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Philip E. Wolfson

Center for Transformational Psychotherapy

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Ketamine for Depression: A Mixed-Methods Study

Philip E. Wolfson

Center for Transformational Psychotherapy
San Francisco and San Anselmo, CA, USA

Prior studies have reported variously on the presence or absence of dissociative effects at subanesthetic doses of ketamine administered for treatment-resistant depression. This mixed-methods study emulated the protocol used for the studies in question, with IV administration of 0.5mg/kg over 40 minutes with eight experienced ketamine users. Quantitative measures were generally insignificant since this was not a population reporting depression; blood pressure increased as expected by 20-30mm systolic and 6-20mm diastolic, falling rapidly by 20 minutes after completion of the infusion. Individual qualitative reports reports of relaxation, pleasant sensation, decreased cognitive function, and some disabling of ordinary capacities. As experienced users, subjects commented freely on what was characterized as the triviality of the experience, and typically expressed skepticism that ketamine could have antidepressant properties when administered at this dose or in this manner, as well as disbelief that it could be beneficial except perhaps as a period of relaxation, or as a partial break from ordinary states of mind in naïve subjects. Group discussion produced a consensus recommendation in favor of threshold- and higher-dosage transformative work beginning with a 40-50mg IM bolus, potentially in a series of sessions with higher dosages if indicated, with the number of sessions to be determined by clinical practice; such work should occur in a closely monitored psychotherapeutic setting.

Keywords: *Ketamine, dissociative anesthetic, intramuscular, psychedelic, antidepressant, treatment-resistant depression, antidepressant, phenomenology, qualitative, mixed methods*

Ketamine is a dissociative anesthetic that has recently shown potential as a significant new antidepressant (Duman & Agajanian, 2012). Unlike existing antidepressants that target serotonin, norepinephrine, and dopamine systems--and that may take a number of weeks to achieve efficacy, ketamine is an NMDA receptor antagonist that affects the glutamate system and appears to provide significant relief to some individuals within only hours or days (Ryan, Marta, & Koek, 2014 [this issue]). These findings are of importance for two reasons: first, because the slow onset of relief from conventional medications leaves a window of vulnerability for individuals suffering from severe depression or suicidality; and second, because current antidepressant treatments fail in approximately 25-50% of individuals treated (Little, 2009; Nemeroff, 2007; Souery, Papakostas, & Trivedi, 2006), and in some cases may actually worsen outcomes (Gueorguieva, Mallinckrodt, & Krystal, 2011).

Even when there is clinical response to current antidepressants, the results are only somewhat better than

placebo (Kirsch & Sapirstein, 1998; Kirsch et al., 2008; Moncrieff & Kirsch, 2005), especially for individuals whose depressive symptoms are mild to moderate at baseline (Fournier et al., 2010). It even has been suggested that the benefits actually conferred may be due to the psychological impact of non-specific physiological effects (Kirsch & Sapirstein, 1998; Moncrieff, 2007), and in any case such benefits may decrease over time (Goldberg, Privett, Ustun, Simon, & Linden, 1998). While individuals with the most severe depression show greater benefits from medication relative to placebo (Fournier et al., 2010), possibly this is the result of a lower response rate to placebo in such cases rather than enhanced drug efficacy (Kirsch et al., 2008). With the limited success of current pharmacological antidepressant strategies and the paucity of progress in the development of new antidepressant drugs (Hendrie & Pickles, 2013), pharmacological treatment has stagnated. The poor long-term outcomes for current depression treatment (Fekadu et al., 2009; Goldberg et al., 1998; Kiloh, Andrews, &

Nielson, 1988; Tuma, 2000), together with its relatively high incidence (Kessler et al., 2003) and great societal impact (McKenna, Michaud, Murray, & Marks, 2005; Murray & Lopez, 1997), suggest that new antidepressant strategies could be of considerable value.

While there has been growing public interest in the potential of ketamine, the robust nature of ketamine as a stand-alone treatment for depression and other psychiatric diagnoses has yet to be convincingly demonstrated. Short-term relief lasting from minutes to a few days has been the rule, particularly with single ketamine sessions (Katalinic et al., 2013), and this may be extremely important in crisis situations where immediate, even if not sustained, relief can be lifesaving. When administration is repeated and provided in concert with a variety of psychotherapies supporting the sustained and/or intermittent use of the drug, there has also been reported success (e.g., Khorramzadeh & Lofty, 1973; Kolp et al., 2014 [this issue]; Krupitsky & Grinenko, 1997). The jury is still out, however, on long-term maintenance dosages of ketamine for treating depressions but, despite this lack of clarity, ketamine as a Schedule III drug with a long history of safe use has become a growing part of the psychiatric arsenal with individuals and clinics—including anesthesiologists—administering the substance in varying ways (Ryan et al., 2014 [this issue]).

Characteristic of the increased popularity of ketamine treatment has been a specific methodology designed to minimize ketamine's potentially powerful psychedelic effects, which are nevertheless difficult to eliminate entirely. The psychedelic properties of ketamine may remain present to some degree, even when administered in the small dosages typically used in studies that attempt to establish its efficacy for depression. Seeing these as undesirable appears to be based on the assumption that such "side-effects" are both negative and separable from its antidepressant properties.

Ketamine has been recognized for its psychedelic properties since 1965, through underground use and a few publications (cf. Jansen, 2004; Kolp et al., 2014 [this issue]). The first study to intentionally examine ketamine's psychedelic effect at subanesthetic doses was published in 1985 by Golechha, Rao, and Ruggu, reporting on the use of 1mg/kg administered intramuscularly (IM) in two males, 51kg and 61kg respectively, with the stated purpose of narcoanalysis. Early reports suggested an emotionally beneficial effect from such doses, which are large enough to produce psychedelic experiences that could be

considered transformational. These often resulted in what was sometimes called a psychedelic afterglow, tending to last for significant periods of time after the ketamine sessions, and suggesting an antidepressant effect. It seems possible that such experiences may have led to the subsequent exploration of ketamine as an antidepressant.

Later research has de-emphasized ketamine's psychedelic properties—perhaps considering these to be a stigma that might impede its psychotherapeutic use. Krystal, along with Charney and other colleagues (1994) at the National Institute of Mental Health, deserve credit for the development of what might be referred to as the "NIMH protocol," with publication of a paper examining its sub-anesthetic effects. In this first paper from a group with Charney as its principal investigator, psychedelic effects were still recognized, even though considered as undesirable. Krystal et al. (1994) reported that:

Ketamine (1) produced behaviors similar to the positive and negative symptoms of schizophrenia; (2) elicited alterations in perception; (3) impaired performance on tests of vigilance, verbal fluency, and the Wisconsin Card Sorting Test; (4) evoked symptoms similar to dissociative states; and (5) preferentially disrupted delayed word recall, sparing immediate recall and post-distraction recall. (p. 199)

Research teams including Charney—illustrating continuity in the development of this research—published results from randomized, placebo-controlled, double-blind studies of ketamine's impact on major depression in 2000 (Berman et al.) and 2006 (Zarate et al.). These two studies demonstrated rapid and robust antidepressant response to a single dose of ketamine using the NIMH protocol, with effect lasting 72 hours or more in 12 of 25 total patients; relapse occurred in all but two patients in less than two weeks post ketamine infusion. By 2010 Aaron Rot and colleagues, again including Charney, had moved from a single dose of ketamine to a series of six infusions administered over 12 days, each infusion at the same dosage that had previously proven efficacious in single-dose treatment. Response criterion was met by nine of ten 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 six days after that. Four of nine patients relapsed less than 2 weeks post-ketamine treatment. Eight of nine patients relapsed between 6 and 45 days, the average being 19 days, with one patient's

antidepressant effect lasting for more than three months. Interestingly, aan het Rot et al (2010) designed this study to be comparable with electroconvulsive therapy (ECT)—which they noted also showed high relapse rates in the month after discontinuation of shock therapy.

Krystal et al.'s (1994) initial report of the effects of the NIMH protocol is markedly different from that offered by aan het Rot et al. when the latter team replicated the NIMH protocol in 2010. They commented, "Ketamine elicited minimal positive psychotic symptoms. Three patients experienced significant but transient dissociative symptoms. Side effects during and after each ketamine infusion were generally mild" (p. 139). Note that Krystal et al.'s (1994) report of "positive and negative symptoms of schizophrenia" (p. 199) changes to "positive psychotic symptoms" in aan het Rot et al. (2010, p. 139); these were now "minimal," dissociative symptoms, were "transient" and limited to a small subset of participants, and side effects were "generally mild" (p. 139). This significant shift in emphasis—little short of a reversal of findings—occurred with the same drug, administered at the same dose, with at least one principal investigator common to both teams; apparently something else had changed.

As a further complication, in 2014 a team led by Zarate (Luckenbaugh et al.)—first author on one of the studies that included Charney—reported that in an analysis of their data from 108 patients who received single subanesthetic infusions of ketamine, the only variable in their data predictive of a sustained antidepressant response was the presence of dissociative side effects. Other agents that, like ketamine, act as NMDA antagonists but lack ketamine's dissociative effects have thus far been ineffective in producing antidepressant effects (Zarate et al., 2013). Conversely, a study of the impact of the dissociative anesthetic nitrous oxide on 20 subjects diagnosed with treatment resistant depression yielded outcomes similar to ketamine (Nagele et al., 2014). Such findings raise the question of whether the antidepressant effect comes from a specific chemical interaction in the brain, whether a particular state of mind may have some beneficial effect irrespective of the chemical used to induce that state (cf. Moncrieff & Cohen, 2006), or whether similar dissociative states may yield comparable benefits through different in brain effects.

The lack of consistency in reporting sensory effects of ketamine during IV administration of the NIMH protocol provided incentive to undertake this study analyzing participants' phenomenal experiences of

the dissociative effects of ketamine using the same dosage rate and method of administration as the NIMH protocol. This represented an effort to gather specific data on the presence or absence, and the nature, of any psychedelic symptoms as reported by Krystal et al. (1994), aan het Rot et al. (2010), and others.

The Study

This study was designed to gather evidence regarding the presence or absence of dissociative effects from ketamine, as well as on the qualities of any such effects and how they might compare with qualities at higher doses, working with experienced ketamine users who volunteered to receive doses consistent with the NIMH intravenous (IV) ketamine protocol followed by the Charney teams (Krystal et al., 1994; Collins et al., 2010). Selected vital signs were measured at intervals, and qualitative reports were collected after the experience. The latter are situated in the tradition of qualitative research on psychedelics, such as DMT, ayahuasca (Bouso, Fábregas, Antonijoan, Rodriguez-Fornells, & Riba, 2013), and marijuana (Lile et al., 2013); it is also resonant with the new Johns Hopkins experienced users study currently enrolling subjects by Griffiths (2015) and his group, which randomizes 20 subjects to five experiences each of 18 different possible psychoactive substances and placebo.

Participants

Eight subjects with at least five prior ketamine experiences at boluses of 50mg or higher, and with no ketamine dependency or negative health effects from ketamine use, were recruited by word of mouth for the study. All but one of these had had more than 20 previous ketamine experiences, with dosage ranging from boluses of 50mg to 130mg; all reported a history of positive and transformative experiences at the higher IM doses. All participants shared a longitudinal awareness of their own and others' ketamine experiences over time—a process years to decades in duration. In pre-intervention interviews, participants expressed a sense of their lives changing over time—with some depressive episodes, relationship upheavals, and emotional difficulties—yet each expressed a sense of gratitude and appreciation for the transformative experience that had occurred with ketamine use, affecting their lives and minds predominantly in a positive manner. None reported depression at the time of the study.

Measures

Blood pressure, pulse rate, oxygen saturation, and respiratory rates were collected, and the Beck

Depression Inventory (BDI; Beck, Steer, & Carbin, 1988) was administered pre- and post-intervention. Qualitative reports were gathered during and after the intervention, and subjects discussed the experience in context of their own previous ketamine use at higher dosages.

Procedure

As a first step, medical personnel took baseline measures of blood pressure, pulse rate, and oxygen saturation for each subject, and the BDI was administered. Subsequently, but prior to ketamine administration, subjects spent 15 minutes relaxing in silence. Ketamine was then administered to subjects, who were lying down, through IV saline drip at a dosage of 0.5 mg/kg over 40 minutes. The intervention took place in a quiet atmosphere, with gentle music deemed to have a “spiritual” quality played throughout the process; the same music was used for all subjects. Blood pressure, pulse rates, oxygen saturation and respiration rates were assessed 20 minutes into the study and 20 minutes after completion of the infusion. Subjective data were accumulated by non-participant administrators who charted, for each subject, observations, periodic inquiries, assessment of mental state, and degree of psychedelic effect observed and reported, if any. Following completion of the IV infusion, subjects spent an additional hour in quiet with communication only as necessary. The BDI was completed again at the end of this reflective period, and a copy was taken home for completion on the following day. After the reflective period, participants engaged in a group discussion.

Results

All eight subjects completed the experience without complications. Return to baseline was reached within 30 minutes to one hour following completion of the infusion. All subjects were fully ambulatory at completion of the infusion with some residual psychomotor slowing. Two subjects reported mild nausea during the infusion. Several subjects ate vigorously after completion of the one-hour post infusion rest phase. One subject complained of an unusual and moderately severe headache for her, which began 3 hours after completion and lasted two hours. Another subject reported mild headache of brief duration.

Pulse rate, oxygen saturation, and observed respiratory rate. These measures did not change from baseline during the course of ketamine administration.

Blood pressure. Blood pressure measurements increased above baseline for all subjects: 20-30mm systolic, and 6-20mm diastolic, falling rapidly by 20 minutes after completion of the infusion.

BDI. There were no significant changes in BDI score, but subjects were not depressed at the onset of the study.

Observations. Reported visual effects and withdrawal from usual visual sensations were the primary sensory effects. Auditory experience was mildly affected if at all, and the tactile sense was not noticeably impacted. Subjects remained responsive to auditory exchanges and responded appropriately to promptings, though at times more slowly and with reduced commentary. Environmental awareness was clearly diminished. Subjects who received higher doses of ketamine tended to report deeper experiences, regardless of their weight.

Qualitative reports. Descriptive comments during the experience included reports of relaxation, pleasant sensation, decreased cognitive function, and some disabling of ordinary capacities (Table 1). As experienced users, subjects commented freely on what was characterized as the triviality of the experience—a period of “OK” relaxation and mildly increased inner awareness, with little if any affective modulation. Subjects typically expressed skepticism that ketamine could have sustained antidepressant properties when administered at this dose or in this manner, and consensus that the experience was best described as a very partial break from ordinary states of mind. Seven subjects indicated no desire to repeat the experience. One female subject felt changed by the experience, later reporting that she felt “emotionally very well” for several weeks, with increased motivation; she said she “would do it again.”

Participant discussion and evaluation. In discussion, a consensus recommendation emerged from the group: for threshold- and higher-dosage transformative work, beginning with a 40-50mg IM bolus, potentially in a series of sessions with higher dosages if indicated with the number of sessions to be determined by clinical practice; should occur in a closely monitored psychotherapeutic setting.

Also informed by the group discussion, it was suggested that goals of ketamine assisted psychotherapy should include facilitating a transformative experience in relationship to one’s own ego that would potentially have as its effect the reduction of obsessions through some breakage of continuity of afflictive mind, reformation of consciousness, reevaluation of the past and, hence, future prospects. In addition, there is the novelty and uniqueness of an experiential state, one that, to paraphrase participants, tends to produce a relaxation of that sense of control that attempts to keep the mind from deviating

Table 1. Notes on Participant Responses and Reports

Subject 1	At 5 minutes—"usual sensations" of beginning of a K experience; "warm and floating"; mild At 20 minutes—"didn't seem like 15 minutes have gone by"; building—"higher than 10 minutes ago" not particularly psychological At 35 minutes—not shamanic, not empathogenic, no disinhibition, no loss of intellectual function; floaty, soft, diffuse sensations in body 10 minutes post-infusion—shouldn't drive, but could; stayed pretty much in contact
Subject 2	At 15 minutes— "something happening," metallic taste At 35 minutes—very pleasant, "definitely K," warm, no hallucinations, mindful, "paper baggy," "crinkly," could read or make phone calls
Subject 3	No report during administration (highest dose, 50 mg). While not clinically depressed prior to trial, had flat-ish affect 2 weeks afterwards—has felt emotionally very well. Baseline reclusiveness seems comfortable and basic inertia is less compelling—a little more willing to get out of her chair "Dose was pretty much perfect"—both out and in, aware and able to talk—and remember most of it; reported that session seemed to go by faster than an hour; "I would do it again"
Subject 4	At 5 minutes—a little relaxation; cold hands At 20 minutes—mildly relaxed, "krinkly paper bag feeling," +2 of 4 (Shulgin scale); would not make phone calls; "now I want to close my eyes"; slightly disabling—feel cognitively sloppy, a little drunk; past experience with 50mg. ketamine lozenge was "stronger than this" At 40 minutes—"paper bag tongue," tinnitus. "I do not think this [treatment protocol] is advantageous or preferred"
Subject 5	At 10 minutes—+2 of 4 (Shulgin scale); would rather keep eyes closed At 20 minutes—"door almost open," +2 (Shulgin scale) At 25 minutes—"I definitely don't want to open my eyes," +2½ (Shulgin scale) At 30 minutes—some nausea, "an ugly 2½" (Shulgin scale) 5 minutes post—"Whew!"; quite "stoned" and nauseated; "I'd never do this again. This is not an anti-depressant!"
Subject 6	At 7 minutes—"something happening," mild, metallic taste, +/- (Shulgin scale) At 20 minutes—high, "loopy," no hallucinations, "can't let go of obsession" At conclusion—"I'd not spend money for this"
Subject 7	At 5 minutes—comfortable, peaceful, "going flowey" At 11 minutes—"very high," smiley, numb hands At 20 minutes—floating, eyes closed, "I don't want to talk" At finish—"laughy, bound in my chest," with open eyes—fuzzy vision, peaceful, puffy eyelids, can't breathe deeply
Subject 8:	At 3 minutes—heaviness in head At 5 minutes—floaty, relaxed, "a familiar falling feeling but very gentle" At 20 minutes—"very, very relaxed," "not particularly insightful, in my opinion—not conducive to therapeutic insight" At 35 minutes—very relaxed, less intense, "very dissolving," could walk with support, "couldn't drive," peaceful, very tuned into all sounds

from what one might believe to be conventional sanity. It is possible that this relaxing effect might lead to a more robust and enduring antidepressant response.

Discussion

Based on participant reports in this small group, the intramuscular (IM) route of administration initially appears to be safe, effective, and less burdened with a

medical context that includes additional and costly technological infrastructure that is necessary when administering ketamine intravenously. It is well known from psychoactive research that a patient's mood and the setting in which that research is conducted may have significant impact on the quality of the resultant experience. In such treatments a medicalized context

has the potential to create an alienating atmosphere that may diminish beneficial effect (e.g., Fadiman & Kornfeld, 2013). Provision of IM ketamine offers the advantage of administration in a comfortable office setting, with appropriate safety measures available.

The effects of ketamine appear to be related both to dose and to subject sensitivity, and only partially to body weight. In this study dosage was based on body weight at a rate of 0.5mg/kg. Subjects with greater body weight who received higher dosages had more of an anesthetic/sensory effect and reported deeper experiences. For example, a female subject who reported significant positive effects had the highest body weight, and received the highest dose (50mg). This outcome is consistent with the researcher's experience that drug effect and body weight are related but not linearly correlated. It is generally the case with psychedelic and other psychoactive substances that individuals have a range of sensitivities irrespective of their actual weight, and that effects are the result of multiple factors, so that a dose that produces intoxication or profound experience in one individual may produce little or no response in another.

Based on extensive experience with ketamine, it is possible to suggest that the sensory effects obtained with dosages used in the NIMH protocol are quite low within the range of effects produced by sub-anesthetic doses of ketamine. As ketamine dosage increases (as to a lesser extent with nitrous oxide) the sensory inputs and perceptual integrations of the senses are progressively turned off at the cortical level, leaving consciousness more and more subject to its own view, experience, and creativity. This state of mind, increasingly separated from external input, bears some similarity to a dream state or a near death experience—a heightened experience of internal consciousness with its own particular linkages fostered by ketamine. Tactile and visual perception are affected at doses of 30–40mg, and olfactory, gustatory, and auditory senses typically shift beginning at around 50mg. As dosage increases, penultimately, this unique consciousness itself diminishes and there is increasing memory loss of the experience—hence the limits on the amount of ketamine that is evocative of the state. Conscious awareness is significantly impacted at 150mg or higher, tending toward anesthesia as dosage increases. Beyond a certain dosage range this impact on consciousness is a self-evident drawback for an assisted psychotherapy experience.

Antidepressant substance treatments can be thought of in categories relating to effects on consciousness

according to the schema I am elucidating below, each illustrated by typical examples, based on my experience as a psychiatrist:

- Interruption of consciousness and breakage of the stream—ECT, narcoanalysis and induced sleep in a continuum to coma
- Disruption of consciousness, mild—NIMH IV protocol of ketamine
- Disruption, ego dissolution, and transformation—higher dose subanesthetic ketamine and other psychedelics
- Direct shifting of mood and new experiences of affect—MDMA and other empathogens
- Slow shifting of affective and anxious/obsessional states—conventional antidepressants such as SSRIs
- Potential affective smoothing, re-focus and obsession release—marijuana

In this context, 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; state shift usually does not persist much beyond the immediate effect of the experience, and ordinary mental states along with the habitual state of depression tend to resume quickly. Small disruptions in consciousness produce minor changes in the course of depression, in part because humans tend to ruminate and obsess, because character is hard to shift, because humans have an ongoing but changing experience of external conditions, because external conditions do not change due to having a ketamine session, and because individuals live in their own history and the history and culture of the external environment.

As noted, Luckenbaugh et al. (2014) indicated that dissociative effects predicted a sustained antidepressant response. Subjects in this study who were experienced ketamine users received doses in accordance with the NIMH protocol that produced relatively mild dissociative symptoms, and most of these reported only minimal beneficial impact. This is consistent with studies that show the antidepressant effect at these low dose levels to be short-lived.

Summary and Conclusion

The effects of ketamine are related to dose and subject sensitivity. For the most part, the higher the dose, no matter what the route of administration, the greater the anesthesia and interference with sensory modes, the

greater the perceived internal stimulation and isolation of consciousness to mind-only phenomena.

The antidepressant effect of the NIMH IV protocol tends to be short-lived and has only been extended by repeated administration of IV infusions and by being a component part of an extended psychotherapeutic modality.

The rapid onset of action of ketamine as an antidepressant appears to be due to its disruption of ordinary consciousness and its anesthetic properties. There is much more work to be done to elucidate a specific antidepressant property of ketamine, separate from or attached to its dissociative effects.

With the possibility that higher doses may produce antidepressant and other positive effects that are more robust and sustained than with the NIMH IV protocol, further explorations of ketamine's effectiveness are highly desirable, given the potential benefits of ketamine assisted psychotherapy. Higher dosages will certainly include a more psychedelic component than occurs in administration of the NIMH IV protocol.

Not all ketamine experiences are positive and easy (see Kolp et al., this issue). Potential use by any route includes the possibility of having difficult experiences, best served by presence in a supportive, safe setting. With positive preparation and administration in a safe and comfortable environment, given the physiological safety of ketamine, subjects may well derive great benefits from dissociative, altered state experiences. This has been the case with the psilocybin work being done at Johns Hopkins by Griffiths, Richards, McCann, and Jesse (2006), and in the MDMA assisted psychotherapy work reported by Mithoefer, Wagner, Mithoefer, Jerome, and Doblin (2011) and the Multidisciplinary Association for Psychedelic Studies (MAPS). One can apply similar models for IM ketamine administration that would constitute a ketamine assisted psychotherapy protocol, without the encumbrances of IV administration and hospital settings.

The fact that there are disparities in reports about the efficacy of ketamine as an antidepressant at doses used in the NIMH protocol, and the possibility that higher doses may produce effects that are more robust and sustained than current formulations, calls for further explorations of ketamine's effects—potential antidepressant, personality transformation, anti-obsession, amongst others. Higher dosages will certainly include a more psychedelic component than occurs

in administration of the NIMH IV protocol. With positive preparation and administration in a safe and comfortable environment, given the physiological safety of ketamine, subjects can generally be expected to be able to emotionally handle their experiences. This has been the case with the psilocybin work being done at Johns Hopkins by Griffiths, Richards, McCann, and Jesse (2006), and in the MDMA assisted psychotherapy work reported by Mithoefer, Wagner, Mithoefer, Jerome, and Doblin (2011) and the Multidisciplinary Association for Psychedelic Studies (MAPS). However, in rare instances profound nadir experiences may also occur (see Kolp et al., this issue). One can apply similar models for ketamine administration that would constitute a ketamine assisted psychotherapy protocol, without the encumbrances of IV administration and hospital settings.

Limitations and Delimitations

The small sample size limits the validity of this study, and qualitative results are not widely generalizable. The fact that subjects were experienced ketamine users may have biased their attitudes toward or perceptions of the effects of the intervention. Participants were not significantly communicative during intervention, so qualitative reports were thin. Group discussion was not recorded and the presence of the researcher in the group discussion may have influenced the recommendations.

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About the Author

Philip E. Wolfson, MD, is the Principal Investigator for the MAPS sponsored FDA approved Phase 2 clinical trial of MDMA Assisted Psychotherapy for Individuals Suffering with Anxiety Due to Life Threatening Illnesses. Practicing psychiatry/psychotherapy in the Bay Area since 1977, Dr. Wolfson has been on the faculties of UCSF School of Medicine, JFK, and CIIS, and has been at the forefront of the development of alternative, progressive psychotherapies. Writing on politics, medicine, psychiatry, psychedelics, consciousness, Buddhism, and bereavement, he is the author of *Noe—A Father/Son Song of Love, Life, Illness and Death*. In creation is The Center for Transformational Psychotherapy, established as a base for offering Ketamine Assisted Psychotherapy and progressive psychotherapy in general.

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