelligence that has an internally felt, unified presence in the world. Because it evolved before the DMN and the ego, the CAS does not see itself as the subject with all other objects as separate and to be acted upon. It is an unconscious dimension that represents a unitary reality and a non-reflective emotional consciousness.

Carl Jung believed the organizing system of the self was predominantly affective and archetypal, and must lie subcortically in the brain stem. He conjectured that such a subcortical affective system might reflect a symbolic, pre-verbal archetypal form of the unconscious that is contained in the brain of all individuals as the collective emotional 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 affective mind.

Panksepp postulated that the CAS's primordial form of conscious affective experience emanates from the brain's emotional control center: the periaqueductal grey (PAG). 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. 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 DMN's filtering mechanism, lie adjacent to the PAG.

A recent brain mapping study at Harvard Medical School found that spirituality, broadly defined as a sense of connection with something greater than one's conscious self, can be localized to the PAG. The PAG has previously been implicated in altruistic behaviors and unconditional love. The Harvard study also found that a spirituality circuit, defined by functional connectivity to the PAG, includes positive connectivity to more ancient subcortical and limbic regions and negative connectivity to cortical regions previously implicated in reasoning, abstract thought, and the DMN.

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, thereby disabling it. This produces several profound effects on awareness that result in a non-ordinary state of consciousness.

An extraordinary effect on awareness is cessation of the ego's habitual filtering of perception so that we undo our automated ways of perceiving the world. This is experienced as a more direct state of awareness that "mirrors" sensory stimuli rather than filtering and distorting them. We "see" and "hear" rather than think and filter, and we perceive directly instead of interpreting and analyzing. The senses are described as keener and richer, and the world looks new and vivid. The "voice in our head" ceases, acquired beliefs are stripped, and the world is seen with the innocent eye of a child in a state of wonder.

There is an intuitive sense of realness and ineffability, as if a veil was pulled aside, and the horizon of awareness is perceived as greatly expanded. Often, there is an unmistakable feeling that one has perceived the true essence of reality.

Another profound effect on awareness is a dissolution of subject-object boundaries as the ego becomes less real or disappears. Instead of the ego separating and analyzing objects in terms of use and purpose, the self expands and merges with objects. Awareness profoundly merges with the present, and a sense of timelessness is often reported. Objects are seen for the first time without the ego's distorting needs, wishes, uses, or purposes, and there is a profound realization that we are more than our ego identity. Objects are perceived as a part of a connected, unified whole, and inanimate objects are perceived as alive and personal. The ego's anxieties and fears, needs and desires, likes and dislikes, and sense of isolation are replaced with openness, trust, and feelings of compassion toward one's self and others.

A final effect is an expansion of awareness to include unconscious emotional stimuli that are disinhibited from ancient brain systems. By gaining awareness of these stimuli that have powerful effects on our mind and body, they can be re-appraised consciously in an accepting, compassionate, ego-free state. These stimuli can also involve eternal genetic memories expressed as motifs, ancestral themes, and archetypes from the collective emotional unconscious: exotic lands, ancient times, kings and queens, chariots, or the face of religious figures.

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

The Core Affective Self and Transcendence

When psychedelics occasion a mystical-type experience, it is consistent with disinhibition of the CAS from ancient brain regions. This primordial territory of awareness precedes language and the ego and exists in the unconscious as an archetypal collective consciousness. The CAS is available as a universal dimension of human awareness but is rarely accessed because it was inhibited and repressed into the unconscious by the DMN and the ego when they came online. The CAS is imbued with an ancestral sense of timelessness and oneness that is perceived as an innate, intuitive intelligence.

The conscious experience of the CAS 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 and allows the individual to see the true essence of the Self.

As the ego dissipates, any initial anxiety is followed by feelings of being transported into a new reality of self-transcendence as the boundaries of the self greatly expand. The hallmark descriptions of this experience are gratitude, grace, and awe. So transcendent is this experience that it is described as a sacred reality that is hidden from everyday sight. Feelings of oneness and a spiritual epiphany are commonly reported, and mystery and divinity are perceived in ordinary phenomenon. The experience is often described as being touched by one's higher Self. It is known as the awakening of the Self in mystical traditions.

This transcendent experience becomes a life-transforming emotional memory of what lies below the surface of everyday awareness. It promotes a deep assurance of meaning and alters perception of one's self, others, and the world. The result is a more integrated mind that strikes a greater balance between affective consciousness and rational consciousness, ego self and core affective self.