The Varieties of Ketamine Experience

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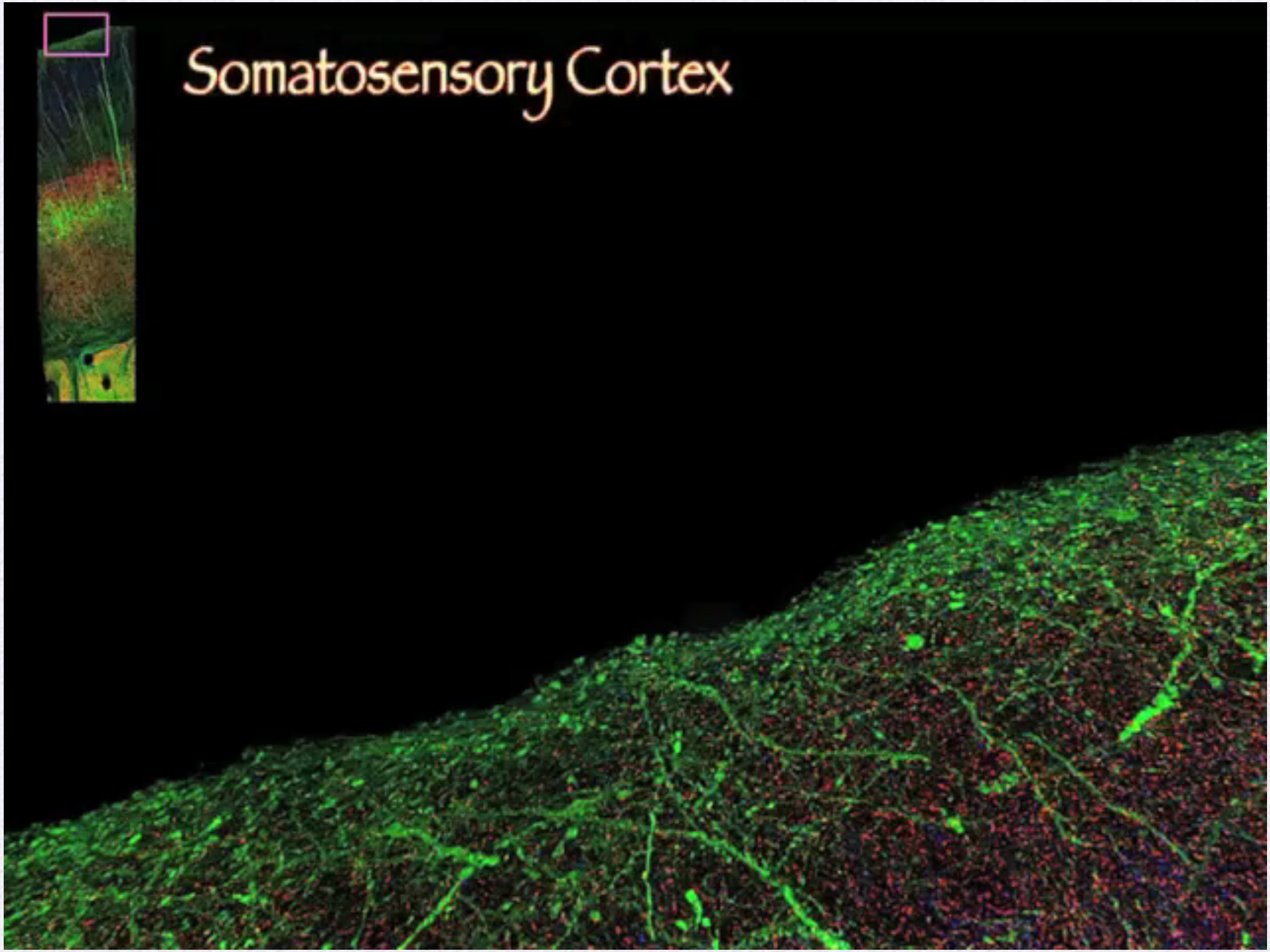
The truth of an idea is not a stagnant property inherent in it. Truth happens to an idea. It 'becomes' true, is made true by events. Its 'verity' is in fact an event, a process, the process namely of its verifying itself, its 'verification'. Its validity is the process of its 'validation'.

William James
from the Preface to *The Meaning of Truth*

and the same for its invalidation. What James did not speak to was the buttressed illusion of validation because of the stamp of approval of an idea from an authority, from special interests especially interested in obtaining a 'truth'

Complexity


Somatosensory Cortex

Complexity dictates a few caveats, among which are:

- *Never trust a single neurotransmitter theory as explanatory. None have worked out.*
- *All attribution of complex mental phenomena have been irreducible thus far to biochemistry, scanning, neuroanatomy, and our various attempts at instrumentalism.*
- *Distrust the latest hype for an internal love substance—e.g., serotonin, oxytocin, the current focus on glutamate, etc.*
- *We remain at the level of observing interactions between drug, setting, and in the broadest sense set.*
- *Embrace complexity and enactivism.*
- *Avoid reducing mind to brain itself.*

---and on a lesser level,

- *Never trust an 'investigator' who is single mindedly making a reputation and a livelihood on a single substance—remember Ricaurte.*

Ketamine—as An Anti-depressant

Ketamine in the News

- Recently, there has been a great resurgence of interest in Ketamine, now touted as a significant new antidepressant, with a novel mechanism of action with congeners of Ketamine in drug company development.
- Ketamine was first synthesized in 1962 and by 1965 was found to be a potent psychedelic.
- John Lilly became the first publicized (self-publicized) advocate for its transformative powers, and for its addictive potential and tolerance with too frequent use. Do read his amazing book *The Scientist*.
- And for by far the best, most thorough writing on Ketamine, do read *Ketamine: Dreams and Realities, by Karl Jansen, MD, PhD.*
- Charney, et al published in 1994 in the Archives of General Psychiatry on the *Subanesthetic effects of the noncompetetive NMDA antagonist, Ketamine in humans. Psychotomimetic, perceptual, cognitive, and neuroendocrine responses.* With this paper, they standardized what has been referred to as the NIMH protocol of 0.5mg Ketamine IV administered by drip over 40 minutes. Interestingly they concluded that Ketamine “produce(d) a broad range of symptoms, behaviors and cognitive deficits that resemble aspects of endogenous psychoses.”

Ketamine—as An Anti-depressant

Ketamine in the News

- In their subsequent papers and to my reading throughout the literature on K, there has been a tendency to diminish the 'psychotomimetic' experiences of subjects, no doubt from an aversion to be linked to its transformative psychedelic powers and any relationship to un-official use as a psychedelic (mind-manifesting) and the war on drugs—of course. I call that 'mystification'.
- For example, in a 2010 paper on the effectiveness of K as an anti-depressant, Charney et al refer to Ketamine as having elicit(ed)_ "minimal positive psychotic symptoms". I would assume that refers to hallucinations, delusions, and other symptoms of schizophrenia under the Schneiderian schema. But it appears to me to be an attempt at avoidance of what Ketamine actually does to people even at low doses.
- This leaves only a putative mechanistic theory, namely that K acts as an antagonist of NMDA, increasing neurotransmission of glutamate and more lately as part of the neuroplasticity fad, that K generates a fantastic explosion of synaptic connectivity and neurogenesis (in rodents) alleviating the atrophy caused by chronic stress (in rodents)
- *Of course, this creates the riddle to which this presentation is addressed: So, what then makes low dose IV K an anti-depressant, and what do people really feel when taking that low dose?—my study to follow.*

Ketamine in the News

- In 1999, K was placed in Schedule III amidst great controversy—pressure for Schedule I inclusion– defended by medical and veterinary advocates for its qualities as a safe and easily administered anesthetic.
- Studies of Ketamine as an anti-depressant, principally using and amplifying the 'NIMH protocol', continued after 1994, with varying results, the hype being—quick action—no blood brain barrier delay issues as per SSRIs and other clinically available anti-depressants and 'sustained' effect for days thereafter. In particular, see Charney and Zarate's work.
- Then, we hit the front page: 5 October 2012, Volume 338, *Science* publishes an editorial and review of Ketamine as an antidepressant touting its novel neurotransmitter mechanism as a potential quick acting entry into the stagnant realm of antidepressant pharmacology. Bold assertions are made such as "depression is associated with reduced size of brain regions that regulate mood and cognition"—rodents are mentioned—and that data has problems. But humans? Primates?
- And, most splendidly: "Recent studies report what is arguably the most important discovery in half a century: the therapeutic agent Ketamine that produces rapid (within hours) antidepressant actions in treatment resistant depressed patients". (page 68)
- *A bugle call to therapeutic action if I ever heard one!*
- But does this only apply to 0.5mg kg IV??? What if that is exceeded? What if a patient trips? Is the anti-depressant action of Ketamine confined to sub-anesthetic and, yes, sub-psychedelic dosage? How is that possible?

The Origins of this Study

- That is the emotional origin of this study
- The intellectual origin is somewhat different. Having known intermittent, non-abusing Ketamine transformationists over many years of use—a longitudinal, historical view—my sense is that Ketamine use has played a valuable and indeed transformative role in their lives, but that there have been episodes of significant and sometimes sustained depression despite Ketamine's use.
- And as a clinician, bringing to bear whatever tools that may apply to assist my patients, Ketamine may be of benefit for depression; or not; or not of sustained support.
- But as a transformative, egolytic, interruption from obsession and despair, Ketamine has a more potent, lasting and valuable impact

The Study

Nature of the Study: Qualitative Research dependent on subjective awareness and reportage with Study Administrators charting and making comments on observations

Motivation to Perform the Study: Curiosity to experience the effects of the IV Protocol and compare these effects with prior high dose experiences. Curiosity to obtain a point of view on the merits of the claims made for anti-depressant effect as a result of the IV Protocol.

Goal: Assessment of the effects of administration of Ketamine IV as per the NIMH protocol for the treatment of depression as reported by subjects experienced with moderate to high dose IM Ketamine effects.

Subjects: 7 Adult Volunteers, K-IM, et al experienced (number of prior experiences 5 or greater) assessing K-IV experience as reference for validation/assessment of IV purported anti-depressant procedure.

The Study

The Study

The Study

The Study

Conclusions Continued

The Nature of a Dissociative Anesthetic

With increasing Drug Dosage—e.g. Ketamine, Nitrous Oxide– the sensory inputs and perceptual integrations of the senses are turned off at the cortical level, leaving consciousness more and more subject to its own view, experience and creativity--this separated from external input, much as in a dream state, or as in a near death experience--so, an experience of heightened cs. Penultimately, cs itself diminishes, then is turned off and unconsciousness occurs.

The Six Channels of Perception and Ketamine as a Dissociative Anesthetic—based on the Abhidharmakosha

Capacity	Field/Object	Integrational Function	Ketamine Dose Effect
Body	Touch	Tactile perception	Analgesia @ 0.5mg/kg IV drip; 30-40mg IM
Eye	Form	Visual perception	Visual Perception disruption@ 0.5mg/kg IV; 30-40mg IM
Nose	Smell	Olfactory perception	Olfactory perception disruption@ 50mg IM and higher
Mouth	Taste	Gustatory perception	Taste Perception Disruption@ 50mg and higher
Ear	Sound	Auditory perception	Auditory perception disruption @ greater than 0.5mgkg; greater than 100mg IM
Mind	Affective and Cognitive Capacities	Consciousness	Cs disruption @ greater than 3mg/kg IV and 300mg IM

All Routes Lead to the K-Hole *from Erowid*

Insufflated / Nasal Ketamine **Dosages by body weight in lbs**	**I.M. Ketamine** **Dosages by body weight in lbs**	**Oral Ketamine** **Dosages by body weight in lbs**
Threshold .1 mg / lb 10 – 15 mg range	**Threshold .1 mg / lb 10 - 15 mg range**	**Threshold .3 mg / lb 40 - 50 mg range**
Light .15 mg / lb 15 – 30 mg range	**Light .15 mg / lb 15 - 30 mg range**	**Light .6 mg / lb 50 - 100 mg range**
Common .3 mg / lb 30 – 75 mg range	**Common .2 mg / lb 25 - 50 mg range**	**Common .75 - 2 mg / lb 75 - 300 mg range**
Strong .5 - .75 mg / lb 60 - 125 mg range	**Strong .5 mg / lb 40 - 100 mg range**	**Strong 1.5 - 2.5 mg / lb 200 - 450 mg range**
The K Hole:1 mg / lb 100 - 250 mg range	**The K Hole: .75 mg / lb 60 - 125 mg range Anaesthetic 1 mg / lb 100 - 200 mg *too low (PW)* *Anesthesia=6.5-13mg/kg***	**The K Hole 3 - 4 mg / lb 500 + mg**

And *Erowid* on the IV Route

I.V. Ketamine Dosages: Anesthetic 1 - 4.5 mg/kg body administered over 60 seconds.

Or, a bolus at 1mg/kg for a 70 kg human would be a hefty 70 mg of sudden K rushing through your blood stream to your brain.

Onset : 1 - 4 minutes (depending on dose and injection location)
Duration : 30 - 60 minutes
Normal After Effects : 2 - 4 hours

Compare to 0.5mg/kg infused over 40 minutes= No K-hole and mild anesthetic effects predominantly on tactile (analgesia), and visual (prefer eyes closed) sensory pathways and reduction in functionality.

focusing on Dose, Method, Duration and Outcome

- The first report of Ketamine use in 'narcopsychotherapy' appeared in 1973, Khorramzadeh reporting on 100 psychiatric patients with various diagnoses with terrific results, 88 of his patients remaining well after 1 year; attributing the success to Ketamine's 'mind-expanding qualities.

- Roquet in 1974 describes the use of Ketamine psychedelic psychotherapy in a group setting—calling his approach 'psychosynthesis'.

- Golechha, et al *Ketamine Abreaction—Two Case Reports* Indian Journal of Psychiatry October 1985 First study for psychedelic, sub anesthetic effect. IM 1mg/kg in 51kg and 61 kg males, so a transformational dose. Purpose: narcoanalysis.

- Krupitsky's Work: 1997 Journal of Psychoactive Drugs *Ketamine Psychedelic Therapy (KPT)—a review of the results of ten years of research.* Treatment of alcoholism in a 3 month long inpatient setting with deliberate preparation for a transformational experience. 2-3 mg/kg IM—a single session. Results: Total abstinence for more than one year in 73 of 111 patients compared to 24% of patients enrolled in conventional treatment.

  Krupitsky goes on to treat heroin addicts, conducting a comparison between a low non-psychedelic dose of 0.2mg/kg vs. 2.0 mg kg—a psychedelic dose, and reports in 2002 " a significantly greater rate of abstinence in heroin addicts within the first two years of follow-up, a greater and longer-lasting reduction in craving for heroin" as compared to the low dose KPT group.

  By 2007, he has created a three session model for KPT and compares two groups--one with a single session and a second with three Ketamine sessions, and finds double the abstinence rate. Interestingly, he reports "No differences between groups were found in depression, anxiety, craving for heroin , or their understanding of the meaning of their lives."

  Kolp, Friedman, Young and Krupitsky seek to duplicate Krupitsky's work in the US concluding that Ketamine is adjunctive and requires, according to Kolp ' a carefully crafted set and setting'. Kolp uses the term 'transpersonal to hypothesize on Ketamine's utility.

A View of Ketamine Clinical Studies

focusing on Dose, Method, Duration and Outcome

- Mills et al, *Treatment of compulsive behaviour in eating disorders with intermittent Ketamine infusions QJ Med 1998, 91:493-503* Patients: 15 chronic, unresponsive to treatment, older female anorectics. Initial IV bolus to sedation endpoint than 20mg IV/hr for ten hours. Opiode antagonists used to block anesthetic effect/ loss of cs. Argument: Compulsive behavior is based on high arousal state leading to involuntary recall leading to long term potentiation (LTP) at the hippocampal level through glutamate—NMDA recepors, blocked by Ketamine. LTP is blocked by K. 9 subjects are responders receiving 2-9 infusions over a 5 day to 3 week period. 6 subjects do not respond with 6 -15 sessions. Response is measured by a reduction in Compulsion Scores. *Comment: While anesthesia was avoided, the long period and frequency of the infusions was a designed interruption of consistent cs in individuals deemed to have an excited compulsive disorder*

Review of Some Studies Labeled as Anti-depressant Ketamine Research

- Charney, et al 2010 *Safety and Efficacy of Repeated-Dose Intravenous Ketamine for Treatment-Resistant Depression* Biol Psych 20120; 67 139-145. Charney moves from single dose K to 6 infusions over 12 days. Patients had previously shown a meaningful anti-depressant response to a single dose of K. They cite: 2 placebo controlled studies reported rapid and robust anti-depressant effects a a single IV doe in symptomatic patients with Major Depressive Disorder, >72 hours in 12 of 25 patients with relapse in all but two patients <2 weeks post Ketamine. In this new study response criterion was met by 9 of 10 patients after the first infusion as well as after the sixth. Patients who responded to the initial infusion maintained their response for as long as they received additional doses and for at least 6 days after that. 4 of 9 patients relapsed <2 weeks post-Ketamine. Eight of nine patients relapsed between 6 days and 45 days, the average being 19 days, with one patient lasting for > 3 months. Interestingly, Charney et al design this study to be compatible with ECT—which they note also shows high relapse rates in the month after discontinuation of shock.

depressant Ketamine Research

Zarate (et al)'s NIMH Ketamine Research—0.5mg/kg IV, Saline placebo

- 2000—Berman, et al develop IV protocol and publish on Ketamine having an anti-depressant effect—7 subjects.
- 2006 Randomized, placebo controlled, double blind crossover study in treatment resistant major depression claiming robust and rapid anti-depressant effects within 2 hours of infusion with 35% of subjects maintaining positive response for at least 1 week.
- Mulitple studies on mechanism of action in mice, rats and humans develop theory of NMDA antagonism and glutametergic excitement. BDNF shown not to be significant in humans—2009. 2010—"preclinical evidence indicates a relevant interplay between AMPA and NMDA in the rapid anti-depressant effect of K". 2010—An ongoing search for clinical biomarkers that will predict positive response to Ketamine: Increased anterior cortical activity due to rapid presentation of fearful faces to Major Depressive Disorder patients said to be a predictor of positive response to K. 2012—NMDA antagonism now thought to be insufficient as explanation for therapeutic effects of K. 2013– rodent studies indicate enhanced synaptic plasticity with K. 2013—hippocampal focus with reduction of neurotransmitter release. *Comment: After all of this work, I have no greater clarity on the molecular basis of Ketamine's anti-depressant action.*
- 2009—Subjects with a family history of alcohol dependence showed significantly greater improvement in MADRS scores compared with subjects who had no family history of alcohol dependence. Subjects studied over 230 minutes at intervals.
- 2010 33 subjects with suicidal ideation show reduction in suicidality within 40 minutes of beginning the infusion, this effect continuing for up to 4 hours. *Comment: Is this really a surprise?*
- *2010*—Repeats depression study in Bipolar I and Bipolar II Patients maintained on lithium or valproate with even better results in terms of rapid response, but shorter maintenance of effect—3 days vs. 7 in the depression study.
- 2011—Extends study to ECT resistant major depression finding improvement of depressive symptoms at 230 minutes.
- 2012—Attempt to extend anti-depressant effects of Ketamine infusion by adding riluzole fails.

The MADRS

Zarate and Others' Main Depression Evaluation Tool

MONTGOMERY AND ASBERG DEPRESSION RATING SCALE*Br. J. Psychiat. (1979), 134, 382-389©Stuart Montgomery 1978, Measures of Depression, Fulcrum Press, LondonThe rating should be based on a clinical interview moving from broadly phrased questions about symptoms to more detailed ones which allow a precise rating of severity. The rater must decide whether the rating lies on the defined scale steps (0, 2, 4, 6) or between them (1, 3, 5) and then report the appropriate number. The items should be rated with regards to how the patient has done over the past week.*

1 - APPARENT SADNESS - ***Representing despondency, gloom and despair, (more than just ordinary transient low spirits) reflected in speech, facial expression, and posture. Rate by depth and inability to brighten up.***

0 No sadness
1
2 Looks dispirited but does brighten up without difficulty
3
4 Appears sad and unhappy most of the time
5
6 Looks miserable all the time. Extremely despondent.

2 - REPORTED SADNESS - ***Representing reports of depressed mood, regardless of whether it is reflected in appearance or not. Includes low spirits, despondency or the feeling of being beyond help and without hope. Rate according to intensity, duration and the extent to which the mood is reported to be influenced by events.***

0 Occasional sadness in keeping with the circumstances.
1
2 Sad or low but brightens up without difficulty.
3
4 Pervasive feelings of sadness or gloominess. The mood is still influenced by external circumstances.
5
6 Continuous or unvarying sadness, misery or despondency.

3 - INNER TENSION - ***Representing feelings of ill-defined discomfort, edginess, inner turmoil, mental tension mounting to either panic, dread or anguish. Rate according to intensity, frequency, duration and the extent of reassurance called for.***

0 Placid. Only fleeting inner tension.
1
2 Occasional feelings of edginess and ill-defined discomfort
3
4 Continuous feelings of inner tension or intermittent panic which the patient can only master with some difficulty.
5
6 Unrelenting dread or anguish. Overwhelming panic.

4 - REDUCED SLEEP - ***Representing the experience of reduced duration or depth of sleep compared to the subject's own normal pattern when well.***

0 Sleeps as usual.
1
2 Slight difficulty dropping off to sleep or slightly reduced, light or fitful sleep
3
4 Sleep reduced or broken by at least two hours.
5
6 Less than two or three hours sleep.

5 - REDUCED APPETITE***Representing the feeling of a loss of appetite compared with when well. Rate by loss of desire for food or the need to force oneself to eat.***

0 Normal or increased appetite.
1
2 Slightly reduced appetite
3
4 No appetite. Food is tasteless.
5
6 Needs persuasion to eat at all.

6 - CONCENTRATION DIFFICULTIES - ***Representing difficulties in collecting one's thoughts mounting to incapacitating lack of concentration. Rate according to intensity, frequency, and degree of incapacity produced.***

0 No difficulties in concentrating.
1
2 Occasional difficulties in collecting one's thoughts.
3
4 Difficulties in concentrating and sustaining thought which reduces ability to read or hold a conversation.
5
6 Unable to read or converse without great difficulty.

7 - LASSITUDE - ***Representing a difficulty getting started or slowness initiating and performing everyday activities.***

0 Hardly any difficulties in getting started. No sluggishness.
1
2 Difficulties in starting activities.
3
4 Difficulties in starting simple routine activities, which are carried out with effort.
5
6 Complete lassitude. Unable to do anything without help.

8 - INABILITY TO FEEL - ***Representing the subjective experience of reduced interest in the surroundings, or activities that normally give pleasure. The ability to react with adequate emotion to circumstances or people is reduced.***

0 Normal interest in the surroundings and in other people.
1
2 Reduced ability to enjoy usual interests.
3
4 Loss of interest in the surroundings. Loss of feelings for friends and acquaintances.
5
6 The experience of being emotionally paralyzed, inability to feel anger, grief or pleasure and a complete or even painful failure to feel for close relatives and friends.

9 - PESSIMISTIC THOUGHTS - ***Representing thoughts of guilt, inferiority, self-reproach, sinfulness, remorse and ruin.***

0 No pessimistic thoughts.
1
2 Fluctuating ideas of failure, self-reproach or self-depreciation.
3
4 Persistent self-accusations, or definite but still rational ideas of guilt or sin. Increasingly pessimistic about the future.
5
6 Delusions of ruin, remorse and unredeemable sin. Self-accusations which are absurd and unshakable.

10 - SUICIDAL THOUGHTS - ***Representing the feeling that life is not worth living, that a natural death would be welcome, suicidal thoughts, and preparations for suicide. Suicidal attempts should not in themselves influence the rating.***

0 Enjoys life or takes it as it comes.
1
2 Weary of life. Only fleeting suicidal thoughts.
3
4 Probably better off dead. Suicidal thoughts are common, and suicide is considered as a possible solution, but without specific plans or intention.
5
6 Explicit plans for suicide when there is an opportunity. Active preparations for suicide.

So, the MADRS—Qualitative or Quantitative? Rater Bias Possible or Not? Simple, common-sense, or some higher scientific value? Subjective or Objective? ‘How do you feel?’ In ten compartments. Your view?

Recent Developments

Because of the short effect profile of Ketamine as an anti-depressant, recent work has moved to extend the number of sessions and even develop a ‘maintenance’ schema for repeated infusions.

- Messer and Haller report using Ketamine in association with ECT in a 46 year old treatment resistant woman, then proceed with 3 additional infusions every other day over 5 days with remission lasting 17 days; then 3 series of 6 infusions over 16 weeks with 3 remission relapse cycles; and then proceed to an infusion every 3 weeks as ‘maintenance with resulting remission > 5 months. ‘Side effects’ included perceptual disturbances, confusion, euphoria and dizziness. Recognizing that body weight in obese individuals raises the dose level to where the psychedelic effects become more in evidence, they move to an ‘ideal body weight’ approach to dosing.

- Murrough et al resort to up to 6 IV infusions administered 3 times /week over a 12 day period with a median time to relapse of 18 days after the last infusion—TRD patients.

- Feifel reports moving to an outpatient setting and following a positive response to an initial infusion, repeating as often as q 2 weeks. He suggests moving to the ease of IM administration.

Depression

- The complexity of our evolved brain/mind/consciousness/connectivity makes reductionist and narrow concepts and explanations for complex and varied states of mind like depression unhelpful, off the mark and superficial. DSM diagnoses are circular and tautological, defining depression as a cluster of the symptoms that in turn define depression. They take the complexity of human beings out of the analysis and create deep mystification in all of us as we think about ourselves and others.
- The concept of Anti-depressants is at its core complex and varied and the restriction in our thinking to drugs only serves Pharma and the 'officials, who are in charge of the self-interested fabrication of depression as disease.
- Within the realm of psychiatric medicine there are many types of drugs said to be anti-depressants and the neurotransmitter—the serotonin model--has been bogus for decades. Over 50% of people put on anti-depressant medications do not respond! No one has ever witnessed a 'chemical imbalance'.
- A very partial list of anti-depressants includes multiple types of chemical anti-deps with very different neurotransmitter actions; and--anti-convulsants, stimulants, marijuana, exercise, meditation, hedonism, temporary satisfaction of cravings, elimination of cravings, oxytocin, sexuality, spiritual practice, money, love, children, activism, justice, a good job, respect, friendship, education, a good book, a bad book, etc, etc.
- Most depressions stop without psychiatrists and therapy. Some depressions start with psychiatrists and psychotherapists.
- There is a continuum between anxiety and depression and mostly they are mingled.
- There are so many aspects of being and being in the world and they all reflect and infect mood. All evaluations are oversimplifications. An at best partial evaluation of our parameters and aspects must include: energy—enthusiasm—motivation—sexuality—engagement—learning and intellect—spirit—love and hate—trauma—grief and loss—failure/success—pleasure/displeasure—hopefulness/hopelessness—health—age—intelligence—blocks and phobias—our social and environmental context—the cultural affect—religion—gender—education—our origins and history of oppression—parenting—grief and loss—responsibilities—family—addictions—etc—etc. Depression can be partial, selective, and total with a slug like existence in which all frames are suppressed.
- for a great read, do try Gary Greenberg's *Manufacturing Depression* Simon & Schuster 2010

View, Path and Fruit

- I have set forth a *view* of Ketamine as a substance in various formats and dosages in interaction with humans.
- The *path* of research and experience has been delineated through the report of my study and a partial review of the studies of others, particularly focusing on the claim for an anti-depressant effect.
- The *fruit* is now ready to pluck—as I taste it:
- *The effects of Ketamine are related to dose and subject sensitivity. In general, the higher the dose, no matter what the route of administration, the greater the anesthesia and interference with sensory modes, the greater the internal stimulation and isolation of consciousness to mind only.*
- *The so-called anti-depressant effect is short-lived and has only been extended by repeated administration of IV infusions. The rapid action of Ketamine is due to its disruption of ordinary consciousness and its anesthetic properties.*
- *The mechanism of action as an anti-depressant has not been elucidated inasmuch as the complexity of the state of 'depression' is enormous and varied and there are undoubtedly many mechanisms at work as there are many states and ways of being depressed. Other mechanisms than the glutametergic one have been proposed such as Ketamine as an antagonist at CNS muscarinic acetylcholine-receptors and opiate receptors and may be a result of interactions with the sigma opiate receptor—all of this coming from animal models and uncertain as to humans.*

The Fruit

continued

- Anti-depressant substance treatments can be thought of in categories:
  - Interruption of consciousness and breakage of the stream—usually repeated—e.g. ECT, narcoanalysis and induced sleep in a continuum to coma.
  - Disruption of consciousness—IV protocol of Ketamine.
  - Disruption, Egolysis, and Transformation—towards the K-Hole, in the K-Hole, other psychedelics.
  - Direct Shifting of Mood and New Experience of Affect—MDMA and Empathogens.
  - Slow shifting of Affective and Anxious/Obsessional States—the continuous brain bath--Anti-depressants like SSRIs, etc.
  - Potential Affective Smoothing, Re-focus and Obsession Release--with Marijuana.

Conclusion

From this perspective, IV Ketamine administration at 0.5mg/kg results in a mild disruption of consciousness, with a temporary release from a depressed affective and obsessional state, that improved state not persisting much beyond the immediate effect of the experience—save for a few people—ordinary mind and the habitual state of depression resuming. I believe this to be because we tend to ruminate and obsess, to have emotional streams and lockups, because we have an emotional view of external conditions, because external conditions don't change just because we are having a Ketamine session, and because we live in our own history and in tandem with the presence, history, and culture of the external environment. Personal change is difficult!

And that is why *transformation* is so attractive and so scary and is not simply a drug story, but requires care, nurturance, input and stimulation, factors that balance us, art and creativity, understanding of our connection to nature, community, and spirit, love and friendship—and more. This complexity to being and to being in the world is why there are no magic, perfect drug bullets.

And as to neuroplasticity, Ketamine seems to me to loosen and reconnect the internal strings, not always in ways that are easy or pleasurable. Perhaps that is what we can actually have as an indirect, sensory experience of neuroplasticity without knowing if the dendrites are actually moving about in there--in more or less one hour of time. I will call that *functional neuroplasticity*---or, *transformation.*

Conclusion continued

As to IV Ketamine infusion's future clinically, I will prognosticate that it is not robust, to use Zarate's hyperbole. The IV Ketamine protocol was birthed in the framework of the NIMH where consciousness of the 'war on drugs' ((or is it 'the war on people who do drugs in some form of other') you would imagine runs high. Schedule III means availability—but the 'officials' make sure to formulate Ketamine at a dose where you can say psychoactivity is under control--not too much, not psychotomimetic, not of the forbidden psychedelic zone. That in itself is a bit of a reach. Ketamine does not know itself of this restriction and does what it does in interaction with the variously sensitive souls to whom it is administered. It has its problems and its plentiful failures.

As an IV practice it is inconvenient and smacks of hospitals and some choose to liken it to ECT—not a point the MadMen would like to have to deal with. There is money to be had, given the ringing endorsements going round, like *Science.* And the effect is not sustained and requires more infusions and more infusions—a bit of a mess—but repetition is the mother of a steady business, so it could have a practitioner base.

But all this belies the main potentiality. Ketamine often has a transformational effect on humans at a moderate dose. There are risks--like bad trips, flashbacks, a very small potential for addiction. But as per Krupitsky, transformational use within a highly supportive framework can produce remarkable changes—like years of sobriety and heroin abstinence. Or, for true change of character and reduction of suffering, for a more open view of self and environment. That is where the Ketamine opportunity lies.

Personal Offerings

If you are interested:

- For many of my articles, check out my website: www,philwolfsonmd.com.

- My book: *Noe – A Father/Son Song of Love, Life, Illness and Death is available for sale here and at the blogsite for the book:* www.noe-thebook.com

- My assessment device--*The Transformation Codex*--is available as a reprint for your use as a tool for assessing your own and others' experiences--big and small--of transformation.

- My article: *A Longitudinal History of Self-Transformation—Psychedelics, Spirituality, Activism and Transformation* Journal of Consciousness Exploration and Research Cotober 2011/Vol2/pp 981-992 is available here as a reprint and contains *The Transformation Codex*

- *Other reprints are available in limited quantities.*

- ***Thanks so much!!!***

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