Ibogaine Therapy in Chemical Dependency and Post-traumatic Stress Disorder:

A Hypothesis Involving the Fractal Nature of Fetal REM Sleep and Interhemispheric Reintegration

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"Banzie (the members of the Bwiti, properly, "those of the chapel") also say that eboga enables a man or woman to return to infancy and to birth - to the life in the womb... by returning initiates to the uterine condition, a condition in any case very close to life in the land of the dead [and so] restores them to their own integrity - their pristine conditions."

—From *Bwiti: an Ethnography of the Religious Imagination in Africa.* James W. Fernandez, Princeton University Press, 1982, p. 491.

INSPIRED FIRST by a synchronistic meeting with Dr. Deborah Mash and Dr. Julie K. Staley, then by enigmatic descriptions of Bwiti lore, I have developed a hypothesis supporting the use of Ibogaine, as well as other analogs or compounds with oneiric [dream inducing] properties for the treatment of chemical dependency and post-traumatic stress disorder (PTSD).

In short, Ibogaine interacts with many neurotransmitter systems to drive amygdaloid-brainstem dynamics into a critical oneiric state, with fractal time patterns of phasic events similar to those existing during fetal rapid eye movement (REM) or Active sleep. In effect, Ibogaine pharmacodynamically destabilizes the functional connectivity of the brainstem and its habitual interactions with bihemispheric temporal lobe structures such as the amygdala, creating a functional state of plasticity in these areas which facilitates the reintegration of traumatic memories by altering psychopathological interhemispheric dynamics, ultimately dissipating addiction-related behavioral patterns. This psychotherapeutic oneiric state is similar to the complex behavioral states of REM sleep and attentional orienting in that they all share the signature of the self-organized critical state, 1/f (one-over-f) patterns of activity involving many levels of the nervous system from the subcellular to the behavioral.

Observed similarities between the neurophysiology of the REM state and that induced by selective psychedelic drugs such as LSD or psilocybin further support this hypothesis as does the observation that REM sleep, which is disrupted by drug abuse and traumatic experiences,[1-5] has been shown to be essential for emotional regulation, learning and memory consolidation.

Recent findings by many researchers, including the author, that stress or abuse in early life induces abnormal hemispheric functional asymmetries, disrupting REM sleep and predisposing patients to addictive and self-defeating behaviors resulting from impaired interhemispheric integration,[6-11] support this new view of the psychobiology and treatment of addiction.

How it all got started

I met Dr. Deborah Mash and Dr. Julie Staley in 1994 while I was working at Florida Atlantic University on my Ph.D. dissertation which involved using fractal geometry to study the structure of REM sleep in fetal animals and its disruption by early stress. The occasion was a guest lecture given at the University of Miami by my mentor at FAU, Dr. Arnold Mandell, a pioneer in the application of chaos and nonlinear dynamics to psychiatry and neuropharmacology.[12-17] Before the talk, Dr. Mash had taken me and others to lunch. There, during the rich conversation that ensued, Dr. Staley spoke of evidence for the oneiric properties of Ibogaine, and it suddenly became clear to me that this might be related to the fractal patterns of REM sleep that I was investigating.

After completing my dissertation in 1995, I began working on the effects of early sexual or verbal abuse in young adults, and continued my work on the effects of early deprivation with Dr. Martin Teicher and Dr. Friedric Schiffer at McLean Hospital.[6,9,18,19] Previous work by Dr. Schiffer and Dr. Teicher has demonstrated the profound and persistent neural and psychological changes induced by early trauma in EEG evidence of asymmetric hemispheric activation during the recall of past trauma.[10] Further, abnormal hemispheric EEG coherence and reductions in the size of the corpus callosum were observed by Dr. Teicher and others with analysis of MRI images from abused and neglected children treated at McLean Hospital.[11] Based on his clinical experience and the seminal work of Roger Sperry,[20] Dr. Schiffer has proposed, that we all have, in fact, two minds or personalities, one in each hemisphere.[21,22] Using a new therapeutic technique called lateral visual field stimulation (LVFS), he has observed clinically a dramatic manifestation of disparate dual personalities in subjects who have suffered from abuse or PTSD during their lives. In effect, Dr. Schiffer proposes that our two hemispheres are like joined minds, mental Siamese twins, who learn in early life to function harmoniously sharing their unique specializations. This harmony is fragmented by abuse or trauma, which unbalances the twins and leads to an unending pathological struggle for dominance resulting in a wide range of personality disorders.[22] For example, one twin, the right in many cases, retains the abuse memory and

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as a result is less mature, and will take control in times of stress or anger, sabotaging the good efforts of the more mature side. This replaces the Freudian concept of the unconscious with Sperry's findings of two minds. Interhemispheric struggles, primarily a result of child abuse, may be the fundamental psychological root of drug addiction. In a seminal chapter, entitled "The euphorohallucinogens," Mandell and Geyer[14] described how normal dual hemispheric organization may be particularly relevant to conceptualizing the neurobiological basis of psychedelic states:

"It seems clear that the lateral specialization of the human cerebral cortex provides two distinct and complementary modes of consciousness and that they function more or less in concert with one another. By virtue of its focal organization and sequential processing, the dominant (usually the left) side is best suited for verbal, mathematical, and analytic thought, whereas spatial orientation, artistic talent, visuoconstructive ability, and abstraction of part-whole relationships may well depend on the more diffuse organization that usually characterizes the right hemisphere. The startling perceptual experiences produced by hallucinogenic drugs may be more comprehensible in light of the capacity of the nondominant hemisphere for simultaneous integration of information. The heteromodal influx of perceptions produced by increased attentiveness and sensitization to sensory stimuli may overwhelm the systematic sequential processing of the language hemisphere and invoke the analogical integrative mode of the right hemisphere to consolidate the perceptual flood. However, with particular doses of hallucinogenic drugs, many subjects experience mind trips, bursts of ecstatic and sequentially logical thoughts, or the insight accompanying discovery (p. 592)."

Further, they anticipated the far reaching implications of interhemispheric warfare in psychotherapeutic approaches to the treatment of psychopathology:

"Supportive psychotherapy, often an alliance between the therapist and only one of the patient's hemispheres based on a common enemy—doctor and patient agree that the mother is the villain—makes one side dominant, eliminating conflict by splitting, just as tricyclics [antidepressants] exaggerate the influence of one lobe (p. 597)."

In contrast, Dr. Schiffer's LVFS-based psychotherapy may allow clinicians to bring the psychopathological struggles between the twin hemispheres to the patient's full awareness, facilitating a degree of resolution and harmony. Within this unique and creative perspective of abnormal relationships between the two hemispheres or minds, LVFS therapy can provide a fundamentally new understanding of traditional psychotherapeutic techniques, as well as controversial and groundbreaking techniques such as eye movement desensitization reprocessing [EMDR[23]] and transcranial magnetic stimulation [TMS[24]]. In addition, this view can inform traditional and innovative psychopharmacological approaches (e.g., the psychotherapeutic use of psychedelics). After researching the ethnological literature and many anecdotal accounts of addicts over the last four years, I believe that Ibogaine, when used in a proper long-term supportive social and psychotherapeutic context, can end drug addictions and possibly the underlying PTSD, by promoting, especially during the cognitive evaluation phase, balanced hemispheric interactions. Just as The Fang adopted the use of eboga to promote social and religious harmony during colonialism-induced social and cultural fragmentation,[25] our world society which is experiencing a similarly deep social fragmentation, accelerated by the soulless march of materialism and concurrent environmental degradation, and marked by escalating drug addiction and suicidal behavior among our youth, may benefit from judicious use of Ibogaine or related agents. Ibogaine, possibly in combination with hemispheric reintegration techniques, may potentially free the minds of many individuals (addicts, rape victims, violent criminals, victims of child abuse, war or natural disasters) suffering from the debilitating emotional disregulation resulting from hemispheric disharmony.

Publishing this paper in MAPS is an attempt to present this hypothesis in the context of new perspectives on the role of fractal patterns and abnormal hemispheric interactions in brain function to an "open minded" or "hemispherically-balanced" audience for wider constructive criticism. In the following sections I will attempt to give the reader a useful introduction to fractal concepts and why they provide an essential point of view for understanding brain/mind. Fascinating connections among REM sleep, attentional and psychedelic states will be established using fractal concepts leading to a description of Ibogaine therapy in the context of the involvement of cortical-amygdaloid-brainstem loops in hemispheric disharmony.

Neurophysiological Similarities Between REM Sleep, Orienting and Psychedelic States

In 1979 Drs. Barry Jacobs and Michael Trulson published a speculative article in the then newly formed journal *Trends In The Neurosciences* entitled "Dreams, Hallucinations, and Psychosis—the Serotonin Connection," suggesting a connection between hallucinogenic drugs, dreams and amphetamine psychosis.[26] Previously, they had developed an animal behavioral model of the effects of LSD and related hallucinogens in cats.[27] This model was based on the observation that cats given LSD demonstrated two dose-dependent behaviors (i.e., limb flicking as if the cats were trying to remove some foreign substance from their paws and abortive grooming as if they had been interrupted during the normal grooming act) that were not present with administration of non-psychedelic drugs. Recordings from the brainstem of cats demonstrating these behaviors confirmed the electrophysiological observations of Dr. George Aghajanian that the behavioral effects of these drugs were associated with a suppression of a complex network of serotonergic neuron cell body groups (I will call this the S-Net) in the brainstem reticular formation (RF), primarily in the dorsal raphe nucleus, DRN.[28] During the late 1970s Jacobs et al. had also been investigating the changes in activity of 300 or so of 60,000 serotonergic (5-HT) neurons which are clustered into 8 interlinked nodes or raphe nuclei, during the sleep-waking cycle in cats and had discovered that the onset of REM sleep was accompanied by the same suppression of activity in the DRN.[29]

They summarized their ideas in the following way:

"Thus, at the cellular level, there is a striking parallel between brain activity following administration of hallucinogenic drugs and [that]

during REM sleep: a significant depression of the electrical activity of the brain's serotonin-containing neurons. The change in raphe unit activity seen spontaneously across the sleep-waking cycle may be the key to understanding altered states of consciousness. In response to a drug such as LSD, a key brain mechanism such as the serotonin system may function in a manner which is appropriate for a different behavioral state (e.g., the discharge rate and pattern during the drug experience may be that of [REM] sleep rather than active waking.) (p.279)."

In short, cats administered LSD appeared to be dreaming while awake, although this idea remains controversial,[30] in part due to new findings of dissociations between drug effects on behavior and average DRN activity.[31] In a later section I will make the case that fractal patterns of reorganized S-Net unit activity, in concert with dynamic changes in other brainstem and forebrain areas are more relevant to understanding drug effects than average DRN unit activity.

Do cats dream?

Work in the early 1970s by Michel Jouvet and collaborators involving small lesions in the pontine reticular formation (PRF) of cats has provided a partial answer to this question.[33] The PRF, located just behind the DRN in the midbrain, is linked with the source of ponto-geniculo-occipital (PGO) waves which are responsible for phasic eye movements and the twitching of whiskers, ears or paws in dreaming cats. Just behind the PRF is the bulbar RF, site of origin for postural atonia or paralysis of body movements and loss of neck muscle tone called nuchal atonia (NA). NA becomes apparent when anyone tries to sleep in an airplane seat; as one goes into REM sleep NA occurs and one's head drops, usually waking him or her up. Oneiric behavior is observed in cats with small lesions in PRF after DRN activity shuts down and they enter REM sleep. As REM sleep begins, the cat, instead of having an episode of NA suddenly raises its head and moves about as if it were watching something. This type of behavior, called an orienting response, is usually associated with a heightened state of arousal and attention. For example, if you have ever watched a cat when birds are nearby, you have probably observed the birds eliciting an orienting response in the cat. During oneiric behavior, the nictitating membranes still cover the open dilated eyes as the cat pursues nonexistent prey.

Many unpredictable patterns of oneiric behavior can occur; for example, predatory attack with play-like pawing, followed by biting and even full rage responses can be observed (sometimes in cats who are always very friendly when awake). Another pattern is the occurrence of non-goal directed grooming behavior. In this case the cat will start licking its forelegs or the cage floor but would not notice a piece of paper placed on its fur. This is strikingly similar to the abortive grooming and limb flicking seen with LSD, with the exception that cats treated with LSD haven't entered slow wave sleep prior to displaying these behaviors.

1/f Fractal Patterns in Time: The Common Ground of REM Sleep, Orienting and Psychedelic States

In the same year as the Jacobs and Trulson paper, Adrian Morrison proposed a connection between REM sleep and attentional states such as orienting.[36] His thesis, that cats and other mammals are in a state of more-or-less continual orienting during REM sleep, is profound in its implications for conceptualizing states of consciousness. This idea was based on his observations that similar amplitudes of PGO waves were evoked in cats during normal orienting responses to loud sounds, during normal REM sleep when behavioral orienting is absent and during elicited oneiric behavior in cats with PRF lesions.[37] Other work has demonstrated that PGO waves are suppressed by 5-HT, so that cats chronically administered 5-HT synthesis inhibitors generate many more PGO waves, more orienting and display disrupted REM sleep for a period of days.[38,39] In support of Morrison's idea, Yamamoto et al.[40,41] have observed common 1/f fractal patterns (explained below) in recordings of interspike intervals in the RF and other regions of the cat brain during orienting to birds and during REM sleep, only not during other types of sleep or quiet wakefulness.

Further, they observed that this 1/f fractal pattern is diminished by serotonergic agonists, indicating that tonic S-Net activity during quiet wakefulness and slow wave sleep (SWS) is not conducive to the 1/f state.[42] In fact, nodes in the cat S-Net, such as the DRN show total inactivation during REM sleep and at the start of orienting responses, but become very active at the offset of these states.[43,44] For example, during REM sleep S-Net activity resumes at the end of an epoch but at twice the rate of quiet wakefulness; this suggests that REM sleep is, at least in terms of 5-HT systems, a prolonged orienting response. Also, brain states when most S-Net nodes are inhibited or destablized, such as during REM sleep, orienting, and after LSD administration, exhibit unique 1/f fractal patterns of activity in time.

Interestingly, a study from 1957 by Schneider and Sigg[45] shows that cats given Ibogaine behave similarly to cats displaying oneiric behaviors. They found that cats given Ibogaine (2 to 10 mg/kg i.v.) show an almost immediate arousal response with rage (similar to that seen with electrical stimulation of the RF): the cats hiss as if trying to scare off an imaginary threat. This may be due to loss of global habituation to the test environment, resulting from Ibogaine's possible effect on the amygdaloid-brainstem pathways. EEG patterns which, prior to the injection, were charateristic of non-arousal, shifted with Ibogaine to a pattern similar to that seen in REM sleep or during orienting responses. In addition, these cats displayed ataxia and a clonic extension of the hind limbs and front legs, not unlike the movement problems encountered in dogs or humans administered Ibogaine.

So, in cats at least, Ibogaine seems to induce a REM-like state with oneiric behaviors more characteristic of PRF lesions, showing more force and intensity than low doses of LSD. I do not mean to imply by this description that Ibogaine merely induces REM sleep; in fact Ibogaine possesses a uniquely complex polypharmacology.[46] This is often seen as a disadvantage for drugs (e.g., drugs are termed "dirty" as opposed to "clean" if they don't target a specific neurotransmitter receptor); however Ibogaine's more widespread actions may in fact explain its extraordinary behavioral effects. Although this drug-induced oneiric state has many of the behavioral and neurophysiological markers of REM sleep without atonia in cats, it has other unique properties which

may result from a sudden massive destabilization of the normal behavioral-state-rhythmicity of the tonically firing S-Net,[43] olivocerebellar systems, and other linked RF and forebrain sites. Ibogaine affects a complex dynamic network of interdependent dopaminergic, norandrenergic, opioid, cholinergic, and NMDA receptors and systems.[46,47] Ibogaine, like LSD, is "switching the channel" from normal attention to a dream-like state, but it is also jolting the S-Net and RF into a unique state, one that may require a return to activity patterns more characteristic of fetal ontogeny to reinstate normal functional organization. In a sense, following Ibogaine treatment, the RF and associated brain regions are functionally "born again."

Now that we have established a few connections between the effects of LSD and Ibogaine and the behavioral states of REM sleep state and orienting in cats, we can explore how Ibogaine may work through long-range fractal correlations provided by a "fetal REM-like" state and reexperienced memories in humans suffering from chemical addiction and/or PTSD. First it is necessary to review the important role of REM sleep during development and some of my recent findings concerning the fractal-in-time nature of fetal REM sleep phasic processes and their disruption by early stress. In the following sections I will describe and apply ideas from the science of complexity that may help us visualize these unique states with 1/f patterns.

The Fractal Geometry of Time in Neurobiology and Fetal REM sleep

Only a decade ago, patterns of bunching or clustering in the opening and closing events of ion channels, quantal release of neural transmitters, or spontaneous patterns of firing neurons, heart beats, and breaths in the fetus or even cars on an expressway were perceived as random and uncorrelated noise-like processes.[48] A revolution in the scientific perception of such noisy natural processes was started with Benoit Mandelbrot's 1983 book *The Fractal Geometry of Nature.*[49] Fractal geometry has evoked a fundamentally new view of how living and nonliving matter is organized into complex recursively nested patterns over multiple levels of space or time. Patterns termed "fractal" or "self-similar" are recurrently irregular in space or time, with themes repeated like the layers of an onion at different levels or scales.

The term fractal applies to objects in space or fluctuations in time that possess a form of self-similarity: fragments of the object or sequence can be made to match the whole object or sequence by shifting and stretching. Another way to think of fractals is in terms of clusters of points or events in space or time. Self-similar clusters have smaller clusters within larger clusters of clusters. Clouds, broccoli, or the surface of the brain can all be visualized as clusters of clusters in space. These clustering patterns, described as bursts within bursts, are a universal characteristic of spontaneous behavior in living systems of cells, neurons and the early motility of embryos of both vertebrates and invertebrates.[50] Self-similar burst-within-burst patterns are ubiquitous, observed in ion channel currents fluctuations,[51] neurotransmitter release,[52] neuronal firing patterns,[53] the searching patterns of animals,[54,55] human judgment and decision making[56,57] and traffic patterns both on expressways and over computer networks such as the World Wide Web.[58] Examples of the burst or clustering patterns are, in fact, familiar to anyone who has driven in or observed highway traffic from a passing airliner. Rush hour or holiday traffic slows to a stand still due to the tendency of nearby automobiles to spontaneously cluster together, forming larger and smaller jams of all sizes. The pervasive nature of these self-similar clustering patterns is again apparent when trying to gain access to the Internet during peak times.

Although the self-organized fractal burst patterns common to both traffic situations appear to be only epiphenomena, they place fundamental constraints on traffic flow. In sharp contrast, biological systems appear to thrive and grow via self-organized fractal burst patterns. In the following, I will attempt to sketch the self-organized critical state, which although still in its infancy, may provide a foundation for understanding the association of 1/f fractal time patterns[59,60] with REM sleep, orienting and the therapeutic effects of oreiric substances such as Ibogaine.

Self-Organized Critical States in Ion Channels and Traffic Jams on the Road or the Web: A Bridge from Clusters of Molecules to Clusters of Minds

At first glance, perhaps, it is disorienting to be reading about fractal patterns of highway and internet traffic in an article on REM sleep and Ibogaine. Nevertheless, complex systems like traffic or large-scale cortical networks share universal characteristics that in one way or another lead to the reoccurrence of similar patterns in very different systems. The great benefit of the sciences of complexity is a perspective that affords open-mindedness to concepts linking diverse fields and applicable to any level of biological or physical description. One such concept is that of the self-organized critical (SOC) state, which describes how complex spatially distributed entities, such as traffic networks, interact across many time and space scales. This concept was originated by Per Bak, a physicist, to explain the widespread presence of 1/f fractal patterns in time[59,60] in nature. The fluctuations of many phenomena—flow of the Nile, light from quasars, ion channel currents, neuronal firing patterns, earthquake distributions, electrical current fluctuations in man-made devices, inter-car-intervals in expressway traffic, and in variations in sound intensity in all melodic music[61]—have been found to exibit 1/f patterns.

The Sandpile model, developed by Bak and his colleagues, provides an intuitively simple description of the mysterious ubiquity of 1/f fluctuations. As grains of sand are added to a pile of sand, a number of processes begin to occur. The added sand will accumulate giving the pile a slope. Now and then, as the sides get too steep somewhere on the pile a single grain causes a sand-slide or avalanche. The sand pile stops growing in height as it reaches a characteristic or "critical" slope, and at this point the sand pile is in what is termed the SOC state. Avalanches of all sizes can occur with the addition of a single grain of sand at the critical state; however, on average, large slides occur less frequently than smaller slides. In fact, over time the pattern of large and small slides is 1/f. The concept of a SOC state allows you a new way of understanding and visualizing the organization and interaction of complex phenomena over many scales of time or space. For

example, work using simplified models of traffic flow indicates that, in situations where the highway is filled with cars on a highway, usually on holidays, fractal clusters of traffic jams of all sizes are more likely to occur. Traffic tends to self-organize into a critical state, where small fluctuations can lead to traffic jams of all sizes or magnitudes and the 1/f signature. What new insights can SOC bring to REM sleep, orienting and psychedelic states?

REM sleep, Orienting and the Psychedelic Experience as Self-Organized Critical States

The concept of SOC has only been used, thus far, to describe behavior in homogenous populations of sand grains or cars, where each interacting element is nearly identical. The brain, in terms of neurons and connections, couldn't be more heterogenous. Heuristically, SOC may help us to visualize a common critical state that exists throughout the brain and brainstem, during states of REM sleep, orienting or those induced by LSD and Ibogaine, resulting in 1/f patterns of interspike intervals as observed by Yamamoto et al.

I propose that PGO spikes and other phasic activity during these states are analogous to the sand slides or traffic jams of all sizes, representing critical fluctuations in neural activity and connectivity. The SOC state during the orienting response may facilitate rapid functional brain reorganization in response to the qualities of the eliciting stimulus. The critical connectivity that exists during these states may primarily involve orienting synergies (among ocular, neck and facial motorneurons). PGO waves may link this critical brainstem-centered connectivity with limbic and cortical structures such as the amygdala and temporal lobes. PGO spike density increases as tonic REM sleep begins, suggesting, as Morrison observed, that REM sleep is a dense, coalescence cluster of PGO activity. From the fractal point of view, REM sleep is a kind of fractal of PGO bursts, and in support of this image, bursts of fine finger twitches during a single REM sleep period appear statistically self-similar to sleep architecture over the entire night. With eyes closed, during the oneiric state, PGO-like spikes among amygdaloid and brainstem sites could generate and direct waking dream sequences. After drug effects subside, with the return of tonic, stereotyped S-Net activity, the natural tendency for PGO spikes to coalescence is forced back into the discrete patterns we know as the nightly periods of REM sleep, constraining the daytime expression of this critical state of connectivity to orienting attentional states.[38] 5-HT neurons during quiet wakefulness fire in an almost stereotyped, clock-like-pattern at 1-5 spikes per second.[43,44] When a cat begins to groom or chew, the S-Net fires at 2-5 times this rate. Jacobs and Fornal have proposed, that in fact, S-Net activity facilitates stereotyped motor output patterns and concurrently inhibits sensory input.[44] If the cat is distracted during grooming, the S-Net pauses to allow sensory processing, and possible motor system functional reorganization, otherwise it returns to grooming. S-Net activity, in concert with dopamine release in the basal ganglia, appears to facilitate functional connectivity among clusters of cortical-striatal thalamic loops during motor output.[44] I would go further, and suggest that complex habitual sequences of motor output (e.g., drug seeking and drug consuming behavior in addicts) represent hypercomplex sequences of cortical-striatal-thalamic activation, triggered by sensory dependent amygdaloid-brainstem modulation of the monoaminergic systems during critical states. The power of Ibogaine to break habitual patterns of addiction may reside in an induced SOC state that disrupts and functionally reorganizes this amygdaloid-brainstem system,[32,63] in effect resetting the brain/mind.

Fractal Bursting and Clustering: Vertical Integration During Brain/Mind Self-Organization

My underlying thesis is that Ibogaine works on many brain systems to drive firing dynamics into a SOC state with avalanches of phasic events similar to that existing during early development. To fully explore this thesis I will show how different development processes and disorders can be reconceptualized in terms of phenomena involving fractal clustering based on ideas such as SOC and vertical and horizontal integration. During embryonic development, cell division creates a ball of cells, which will if all goes well, self-organize into a coordinated interconnected system of tissues. Concordant with cellular and molecular differentiation into tissues and organs is the development of functional connectivity among these complex systems of cells. This formation of functional connections and interactions from molecules and cells to tissues and organs, I will term "vertical" integration.[64,65]

Biological systems are in a constant state of criticality and self-organization. In contrast to highways and traffic jams, analogous critical states in developing brains may lead to the enhancement of synaptic connections, sparing of axons, and synchronizing twitches that allow distant regions of the organism to link and coordinate gene expression and neural-motor development. Traffic jams on the internet are almost as complex because of the highly interconnected nature of computer networks, and the vastly different timescales, from microseconds to seconds and hours, are closer to those present in developing organisms and the brain. Long patterns of bursting have statistical self-similarity and 1/f power spectra; in some cases, they appear very similar to the bursting patterns of ion channels, neurons and phasic REM processes such as PGO waves. WWW bursting patterns originate in the complex interactions among computer processes, network dynamics and user "think times."[62] For example, the cognitive psychologist D. Gilden[56,57] has found that fractal time variation is a basic element of human judgment and decision making, implying that the user and his or her fractal processes, through vertical convergence over the network, may supply some of the fractal bursting present in the WWW.

Psychedelic Drug Induced Fractal Clustering in Serotonergic Network Output Patterns

Fractal clustering provides new ways of thinking about the behavior and interrelationships of networked brain systems. For example, the S-Net enmeshed in the RF[43] and interlinked with other monoamine, cholinergic and peptide systems could, like the WWW, be visualized as a backbone of primary nodes, with links to secondary networks and nodes. The differential effects of psychoactive drugs could be mapped to changes in the SOC state of the S-Net, knocking out the activity of some nodes and

resulting in atypical fluctuations in 5-HT release in different brain regions.[63] For example, LSD, 5-methoxy-DMT and psilocin have primary effects on the DRN, the nucleus centralis superior (NCS) but little effect on nucleus raphe pallidus (RPA) activity. On the other hand, phenylethyamine hallucinogens have few effects on NCS or RPA activity.[66]

These fractal fluctuations in S-Net activity may synergise with drug effects in other neurotransmitter systems to bring new qualities to self-organized critical oneiric states. LSD, unlike 5-methoxy-DMT and psilocin, has effects on cortical-limbic dopaminergic cells in the ventral tegmental area (VTA) of the midbrain, resulting in enhanced dopamine release in the amygdala and prefrontal areas. The duration of these drug effects has broad range of time scales, and may fluctuate wildly as the S-Net tries to reinstate stereotypical stability. The resulting alterations in synaptic flux of monoamines may influence the degrees of segregation or clustering of functional subcircuits of various bilateral brain regions such as basal ganglia, amygdala and cortical areas which in turn feed back on the subnets of monoamine cell body groups. Ibogaine, due to its complex polypharmacology and active metabolite which is a selective 5-HT reuptake inhibitor (SSRI), Ibogaine may prolong S-Net reorganization during therapy. Thus, systems with fractal bursting patterns over many time scales, such as the WWW, may provide general models for drug action or neurodevelopmental processes.

The Fractal Structure of REM Sleep in Fetuses

The REM-like sleep state is pervasive during fetal life, playing an essential, but up to now, unexplained role in the developmental organization of brain and behavior.[68] In 1996, Dr. Mandell and myself proposed that the correlated fractal bursting nature of REM, or Active sleep, as it is sometimes called in the fetus and newborn, provides a fractal time framework in which cortical and subcortical networks can organize and consolidate changes.[69] The central focus of my doctoral research, underway at the time I met Dr. Mash, was to test this proposal.[70,71]

I measured the durations of NA (nuchal atonia, loss of neck muscle tone) over extended periods in fetal sheep and neonatal rats, species which are in a REM sleep-like state > 50% of the time. I found that the recorded NA episodes demonstrated the expected developmental changes reported for other REM sleep markers, as well as non-random fractal clustering patterns in time during the last trimester in fetal sheep,[71] and during the first 12 days of life in neonatal rats. These findings are striking in that they illustrate that phasic REM-associated events, at least during development, are not fundamentally independent random processes, as is implicit in Allan Hobson's activation-synthesis model of REM sleep,[72,73] but rather are fractal in time.

Disturbances of phasic REM processes are also a common thread in many disorders of sleep in infants, children and adults.[4,74-76] As mentioned earlier, PTSD is linked to a fundamental disturbance of phasic REM sleep mechanisms resulting in recurrent stereotypical anxiety dreams as well as disturbed limbic system and brain stem-mediated functions such as abnormal startle responses.[1-5] Chronic use or abuse of many drugs results in alterations of phasic REM sleep processes.[75] Delirium tremens or "the DTs" that follow withdrawal from chronic alcohol use appears to represent an intense period of rebound REM sleep accompanied by waking hallucinations.[77] Analogous to Ibogaine therapy (see below), recovery from an episode of DTs is followed by a prolonged bout of deep, refreshing sleep called "terminal sleep" from which the patient awakens essentially recovered from withdrawal.[78] Temporal lobe dysfunction involving limbic structures such as the amygdala and hippocampus are frequently associated with sleep disturbances and REM sleep-related events such as sleep-walking and parasomnias.[35,79] Disorganization of sleep architecture over many timescales (from microstructure to circadian structure) is commonly associated with many psychiatric illnesses, including anxiety disorders.[80] Hemispheric asymmetries, resulting from lateralized temporal lobe dysfunction and alterations of commissural development,[11] the aftermath of childhood stress or trauma, could represent another key factor in sleep disorders.[81,82]

General models proposed for REM sleep function in adults do not usually provide a common theoretical foundation for understanding and incorporating these disorders. In the following I will describe how alterations in the vertical consolidation of self-similar bursting patterns of phasic sleep events can provide a conceptual bridge between the disorders of REM sleep in adults and in children. This conceptual foundation underlies my hypothesis of Ibogaine action in bihemispheric reintegration.

Dueling Amygdalae in Sleep Pathology: Insights into Autism and Interhemispheric Reintegration Via REM Sleep

Recent work on the neurobiology of autism has implicated bilateral medial temporal lobe structures such as the amygdaloid complex as key brain sites of the socioemotional abnormalities seen with this severe developmental disorder[83,84] although many other brain regions have also been implicated. The amygdaloid complex composed of two almond-shaped structures deep in the medial temporal lobe (amygdala is latin for "almond") appears to be involved in REM sleep onset, sleep architecture and ultimately dream content. For example, amygdaloid stimulation in unrestrained cats evokes significantly increased PGO number, spike and burst density.[85] Regional cerebral blood flow in the human amygdala is positively correlated with REM sleep.[86] The central nucleus of the amygdala is reciprocally innervated by brainstem regions, such as the parabrachial region which is involved in alerting and in the generation of REM and PGO waves.[67] Also cholinergic activation of the central nucleus produces long-term facilitation of REM.[32] In addition, the amygdala receives most of its serotonergic innervation from DRN which has a strong inhibitory influence upon amygdaloid neurons.[87]

LSD may disinhibit amygdaloid neurons and has also been reported, at low doses, to increase the duration of REM sleep periods.[14] Symmetric activity in bilateral amygdaloid-parabrachial pathways may be required for the occurrence of typical global sleep architecture during a nightly sleep period. As it seems in amygdaloid kindling in cats,[88] asymmetric hemispheric activation of amygdaloid-parabrachial pathways results in abnormal sleep

architecture and pronounced changes in the patterns of phasic REM events.

How might temporal lobe dysfunction associated with amygdaloid-parabrachial pathways in autism manifest in patterns of phasic REM sleep? Tanguay et al.[89] have investigated the phasic clustering nature of REM in autistic and normal children, through their observation of ontogenetic changes in the bursting structure of eye movements (EM) during REM sleep. They found that eye movements in normal children on the whole did not become organized into bursts until 40 weeks gestational age; thereafter changes in the clustering of the bursts of EM were correlated with developmental age. Also, from 2 to 24 weeks postnatal, as total REM decreases, the number of EMs remain constant resulting in an increase in the mean number of EMs/sec of REM. This recurrent theme in many developmental processes, horizontal integration or the coalescence of clustering with age, as described for NA, was observed in normal children between 3 months and 5 years of age. At this age, a major organizational change occurred in the patterns of EMs, marked by the increasing tendency of bursts of EMs to cluster, with more and shorter EMs packed into bursts within bursts. However, autistic children were found to have substantially less clustering of EMs. In fact, no significant differences between burst structure in 2-5 year old autistics and younger (<18 month) normal children could be found. Autistic children seem to display a failure to complete integration at this stage of development. It's as if they are stuck at one dynamic stage of development, unable to progress. Perhaps the functional dynamics of abnormal asymmetric cortical-amygdaloid-parabrachial pathways are involved[83] and hinder vertical integration, resulting in excess phasic activity and the appearance of immature global sleep architecture. Increased phasic activity, analogous to fetal activity, could be an attempt by the brain via enhanced bursting to establish long-range correlations and promote horizontal integration. Successful behavioral therapy for the treatment of autism by sustaining long-range fractal correlations between events in the emotional-behavior experience of the autistic child may enhance integration within these pathways. Ibogaine therapy may also provide fractal long-range correlations during waking dream and reevaluation phases.

Emotional Memory, the Amygdala, and Tripping in Fractal Time: Going Back to the Womb with Ibogaine

During Ibogaine therapy, patients have reported a dose-dependent experience of dream-like states, except that they are awake and can respond to questions. What follows is a general description of the Ibogaine experience and many variations in the length, occurrence or quality of stages are often observed. Soon after administration, the patient:

1) First experiences a loud humming or oscillatory sound, changes in visual perception and signs of ataxia when trying to walk;

2) Within 1 to 2 hours this auditory experience ends and images may appear, especially after eyes are closed. The patient then notices a rapid visual presentation of various images, sometimes specifically reviewing traumatic events or circumstances from their childhood and/or life of addiction for a long period (3 to 8 hours). Distortions of time perception by the patient are also reported, in which the dream experience is perceived to take much less time.

3) Following the end of dream stage (3 to 9 hours post administration), a period of intensive reevaluation of previous life experiences can take place. The stimulant or opiate-addicted patient may then sleep for long periods, and awaken without characteristic withdrawal symptoms (analogous to "terminal sleep" following DTs).

4) Long term effects of the Ibogaine treatment sometimes include a reduction in the need for sleep to 3-4 hours per night for up to a month or more and the elimination or amelioration of the craving and desire to do drugs.

The Pervasive Oscillatory Sound

During this stage, the pharmacological effects of Ibogaine and its primary metabolite may start to destablize the habitual amygdaloid-brainstem modulation of global bihemispheric monoaminergic systems. The disturbing effects of lights and sounds could result from loss of normal global habituation due to RF destabilization, resulting in the fear and rage responses observed in cats. Trauma or drug abuse history is strongly associated with asymmetric hemispheric function[7-11,90,91] and recent anatomical MRI and fMRI data show that temporal lobe structures such as the hippocampus and amygdala are particularly sensitive to the effects of child abuse and trauma.[9,21] The oscillatory sound could indicate rapid shifting or cycling of attentional resources between the left and right hemispheres, possibility in association with pharmacological downshifting of the normally constant 10 Hz rhythmicity of the olivocerebellar system.[94] This sign may be stronger in subjects with more pronounced asymmetric hemispheric function and awaits further investigation. As this oscillatory auditory effect downshifts, possible flooding of the left hemisphere by material from the uninhibited right may take over primary conscious focus, as outlined by Mandell and Geyer.[14] This sets the stage, along with phasic fluctuations of the S-Net and uninhibited PGO, for the sudden onset of the self-organized critical state and the waking dream period.

Waking Dreams: A Healing Journey Through the Fractal Hyperspace of Emotionally Indexed Childhood Memories

I propose that the basolateral amygdala (BLA) is a critical neural substrate of the waking dream stage as fractal neural bursting in this subcortical cortex-like structure may represent access points in a fractal hyperspace of emotionally indexed memories. The effects of early trauma on the development of the amygdala and other temporal lobe structures may interfere with its normal bilateral function during REM-sleep mediated consolidation of emotionally significant events. The recall of traumatic childhood experiences in adults, due to the immaturity of limbic structures at the time of trauma, my require electrical stimulation or intensive PGO-like activity present during the Ibogaine oneiric state. Habitual disruption of normal sleep processes by stress associated with combat, bereavement, divorce, child abuse, neglect or chronic drug abuse interferes with the natural restorative function of phasic REM process, resulting in patho-neurophysiological sequelae of events further exacerbating physiologi-

cal and psychological addictions and rigidifying emotional traumas into PTSD and chronic hemispheric imbalance. Ibogaine-mediated exploration of the subspaces of emotional memories associated with these traumas may help to free these rigidities, restoring after cognitive reevaluation and horizontal and vertical consolidation of amygdaloid brainstem systems some degree of normal hemispheric balance.

The amygdala is also known from many studies in animals and humans, to act as the meeting place between emotions and the mind. Vietnam Veterans with PTSD, for example, have increased regional cerebral blood flow in the right amygdala when generating mental images of combat-related pictures.[90] We each have bilaterally interacting right and left amygdala which give us our internal emotional experiences by processing and attaching affective response to the rich flow of information from all the five senses and modulating our perception and the autonomic centers of the brain. Extensive research involving patients with temporal lobe epilepsy originating in the BLA has demonstrated that emotional experiences, in some cases highly charged, can result from electrical stimulation of this area. Although these experiences cover the full range of human emotions, fear and anxiety are the most common and are evoked frequently from the right amygdala. The following, from Gloor et al.,[91] is a description of a childhood trauma memory evoked during electrical amygdaloid stimulation in an adult male prior to surgery:

"When the right amygdala was stimulated with a 1 mA current, {the patient} experienced something that he found difficult to describe but finally likened to a feeling of falling into water. {after another stimulation} The patient immediately opened his mouth with an astonished look on his face, sat up, and said that now he knew what it was: it was the feeling of being at a picnic in Brewer Park in Ottawa. "A kid was coming up to me to push me into the water. It was a certain time, a special day during the summer holidays and the boy was going to push me into the water. I was pushed down by somebody stronger than me. I have experienced that same feeling when I had petit mals before. {...} When questioned whether he actually saw himself being threatened by the "big fellow" he said no, but it was a feeling as if he were there and was being chased."

Thus it appears from the work of Gloor[91,92] and many others that the amygdala, particularly the right BLA,[93] is where the "right mind" and brain meet to generate and bring to awareness the associated memories and emotions of a traumatic experience. Ibogaine may evoke the appropriate fluctuating milieu of neurotransmitters and neuromodulators to trigger a SOC state in the BLA, amygdaloid-brainstem pathways, and extrastiate areas activated during dreaming.[95] The unique morphology of the BLA pyramidal cells and lack of tangential or radial cortical organization may reflect functional connectivity specialized for non-sequential interactions over multiple timescales (or broad-band synchronization) with other temporal lobe cortical and subcortical regions. Distortions of time perception noticed by patients may reflect the "rescaling in time" afforded by the fractal bursting of BLA pyramidal cells during this critical state.[69] Taken together, these observations, speculations and experiences point to the role of common self-organized critical states states in the amygdalae, extrastriate cortex and brainstem as the emotional and visual and substrates for Ibogaine "experiential" dream-like phenomena.

Reevaluation & the Long "Terminal Sleep"

After the end of the SOC dream-like state and rapid image experience, subjects are able to reflect on and integrate the experience, free of craving or withdrawal symptoms. The subject has experienced "the big picture" and a unique perspective on his or her life. If struggles between the twin minds underlie drug addiction, then the "experiential" recall of trauma experiences may help bring understanding and insight to these struggles. Many addicts report a feeling of "getting in touch with their soul" or a feeling of oneness with the universe and that "...all the people in the universe and all things in the universe are only one." These experiences and feelings, in part, may result from a new sharing and harmony between long dissociated twins. A long period of sleep may then ensue, and patients after waking have reported having had "the best sleep of their lives." As described above the sequence of stages in Ibogaine therapy has some interesting similarities with Delirium tremens and terminal sleep that follow withdrawal from chronic alcoholism and other kinds of drug addictions. In this regard, the Ibogaine state may represent a kind of facilitated "REM-rebound" process, making up for sleep loss since trauma or abuse first affected sleep architecture.

Recovery and Insomnia

In the month following Ibogaine therapy insomnia may be due to the presence of a long-lasting metabolite (Mash, personal communication) and/or a reduction in the physiological need for sleep because of the intense emulation of dreaming (or REM rebound) which occurs during the treatment. This intensifies adjustment problems for addicts, due to the loss of old patterns of behavior and social support during this phase. Among The Fang, where eboga is used ritually, a strong social network already exists. After initiates recover from their "journey to the land of the dead," they are reborn socially, and have new social status. One insight that the fractal perspective can bring to psychotherapy is the necessity of the "long-view." Although the brain generates long-range correlations, abuse, trauma and the stress of modern life can quickly destroy these correlations.

Ibogaine in context

While the Ibogaine experience may restore long-range correlations through the self-organized critical state and horizontal and vertical processes, it is also necessary to complement these sources with support groups, long-term therapy or follow-up as well as community involvement and reintegration. A supportive social network, as with The Fang, should be a fundamental part of any large-scale Ibogaine treatment program.

Summary and Future Directions

I have presented a comprehensive hypothesis supporting the use of Ibogaine (and other oneiric substances) in the treatment of chemical dependency and PTSD due to its unique neuropharmacological and psychobiological properties. These two disorders are usually interrelated in that the majority of drug addicts have a

history of traumatic abuse that may result in functionally abnormal hemispheric interactions precipitating emotional instability and addictive behaviors. In the hypothesis I proposed that Ibogaine works through multiple neurotransmitter systems to create within amygdaloid-brainstem systems a self-organized critical oneiric state or state of plasticity, similar to states of plasticity existing during fetal development. This critical brain state may facilitate the consolidation of traumatic memories, reversal of abnormal hemispheric functional and the dissolution of habitual motor patterns associated with addiction. It is the hope of the author that this hypothesis may provide a spring-board for experimental investigations of many of the related ideas presented, providing an integrated theoretical view of the action of Ibogaine and other oneiric drugs, with the final goal being the introduction of Ibogaine or other oneiric compounds into widespread clinical use. The following are a few proposals for further research with this goal in mind:

Measurement of Phasic Events In Addicts Pre- and Post-Ibogaine:

With relatively little expense, non-invasive measurement of eye movements or galvanic skin response (GSR) before, during and after Ibogaine therapy could be carried out in addicts undergoing treatment. Changes in the fractal clustering of phasic events such as EMs or GSR may provide a useful objective assessment of the progress and long-term effects of therapy. Also, lateral visual field stimulation goggles and ear temperature measurements could provide correlates of hemispheric asymmetry changes.[18,19,21]

Measurement of changes in hemispheric functionality with Ibogaine:

A much larger study to assess changes in hemispheric asymmetry using quantitative EEG, PET imaging or functional MRI measures of brain activity pre- and post-Ibogaine, could test the dual hypothesis that hemispheric asymmetry is involved in addictive behavior and that Ibogaine may ameliorate these asymmetries. Pre- and post-Ibogaine sleep studies could also explore the relationship between hemispheric asymmetry, addiction, phasic events and general sleep architecture. Due to the more invasive nature of this testing, and the lack of testing facilities in countries where Ibogaine is legal, these studies could not be performed at this time during actual Ibogaine treatment. •

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