KETAMINE-ASSISTED PSYCHOTHERAPY FOR INFUSIONS (KAP-I): GUIDELINES FOR PRACTICE

by

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Abstract

Ketamine has shown remarkable promise in mental health treatment, yet few guidelines have been published for the purpose of assisting psychological providers with key points to consider when delivering therapy concurrently with this procedure. This dissertation explores the effects of ketamine, the historical aspects of psychedelic treatment, and how to deliver therapeutic interventions while participants are under the influence and makes suggestions around how to deliver treatment to improve patient outcomes. Guidelines related to assessment, appropriateness, and timelines are discussed, along with logical and theoretical underpinnings, psychopharmacological information, and appropriate treatment strategies for practice are proposed.

Dedication

There are far too many people to thank for the years of effort, time, and investment in realizing and completing this project. First off, I need to thank my husband, Jon, for supporting me through this rigorous time and always being a beacon of hope to finish this project. My mentor, Dr. Natalie Marr, for pushing me into this topic and her countless hours of support for me along the way. My friend and colleague, Dr. John Huber, as none of this would be possible without him. To Dr. Carl Bonnet, who brought me into the world of ketamine and opened my eyes to the possibilities and realities of this treatment methodology. To my parents, Cliff, and Connie, who have always supported me and my endeavors, being my biggest fans and emotional support. I lost my father during the final phases of this project, and I could not have gotten to this point if it were not for him and my mother. And to the hundreds of colleagues, friends, and even patients, who have walked alongside me throughout this journey. This seminal work is dedicated to all who have been there for me, who I cannot graciously thank enough.

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CHAPTER 1. INTRODUCTION

Background of the Problem

For centuries, humankind has been endeavoring to understand their own internal processes. Writings in the time of Plato referred to this phenomenon as *enkrateia*, or a sense of mastering one's sense of self (Dorion, 2007). As centuries progressed, the study of psychology and human understanding emerged from the late 19th century, developing into the practice it is today (Hunt, 2007). From time immemorial, indigenous societies have engaged in the use of hallucinogenics in religious ceremonies, for the application of rites of passage, and other cultural purposes (Davis, 2004). In recent years, the synergizing of hallucinogenic and therapeutic modalities has appeared to produce beneficial effects which have broadened the application of these two separate paradigms into one emerging field: psychedelic-assisted therapy (Dore et al., 2019; Wolfson P. E., 2014; Wolfson & Hartelius, 2016). One of the most prominent substances that has emerged in this field has been the off-label use of ketamine.

Ketamine, as a drug, has been in use for approximately 60 years (Dorandeu, 2013). After its discovery in 1962, known then as CI-581 after its successful synthesis from phencyclidine, ketamine began to be used in clinical trials in 1964 and was later integrated into general practice (Dorandeu, 2013). By 1970, it had been approved by the Food and Drug administration for the established purpose as a dissociative anesthetic (Hyde, 2015).

Historically, ketamine has been implicated in numerous applications other than an anesthetic. Treatment for various maladies began in the 1990s for treatment of substance use disorders related to alcohol and opioids, and for psychological disorders, including obsessive-compulsive disorder, eating disorders, and depression (Hyde, 2015). The most remarkable

efficacy has been identified as that with major depressive disorder, and while there are wide implications for other treatments, the guidelines that are herein described will apply only within the confines of the treatment of depressive disorders, generalized anxiety, and posttraumatic stress disorder.

While ketamine has been utilized in treating depression, the option of integrating talk therapy as an adjunct has been typically overlooked or even dismissed within the medical community due to it being an intoxicant and historical drug of abuse (Perry et al., 2007). Though it has been applied and chronicled by a few psychiatrists such as Philip Wolfson, M.D. (Wolfson & Hartelius, 2016), no readily obtainable guidelines appear to exist for the application of talk therapy with the novel intravenous infusion method of ketamine. As a result, the purpose of this dissertation is to establish worthwhile guidelines of practice to assist clinicians across the mental health field to become trained and aware of ketamine as an adjunctive method of treatment.

Statement of the Problem

Currently, no easily identifiable guidelines exist to develop training or manualization of psychotherapeutic methods related to psychedelic medicine. Because of a lack of understanding regarding ketamine and its purposes in use by most psychotherapists, documenting findings, outcomes, and potential recommended practices for the delivery of psychotherapy with ketamine as an adjunct to therapy does appear to be a prudent area for development. Recent literature has identified these limitations and have also echoed these concerns regarding *substance-assisted psychotherapy* (Thal et al., 2021), of which ketamine would fall under. Because of these remarkable limitations, this program will endeavor to bridge the gap that is currently missing.

Another area of consideration is around cost and accessibility. Ketamine as a treatment comes at a considerable cost to the patient. Adding further interventions, such as adjunct psychotherapy, can also increase those costs. While these costs may impact a patient's ability to pursue these treatments, it does not mean that ketamine should be left without thoughtful approaches to delivery guidelines. As such, ketamine treatment centers do appear to continue growing across the country as demand increases (American Society of Ketamine Physicians, Psychotherapists, & Practitioners, 2022).

Purpose of the Program Development

The purpose of this program is to delineate and define necessary guidelines of what the best approach is to Ketamine Assisted Psychotherapy for Infusions (KAP-I). While a practice related to Ketamine Assisted Psychotherapy (KAP) has been utilized with other ketamine delivery methods, i.e., intramuscular injection, oral administrations, and blended applications with other substances (Wolfson P. E., 2014; Wolfson & Hartelius, 2016), extraordinarily little documentation or guidelines exists in the delivery with intravenous (IV) infusions. Due to the bioavailability and absorption differences between these methods, experiences do tend to be varied between them (Mathew & Zarate, 2016; Salvadore & Singh, 2013). Therefore, the establishment of specific guidelines and boundaries of practice toward a ketamine infusion model is the purpose of this dissertation. Assisting clinicians to better understand the various ketamine delivery methods, which can and do affect patient experiences, appears to be necessary to assist in better patient outcomes and for practitioner awareness. The primary focus in this dissertation will be primarily related to delivering KAP-I.

Need for the Program Development

The goal for this type of program creation is to provide a primer for mental health professionals who are interested in psychedelic medicine to become familiarized with the purposes and approaches of ketamine treatment, while also understanding the psychological effects of dissociative experiences and how therapeutic interventions can assist during these encounters. Furthermore, it can also be a resource for clinicians who are practicing ketamine-assisted psychotherapy for a more in-depth training to continue to facilitate their education related to ketamine and its effects. In order to expand understanding of how to best approach these treatment strategies, clinicians will be better enabled to understand the medical approach for treatment while augmenting patient outcomes with integrated mental health intervention. By creating this synergy, patients can be assured that mental health providers understand what is required for this medical procedure to help unlock their true potential through ketamine treatment.

Because ketamine is becoming more readily available in clinics across the country with now over 400 clinics operating in most of the United States (American Society of Ketamine Physicians, Psychotherapist & Practitioners, 2022), reasonable guidelines and educational around ketamine is highly recommended to ensure that mental health professionals who are being brought into ketamine treatments are prepared for such a task. Early use of ketamine as a mode of treatment tended to be limited to geographic areas where the use of psychedelics was acceptable to local providers and were performed in an underground capacity to observe the effects and measure any observable benefit (Wolfson & Hartelius, 2016).

Early pioneers of the practice would gather and discuss their own experiences of ketamine use, often while using other substances as well, and were documented for the purpose of detailing their experiences with the costs and benefits of the practice (Wolfson & Hartelius, 2016). This practice shared a similarity to other's experiences with dimethyltryptamine (DMT) and documented by the clinicians of those studies as well (Strassman, 2000), or with the use of lysergic acid diethylamide (LSD) and psilocybin mushrooms (Hofmann et al., 1959; Lee & Shlain, 1985).

Currently, there are differences of opinion and philosophy regarding the safety and efficacy of ketamine for patient care (Bonnett, 2018; Foster, 2021; Han et al., 2016; Wolfson, 2014). These philosophies can change between medical providers due to their comfort levels with using ketamine intravenously (Bonnett, 2018). This is due to the ideas that ketamine is not considered a primary treatment but should be secondary or tertiary only after the use of other classes of pharmacotherapies or treatment strategies (Foster, 2021). By empowering mental health providers to be up to date in current and emerging practices is key to assist in developing a more centralized methodology rather than ad hoc approaches based on individual experiences.

This approach will utilize a framework of collaborative care with medical providers to best address patient outcomes and ensure better communication between providers (McDaniel et al., 2014). This approach will assist in creating a more worthwhile understanding for mental health providers, while also helping ketamine providers know what to expect from mental health professionals who are collaborating on patient outcomes and coordinating treatments.

Significance of the Program Development

This program is set to establish wide-ranging guidelines in the practice of dissociative therapy treatments. Approaches that blend other elements of understood methodologies that would not work by themselves has come from years of integration into medically delivered practices (Bonnett, 2018; Foster, 2021) and learning what patients are able to accomplish while under the influence of ketamine will continue to expand the application of this modality (Huber, 2018). Currently, very little, if any, literature exists which is accessible to a widespread audience. Therefore, the availability of such information is considered beneficial to the greater mental health community at large.

Assumptions and Limitations

Ketamine is not a universally accepted form of therapeutic intervention in the medical or mental health community at the current time. There appears to be a belief among medical providers that ketamine should be a tertiary level of treatment option and not one that is a reasonable form of primary treatment (Bonnett, 2018; Foster, 2021). Some believe that other forms of treatment, such as multiple SSRI/SNRI intervention, electroconvulsive therapy (ECT), transcranial magnetic stimulation (TMS), or other such medical interventions should be attempted prior to the administration of ketamine (Bonnett, 2018; Foster, 2021). As ketamine has had a long-standing effectiveness and well documented effect panel (Fadiman, 2011; Fourcade & Lapidus, 2016; Mathew & Zarate, 2016), it is suggested that these preconceived notions do not reflect the current understanding of the available literature.

While ketamine is gaining popularity, the realities of differing philosophies around delivery do exist. Clinics may utilize intravenous, intramuscular, or oral administrations to treat

patients, which is ultimately their choice, and appears to vary based on the philosophy of the medical provider (Bonnett, 2018; Dore et al, 2019, Foster, 2021). It is not the purpose of this dissertation to establish or dictate medical guidelines, but to instead give mental health providers the information to determine the efficacy of treatment through patient reports and observations, and to collaborate with medical providers to provide feedback.

It is also prudent to assist mental health professionals to learn to navigate these philosophical differences with medical providers to assist in delivering the best practices of psychedelic medicine, as input to treatment may be sought by medical providers from the mental health professionals. It is suggested that the quality of the experience of the patient is best described by the mental health provider to the medical provider for treatment planning and dosage.

Definition of Terms

AMPA: α-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid: a compound which mimics Glutamate, and is an agonist for the AMPA receptors in the brain, believed to be implicated in memory formation (Ago et al., 2019; Purves et al., 2017)

Dissociative Response: The onset of an association of unrelated perceptions or ideas from the inability of the mind to perform operations of judgement and reason (Moskowitz et al., 2008). This condition is directly attributable to the use of ketamine in a clinical setting and is the impetus of having a therapeutic response.

Ego Dissolution: a disruption of ego-boundaries, which results in a blurring of the distinction between self- representation and object-representation and precludes the synthesis of

self-representations into a coherent whole (Nour et al., 2016). Overall, it is a compromised sense of self which is onset during a psychedelic experience with ketamine.

Enantiomer: either of a pair of chemical compounds whose molecular structures have a nonsuperimposable mirror-image relationship to each other (Merriam-Webster, n.d.).

Glutamate: an excitatory neurotransmitter which is known to interact with other neurotransmitter systems (Carlson, 2017). It is considered the principle excitatory neurotransmitter that exists in the brain with numerous applications and facilitations that occur in various organ systems and the nervous system (Meldrum, 2000).

Mnemonic Processes: the cellular and molecular action of memory consolidation, retrieval, and reconsolidation (Inserra, 2018).

NMDA: *N*-methyl-$_{D}$-aspartate or *N*-methyl-$_{D}$-aspartic acid: Receptors which are implicated in long-term potentiation in learning and memory formation which have also been associated with ketamine due to its antagonist effects on the NMDA Glutamate receptor (Carlson, 2017).

Psychomimetic: producing effects (as hallucinations or paranoid delusions) that resemble or are identical with psychotic symptoms (Merriam-Webster, n.d.).

Psychotomimetic: tending to induce hallucinations, delusions, or other symptoms of psychosis, typically though the use of a drug (The American Heritage Dictionary of the English Langugage, n.d.).

Treatment-Resistant Depression: Being treated for depression through available means (i.e., pharmacotherapies, psychotherapy, etc.) and not seeing an improvement in overall symptoms from the use of these standard means (Mayo Clinic, 2021).

Expected Findings

With the implication of an emerging field, it is difficult to determine the documented efficacy of this treatment and methodology. Few double-blind resources do exist, mostly among military researchers (Burger et al., 2016), and are more oriented towards suicide prevention while also examining the effects of ketamine on depression. It is widely documented that ketamine does a remarkable job in counteracting acute suicidal thoughts (Ago et al., 2019; Aleksandrova et al., 2017; Burger et al., 2016; Grunebaum et al., 2017; Hartberg et al., 2018; Mathew & Zarate, 2016; Niciu et al., 2014). It is expected that many of the necessary applications of treatment will be laser focused on the specific group being studied. It is the purpose of this dissertation to be a more widely scoped delivery to a widespread population for an integrative effective of treatment management and design. It is also to introduce the therapeutic process into ketamine infusions for a synergy-based approach in delivering mental health treatment with medical intervention.

Organization of the Remainder of the Dissertation

The following chapters will provide a layout for understanding patient responses, establishing pre- and post-treatment results to determine efficacy, and to outline potential methods of addressing situations as they occur in treatment. Chapter 2 will discuss the history of ketamine and its known effects on mental health conditions along with a literature review on specific populations which are considered benefitted from treatment. Chapter 3 discusses the needs for this type of program due to the lack of information that exists in the current mental health and medical climate. In Chapter 4, an outline of the various steps that need to be taken in addressing patient needs, provider relations, and the realities of scheduling time for patient care

in this capacity are discussed while also outlining a step-by-step approach to patient strategizing, delivery of services, and post-infusion series steps to determine efficacy and re-assessment of symptom severity. Chapter 5 discusses future exploration of the realities of ketamine treatment and next steps in fine tuning the delivery method described in this program.

CHAPTER 2. LITERATURE REVIEW

Introduction to the Literature Review

Current research regarding the use of ketamine as a mental health facilitated treatment has been slowly emerging over the past 20 years. It is believed this is due to the continuation of the burgeoning field of psychedelic medicine in treating various mental health concerns as a fringe element of the literature. A cursory review of the current literature appears to indicate that the emergence of research that is being published seems to recapitulate existing research with the continued understanding that there is a potential benefit from utilizing psychedelic medications like ketamine but are not limited to this medication. Current access to hallucinogens, such as psilocybin mushrooms in Oregon, is being overseen by the Oregon Health Authority Public Health Division's Center for Health Protection and is being implemented for public access to these mushrooms in 2023 (State of Oregon, n. d.) which seems to reflect the trend of increasing access to these substances. This broadening of the application of hallucinogenics and psychedelic medicine with ketamine, which is currently offered in numerous states around the US, appears to be the most accessible, for now, due to its long history of accessible side-effects and a broad understanding of the mechanisms of action (Mathew & Zarate, 2016). The research presented reflects the more recent understandings of how researchers have utilized ketamine to elicit certain treatment effects, primarily around depression, anxiety, and posttraumatic stress, but also delves into some of the historical contexts for these applications.

While there does appear to be further applications outside of treatment related to depression, anxiety, and PTSD, it is outside the scope of this project. What information is available related to substance abuse treatment or for the treatment of obsessive-compulsive

disorder by utilizing ketamine will not be thoroughly explored in this project but will be discussed in the relevant research presented for this literature review.

Further understanding of how hallucinogens are utilized will also be a significant component of this project. It is believed that hallucinogenic use for introspection is not a new concept, and has existed for centuries (Warms et al., 2004). However, the most recent emergence of these practices is what is considered the center of this type of project, and will build upon the existing literature, its history, and its application. While it is not presumed to be groundbreaking information, it is believed to be presented in a linear fashion to provide a basis of understanding of ketamine, psychedelic medicine in general, and its application.

Theoretical Orientation

The use of ketamine as a facilitator for psychotherapy is a burgeoning field that has no clear operating boundaries outside of early documented usages from an *off-label* approach (Wolfson & Hartelius, 2016). As psychedelic medicine is not a new concept (Fadiman, 2011; Wolfson & Hartelius, 2016; Wolfson, 2014), the use of psychedelic medications for the treatment of depression and PTSD (American Medical Association, 2014) is growing and is becoming more and more mainstream from a medically oriented standpoint (Dore et al., 2019). In the meantime, various mental health providers are seeing this as a potential cutting-edge treatment, though there are no formal guidelines that readily exist for the delivery of talk therapy, leaving the opportunity to develop such a course of treatment as a potential area for program design. The purpose of creating guidelines around delivery of therapeutic intervention during the administration of ketamine is to foster knowledge to clinicians about best practices of what type of approach to take when people are under the influence of ketamine.

It has been proposed that a new paradigm of psychology, proposed to be *psychedelic social psychology*, be founded for the purpose of integrating psychedelics into practice to assist individuals to dig into their internal processes through the implementation of psychedelic substances (Lyubomirsky, 2021). While Dr. Lyubomirsky contends that social psychologists are prime to be brought into the current era related to psychedelics, the same can be said for clinical psychologists and mental health professionals. It is suggested that this broadening be more pointed into the current approach of facilitating psychedelic use for the purpose of wellness and trauma-related relief.

A group of varied professionals, to include psychologists in Canada, are also calling for the expansion of treatment through the implementation of use of psychedelics (Rochester et al., 2022). These professionals contend that research has been conclusive in implementing this type of treatment among psychiatrists, psychologists, palliative care providers, anthropologists, ethicists, religious professionals, and legal practitioners (Rochester et al., 2022) and suggest expanding the accessibility to these alternative treatments.

A potential underpinning of this type of approach is mirroring that of Cognitive Processing Therapy (CPT) which was developed to assist in overcoming symptoms related to Posttraumatic Stress Disorder in veterans, but has also shown efficacy in treating sexual assault, childhood-related traumas, combat-related events, and even weather events and natural disasters (American Psychological Association, 2017). The aspects of this type of treatment that are important are related to psychoeducation during which educates patients around their experiences, emotions, and regulation before and during their individual sessions. It is considered that CPT is highly manualized with a specific topic or agenda to discuss during each

session and maps out homework or writing assignments to be completed between sessions to explore during the next session (Monson et al., 2014); however, it is noted that CPT is not the only approach that utilizes this method. These approaches are integral in establishing the therapeutic process throughout treatment and creates a model for application throughout a 12-session framework (Resick et al., 2008). This model does appear to lend itself to this type of intervention and program as the patient's participation is necessary. It is posited that by removing the ego temporarily will assist in facing these issues without the trauma-response that is elicited when bringing these memories to mind in an otherwise therapeutic session, though it can also be beneficial for other concerns that are not especially trauma-oriented.

As the majority specialization is around Cognitive Behavioral Therapy (CBT) in training new practitioners, a model related to CBT will also be integrated into the approach that is presented. Many of the approaches that are considered around processing through trauma from a trauma-focused perspective with positive results (Burger et al., 2022), addressing depression through self-regulation (Barton & Armstrong, 2019), and managing anxiety through exposure and response management (Morrow & Dupont, 2018). These approaches are founded in guided imagery to implement cognitive restructuring (van Teffelen et al., 2022) to bring about effective change in these populations. Several of these approaches will be discussed throughout the following chapters.

Review of Research Literature

Ketamine as a drug was synthesized from phencyclidine in 1962 by Calvin Lee Stevens, Ph.D., who was an Organic Chemistry professor at Wayne State University (Dorandeu, 2013). It has long been considered a safe anesthesia that could be used in the field or in the surgical suite,

though there were further implications of other use that were later discovered (Dorandeu, 2013; American Medical Association, 2014). In 2019, it was approved by the Food and Drug Administration to treat depression and has been called “miraculous” in its application (Moghaddam, 2021). It is the approach of this dissertation to lead to wider understandings in helping individuals become more empowered in making informed decisions of alternatives to antidepressant medications that may have been determined to not have worked for them (Pollan, 2018).

Integration of varying styles of treatment when used in conjunction with each other can promote better understandings of outcomes (Agency for Heathcare Research and Quality, 2013). Understanding that methods that exist independently can also be augmented by utilizing different methods to observe potential outcomes. Ketamine infusion therapies have already shown potential benefits and do appear to have potential benefit when integrated with psychotherapy (Dore et al., 2019). However, ketamine has shown to have wider benefits than that of the early discovery of the drug, as evidenced by the emerging research around its potential uses outside of the surgery suite.

The Historical Emergence of Medicine and Psychedelics

The current idea related to the implication of medicine is a recent application (Roder, 2004). Historic tribes in Nigeria and throughout most of Africa relied on the use of witchdoctors to overcome maladies (Roder, 2004). The same can be said for Central and South American cultures and the prevalence of ritual shaman or *curanderos*, also known as folk healers (Krassner, 2004). These practitioners would perform therapeutic healing and implemented *universal therapeutic techniques*, such as having a shared faith, intertwining the emotional

implications of psychotherapy, exploring the role of groups and social influences, reflecting the influencing power of therapy and of the therapist, and guiding individuals through the process of catharsis (Krassner, 2004). These practitioners also shared similar worldviews with those they worked with, exhibited therapeutic qualities, performed processes which raised expectations in those receiving therapy, and exhibited a command of therapeutic techniques, all of which were considered beneficial for others to accept their help (Krassner, 2004).

Davis (2004) states that there are three types of substances that produce mind altering effects: *psychotomimetics*, or psychosis mimickers, *psychotaraxics*, or mind disturbers, and *psychedelics*, or mind manifesters. Each type tends to induce dreamlike experiences with perceptual alterations in sensory perceptions (Davis, 2004). He also suggests that most hallucinogens are plant-based and have been either duplicated or mimicked in chemical form (Davis, 2004). One of the most remarkable and well-known substances, *ayahuasca*, has been in use in indigenous populations for centuries, which some estimate has occurred since before 2000 BCE in Ecuador (Naranjo, 1986).

These ancient ceremonies have relied on the ability for humans to seek internal understanding using psychedelic experiences (McKenna et al., 1998). It has been suggested that humankind has always relied upon the use of facilities to gain awareness and knowledge of their internal processes (McKenna et al., 1998). However, medicine, it seems, is mostly accepted now in a wide range of societies, however certain applications appear limited in others (Davis, 2004).

In the early 1980s, it became clear that the research had become antagonistic towards the exploration of psychedelic medicine (Walsh, 1982). Walsh (1982) argued that through the application of misinformation and sensationalism, psychedelic experiences were considered

negative or dangerous with no potential for beneficial outcomes. Through his years of research, he determined that psychedelics were more positive and beneficially influencing to those who would use them more than negative (Walsh, 1982). Ultimately, he would argue that psychedelics could assist people in developing beneficial outcomes through their use (Walsh, 1982).

Early Literature on Ketamine

While ketamine has been in use since the 1960s, with its first human trial occurring on August 3, 1964, it took researchers approximately 30 years to begin performing research in the 1990s related to identifying the potential other uses of ketamine outside of anesthesia, such as the antidepressant effect (Mathew & Zarate, 2016). This early history included identifying detangling the stigma from phencyclidine, which was a predecessor of ketamine (Mathew & Zarate). Much of the research in the early 1990s was performed on varying animal models to measure the effects on the *N*-methyl-$_{D}$-aspartate (NMDA) receptors (NMDARs) and the processes it elicited (Mathew & Zarate, 2016). But this was only the beginning of the research that would come forth after these initial findings.

By the mid 1990s, ketamine had become more identifiable in the research due to the growth of an illicit user base which led researchers to endeavor to find out why the drug had become one of abuse (Dalgarno & Shewan, 1996). The researchers utilized a semi-structured interview style to gather information from these illicit users who resided in Scotland (Dalgarno & Shewan, 1996). The users described the sensation of ketamine to the researchers in the following manner: as feeling a sensation of light throughout the body and colorful visions; a complete loss of any sense of time; distortions of body size and shape in bizarre manners and skewed perceptions of bodily integrity; feeling like they were floating; feeling as if they left their

own body; profound internal insights related to existence or the sense of one's self; being "at one" with the universe; and having visions of supernatural or spiritual beings (Dalgarno & Shewan, 1996). Among the sample of 20 users that the researchers talked to, most said they had used ketamine occasionally, but the use ranged from once to approximately 100 times and would typically use the drug intranasally in approximately $1/16^{th}$ to 1/4 of a gram size doses, though several had utilized the drug via smoking, swallowing, or snorting as a nasal spray, with only two having injected it intramuscularly (Dalgarno & Shewan, 1996).

Krystal, et al. (1998) described the ketamine effect as being *psychomimetic*, or producing effects (as hallucinations or paranoid delusions) that resemble or are identical with psychotic symptoms (Merriam-Webster, n.d.), as rated by the Clinician Administered Dissociate States Scale (CADSS). This instrument assesses if the patient experiences things in slow motion, unreality, separation from experiences, feeling outside their body, and so forth. The crux of these ideas appears to capture the feeling of being dissociated in conjunction with ketamine intoxication. The necessity for understanding here is that ketamine will produce various effects, but it is believed that dissociation is a shared experience among most users (Krystal et al., 1998).

Krystal and his team (1998) administered ketamine to 23 healthy individuals through an intravenous method in conjunction with lorazepam to determine the differences these two medications elicited when combined. It was found that ketamine produced behavioral responses that would be seen in patients with schizophrenia and the associated positive and negative symptoms and dissociative symptoms (i.e., perceptual alterations) (Krystal et al., 1998). Interestingly, it was found that lorazepam amplified the effects of ketamine related to sedation, attentional impacts in functioning, and amnestic effects, but had no meaningful synergistic

effects on a pharmacokinetic level (Krystal et al., 1998).

Krupitsky and colleagues (2002) set out determine how well ketamine could assist in detoxifying from heroin and found that the psychedelic experience has been promising in treating substance abuse due to the effects that are elicited, though acknowledged it was difficult to generalize the findings due to a wide array of results. In their study (Krupitsky et al., 2002), the researchers screened 70 subjects for treatment with ketamine between two groups of high and low-dose groups composed of 35 participants each and were long-term users who were abstinent from heroin for approximately the same duration of time. Multiple assessment measures and instruments were used to assess the presence of psychiatric conditions and to account for their individual psychopathologies in order to measure patient ratings pre- and post-infusion sessions (Krupitsky et al., 2002). Follow up sessions were completed monthly through a 24-month schedule on a blind basis so that the rating psychiatrist were unaware of which conditions the participants were assigned to, and to examine any relapse or drug use after the completion of the infusion series (Krupitsky et al., 2002).

The therapeutic interventions were divided into three stages, being a preparation stage, during which time there were guided sessions related to the subject's dependence on heroin, the ketamine infusion that was accompanied by music and psychotherapeutic intervention, and then follow up psychotherapy sessions that took place several days after the ketamine sessions (Krupitsky et al., 2002). The study's results suggested that high-dose ketamine (2.0 mg/kg) when combined with psychotherapy reflected the most effect when compared to the low-dose group (0.2 mg/kg) (Krupitsky et al., 2002). Interestingly, both groups showed beneficial effects related to anxiety, depression, mood, and activities of everyday life, which was posited to benefit those

who were prone to relapse by the reduction of depressive symptoms (Krupitsky et al., 2002). Both groups also reflected positive outlooks, gained confidence, and found themselves being more emotionally available after the treatment (Krupitsky et al., 2002). The study concluded that high-dose ketamine group benefited for a longer term within the 24 month follow up period than those in the low-dose group, suggesting that the psychedelic experience was more likely to produce that effect than a sub-psychedelic experience (Krupitsky et al., 2002).

Establishing Ties with NMDA and AMPA

A push to understand ketamine's effects and why it has the outcomes it produces are widely seen throughout the current literature (Ago et al., 2019; Dore et al., 2019; Fourcade & Lapidus, 2016; Mathew & Zarate, 2016; Moghaddam, 2021; Salvadore & Singh, 2013; Zorumski et al., 2016). While its early beginnings were related to battlefield use as a field anesthetic, which is still in use today (McGhee et al., 2008), its novel use turns to the realities of treatment for mental health by the effects of dissociation, and effects on N-methyl-D-aspartic acid (NMDA), and α-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid (AMPA) responses (Dore et al., 2019; Mathew & Zarate, 2016).

NMDA and AMPA are implicated in the process of neuroplasticity and are believed to underpin the learning and mnemonic processes that occur through lived experience (Yee et al., 2007). Yee et al. (2007) utilized 18 mice who were bred to overexpress adenosine kinase (ADK), an enzyme which is implicated in regulating adenosine, which is an organic compound that assist in the transmission of glutamate and dopamine, which are believed to have implications related to behavioral regulation and cognitive functioning. The research endeavored to identify how pharmacotherapies affect the symptoms of schizophrenia and how it develops in humans (Yee et

al., 2007). Through a series of behavioral assessments, the mice were exposed to several different conditions where their learning and behavioral regulation were measured along with any implications of working memory deficits that may have developed (Yee et al., 2007). The important implication of this research is through the glutamate and NMDA effects on learning and how this process is implicated in producing new information from being retained, even when affected by genetic disruptions (Yee et al., 2007). These processes appear to be the underpinning of a processes referred to as mnemonic processing.

Mnemonic processes have significant implications in the treatment of trauma disorders, depressive disorders, and anxiety disorders, as these can be the result of learned behaviors or experiences that occur throughout the lifespan (Lakhan et al., 2013). Research by Lakhan et al. (2013) endeavored to understand their role in how these disorders manifest because of NMDA pathway disruptions, resulting in the onset of schizophrenia, mood dysregulation, and even substance-related psychosis. The authors posit that these NMDA pathways may have deeper implications with these disorders, along with the hypothesis that affecting the NMDA pathways can assist in overcoming the onset of psychiatric conditions through pharmacotherapy due to the ubiquity of NMDA receptor sites, especially in the hippocampus and within the limbic system structures (Lakhan et al., 2013). The researchers suggest that the use of NMDA agonists can assist in overcoming many of these psychiatric maladies specifically because of the pathways that are implicated in the onset of these disorders, and that combination therapies can result in more robust outcomes (Lakhan et al., 2013).

Further, mnemonic processes appear to be the basis of how information is sorted, stored, and consolidated in memory formation (Moskowitz et al., 2008). Moskowitz et al. (2008)

compiled research from historical perspectives which attempted to account for traumatic events resulting in dissociation and psychotic episodes and how these perspectives shifted throughout the nineteenth and twentieth centuries, while also exploring the fragmenting of ego through the lens of a schizophrenic break. Further implications of childhood trauma and the results of psychosis are also explored and are expressed through the onset of psychosis and dissociation through the lens of childhood experiences (Moskowitz et al., 2008). These aspects of understanding which are related to the onset of psychiatric disorders in adulthood are necessary components of unwinding an individual's ego and deeper perspectives in order to uncover the genesis of mood dysregulations, anxiety, and trauma.

In relation to the AMPA effects, research by Akinfiresoye & Tizabi (2013) reviewed how the stimulating of AMPA alone can produce antidepressant effects, and how synergizing AMPA and ketamine can further add benefit in genetically modified rats that were bred to exhibit depressive symptoms. The rats were subjected to various behavioral conditions to measure their reactions to both standalone AMPA and AMPA combined with ketamine (Akinfiresoye & Tizabi, 2013). The researchers determined that AMPA treatment alone produced a quasi-antidepressant effect, while the AMPA-ketamine blend showed more improved findings (Akinfiresoye & Tizabi, 2013). Their conclusions suggest that AMPA alone does indicate evidence for an antidepressant effect, further reflecting prior research findings, as well as further showing support for the reduction of depressive symptoms through the administration of ketamine (Akinfiresoye & Tizabi, 2013).

Ketamine has previously been considered a medication that can elicit psychosis, also known as a *psychomimetic response*, due to it mimicking psychotic features, (Julien et al., 2011).

These effects are considered simlar to those of schizophrenia without the long-term effects or permanency of an organic brain dysfunction due to the impact on NMDA receptors and glutamenergic responses (Julien et al., 2011). Interestingly, and uniquely, ketamine does have some interactions with acetylcholine, dopamine, or serotonin, and still produces effects that are perceptual in nature, though the mechanism that controls these effects as a side effect of the drug is considered complex (Julien et al., 2011). It is suggested that the ketamine-NMDA response is similar to that of a benzodiazepine-GABA receptor response, in that the affected glutamenergic response results more in analgesia and an amnestic response (Julien et al., 2011).

The mechanism behind other hallucinogenics, such as psilocybin or LSD, rely on serotonin and dopamine, and produce auditory and visual effects that typically last several hours (Zorumski et al., 2016). While ketamine does directly affect these neurotransmitters, it is not believed to be attributed to the visual heightening and auditory enhancements (Mathew & Zarate, 2016). These effects are not considered as vivid as those with other hallucinogens but do appear remarkable and worthy of understanding (Mathew & Zarate, 2016).

Mathew & Zarate (2016) compiled reports from multiple authors to expand the understanding of ketamine for multiple applications, specifically around TRD, suicide, tolerability related to cognitive efficiency, antidepressant applications, along with applications related to obsessive-compulsive disorder and substance use disorders. This compendium is a novel tool in developing deeper understandings of the medical literature related to ketamine and its myriad applications. The authors note that research for OCD, PTSD, and substance use disorders are necessary to understand wider implications of the use of ketamine (Mathew & Zarate, 2016).

Zorumski, et al., (2016) examined the effects of ketamine to measure the psychomimetic properties as well as the antidepressant effect from a molecular perspective and to understand its effects on cells and neural networks. Exploration of the NMDA receptors, or NMDARs, was the primary focus on measuring the impact of the effects, and how blocking these receptors can lend itself to enhancing an individual's mood state, but the true mechanism appears unclear (Zorumski et al., 2016). The authors posit that there are ongoing investigations to ketamine's mechanism of action which produce these antidepressant effects, especially in relatively small doses, but do not appear to be produced when ketamine is used in anesthetic doses, implicating that dosing is important when utilizing ketamine for the robust antidepressant effect (Zorumski et al., 2016). Further findings of their research suggested that the action on glutamate and the release that is inhibited from the NMDAR response appears to be tied to the antidepressant effects and its durability after infusions are performed (Zorumski et al., 2016), which has been documented in other studies as well (Behrens et al., 2007; Homayoun & Moghaddam, 2007; Schobel et al., 2013, as cited in Zorumski et al., 2016).

Aleksandrova et al. (2017) reviewed the literature related to the synaptic signaling produced by AMPA and NMDA and ketamine's effect on both these pathways and how hydroxynorketamine (HNK) also affected these mechanisms. The purpose of the research was to determine alternatives to ketamine while also identifying potential mechanism that could be produced in alternative pharmacotherapies (Aleksandrova et al., 2017). The authors note that much of the currently available medication options have significant shortcomings, such as a prolonged desired effect time, limited efficacy, and increased risk of suicidal ideation (Aleksandrova et al., 2017).

Pharmacology of Ketamine

The effects of ketamine onset briefly due to its short half-life, believed to be seven to eleven minutes (Fourcade & Lapidus, 2016). Fourcade & Lapidus note that the chemical name for ketamine is (*R,S*)-2-(2-Chlorophenyl)-2-methylaminocyclo-hexanone (2016) and is classified as a complex pharmacological agent that is considered a chiral arylcyclohexalamine (a class of designer drugs) that has an affinity for multiple receptors, such as the opioid Mu (***μ***), Kappa (κ), and Sigma (σ) receptors, of which the highest affinity is for the ***μ*** receptor, NMDA receptors, AMPA, and the excitatory neurotransmitter glutamate. After ketamine passes through metabolization, it produces several metabolites, namely norketamine (NK), dehydronorketamine (DHNK), six hydroxynorketamine metabolites (HNK), and hydroxyketamine (HK) (Zarate et al., 2012, as cited in Fourcade & Lapidus, 2016). These metabolites are believed to be responsible for the amnestic and analgesic effects due to their amplification after metabolization (Fourcade & Lapidus, 2016).

Ago et al. (2019) endeavored to understand the molecular mechanisms of ketamine effects, how it created an antidepressant effect, and to deepen the understanding of the metabolites that ketamine produces. They examined the effects in the prefrontal cortices of mice in relation to (R)-ketamine, (S)-ketamine, (R)-norketamine [R-NK], (S)-norketamine [S-NK], (2R,6R)-hydroxynorketamine [(2R,6R)-HNK], and (2S,6S)-hydroxynorketamine [(2S,6S)-HNK] (Ago et al., 2019). The authors note in their findings that (R)-ketamine does have a higher potency effect along with longer lasting duration of the antidepressant relief, while also increasing dopamine release and AMPA reaction, where (S)-ketamine does not, but (S)-ketamine does cause an increased serotonergic reaction (Ago et al, 2019). The authors also suggest that

both (R)-ketamine and (S)-ketamine do show increases in serotonin (5-HT) production, but that (R)-ketamine showed a greater increase, while (S)-ketamine reflected a higher amount of dopamine production (Ago et al., 2019). The authors also state that the metabolite effect from (R)-NK, (S)-NK, and (2S,6S)-HNK did not affect 5-HT activity in the prefrontal cortex, but that (2R,6R)-HNK did slightly improve 5-HT production (Ago et al., 2019). The study suggests that the complexity of ketamine and its metabolites provide a wide range of understanding that continues to be developed in the literature.

The effects of ketamine are believed to be short-lived and only tend to occur during the active infusion itself, resulting in relatively rapid recovery times after the infusion is completed while metabolite responses are seen for up to five days after the completion of the infusion (Salvadore & Singh, 2013). Salvadore & Singh (2013) argue that much of ketamine's abuse potential tends to be from self-reported abusers versus analysis of clinical studies but do suggest that adverse reactions such as memory impairment in the short-term for those who abuse ketamine, and that functioning does appear to return to a relative baseline level of functioning after discontinuing abuse. They also suggest that administration conducted under supervision is best to maintain antidepressant effects (Salvadore & Singh, 2013). That is not to say that ketamine cannot be abused but should be kept in clinical applications and under strict supervision (Salvadore & Singh, 2013).

Known Safety of Ketamine

Ketamine has a long history that is shown to be safe and effective in clinical settings (Perry et al., 2007). Research by Perry et al. (2007), reviewed over 800 administrations of ketamine through a sample population of 450 individuals, and found that of those who

experienced any adverse effects was approximately 2% of the sample with minimal residual effects noted after the discontinuation of ketamine, suggesting that the use of ketamine for most healthy individuals was considered safe. The individuals were observed between sixteen different studies between 1989 and 2005 and were administered intravenously through an infusion model or bolus style with an infusion to follow (a bolus is a rapid delivery method of a substance through IV or oral delivery methods) (Perry et al., 2007). In all, no serious adverse effects were noted in the study sample, and of the sample, 2% of subjects were shown to have any impact to mental status that was returned to baseline at the conclusion of the day (Perry et al., 2007). This finding is important in the understanding of how ketamine can have some mild adverse side effects; however, these effects are usually resolved quickly.

A response that is attributed to hallucinogens which is unknown to an individual who has not experienced it before can be jarring and uncomfortable (Newcombe, 2008). In the spirit of first-hand experience to establish a personal understanding of the ketamine experience through field research, Newcombe set out to understand the effects firsthand in the style of the psychonaut experience with the help of a medical doctor, a psychologist, a mental health nurse, and two writers (2008). The project that was set up in the United Kingdom brought together psychologists, writers, and other professionals who were interested in studying the effects of certain drugs and documenting their experiences (Newcombe, 2008). They administered the dose of ketamine through intravenous injection in two doses spread out over a period of two hours of approximately 40mg per dose (Newcombe, 2008). The group tape recorded their sessions and held discussions afterwards to document their experience along with taking notes throughout the trip and later wrote up a completed report (Newcombe, 2008). Remarkably, one of the

participants noted their relief from depressive symptoms, along with not having any notable hang over effects that are observed with other hallucinogens (Newcombe, 2008). The authors argue that their experiences are beneficial to the public due to their willingness to provide an insider's view of what the effects of ketamine are and how they can be applied in further research (Newcombe, 2008).

Statements related to the applications of ketamine that were discovered in the Journal of the American Medical Association (JAMA) Psychiatry communication suggests that there are rapid and robust effects on depression among those who suffer from anxiety and mood dysregulation using ketamine with rapid and repeatable results (Sanacora et al., 2017). The statement also suggests that small sample sizes and long-term research is lacking and calls for further research into these effects (Sanacora et al., 2017). However, they note that the research that does exist appears to support the findings that ketamine does show promise for patients for treatment of depressive disorders in both the short- and long-term through minimal and repeated dosing (Sancora et al., 2017). The statement acknowledges that the lack of research does produce some reticence in their recommendation for wide-spread use due to the uncertainty around populations outside of mood disorders but do remain open to the possibility that ketamine can work in other populations (Sancora et al. 2017).

Ketamine as an Antidepressant

Kennedy (2009) suggests that antidepressant medications are a necessary component of the current treatment of major depressive disorder, and that this form of treatment should offer rapid relief of the debilitating symptoms while also assisting in preventing another episode from occurring. It is suggested to be a necessary step in the overall treatment of acute mental health

concerns around depression and is beneficial in assisting patients in returning them to a functional life (Kennedy, 2009). Kennedy (2009) argues that medications are beneficial when compared to placebo groups in randomized control trials and are found to assist in patients finding benefit from it, but also that limits in their application go beyond the typically prescribed medications, such as venlafaxine versus atypical alternatives, such as agomelatine. This argument does seem to also apply to other alternatives, such as ketamine, for the effective treatment of depression.

Dissociative responses are believed to aide and mediate the antidepressant effects of ketamine (Ficek et al., 2016; Krystal et al., 1998; Luckenbaugh et al., 2014). Luckenbaugh, et al., performed research on over 100 patients who were diagnosed with depression and bipolar disorder to determine if one infusion of ketamine was beneficial after seven days (2014). The findings suggested that the more powerful the dissociative response, the more robust and prolonged effects were observed, suggesting a more durable response was associated with the onset of dissociation (Luckenbaugh et al., 2014). These findings were supported in patients with moderate to severe depressive symptoms that had been ongoing for an average of 55.7 months, yet showed marked improvement over a seven-day, post-infusion period, and were reflective of dissociation as a marker for efficacy among participants (Luckenbaugh et al., 2014).

Other studies suggest that the efficacy of decreasing suicidality is a potential benefit of ketamine, which offers a novel, fast-acting treatment for active suicidal ideation, typically early as 40 minutes after a single infusion, along with a significant decrease in acute depressive symptoms after an infusion within 4 to 72 hours (Soleimani & Murrough, 2015). It has also been documented to address those with treatment resistant depression (TRD) to have a clinical

response after a two-week infusion series (Soleimani & Murrough, 2015). Their review of the literature found that suicidality appeared to be abated within approximately 40 minutes after a single infusion and in studies among four clinical trials that acute suicidality was decreased 230 minutes post infusion (Ballard et al., 2014, as cited in Soleimani & Murrough, 2015).

Han and colleagues (2016) performed a meta-analysis to examine the effectiveness of ketamine in treating individuals who had been diagnosed with major depression. The authors reviewed medical research databases and literature that utilized double-blind, placebo-controlled studies and compared them to placebo-only studies, and analyses were performed to examine results at day 1, day 3, and day 7 (Han et al., 2016). Overall, the data utilized included 368 patients across nine studies, and results suggested that ketamine was significantly more effective when compared to placebo, and the results indicated that ketamine was effective in the rapid decrease of acute symptoms of major depression which they detail is symptoms related to low self-esteem, changes in appetite, and loss of interest in pleasurable activities (Han et al., 2016).

Ficek et al. (2016) reviewed ketamine's dissociative response as it related to the antidepressant effect in mice who were bred to be utilized in a wide array of medical research applications, known as C57BL/6 J mice. By utilizing genetic sequencing and quantitative PCR testing, the team were able to identify that NMDA responses with ketamine were similar to other psychotropics, such as antidepressant medications, antipsychotic medications, anxiolytic medications, psychostimulant medication and opioid medication (Ficek et al., 2016). The findings suggested that ketamine produced comparable effects to memantine (a medication utilized in slowing the progress of Alzheimer's disease) and phencyclidine (PCP). Through these NMDA responses, the authors posit that the effects of ketamine are like those of a

monoaminergic antidepressant and suggests that the antidepressant effect is likely due to this mechanism of action (Ficek et al., 2016).

Niciu and associates (2014) set out to determine if a family history of alcohol use disorder produced any effects on durability related to ketamine treatment. The team examined 52 individuals with a diagnosis of treatment resistant depression and assigned them all to receive ketamine infusions but supplemented their infusions with an adjunct dose of riluzole (a sodium channel inhibitor) or placebo approximately five hours after the infusion (Niciu et al., 2014). The team assigned the individuals between four conditions related to a positive/negative family history for alcohol use disorder and riluzole/placebo groups. Interestingly, the results suggested that the riluzole had no significant effects; however, the individuals who had a positive family history of alcohol use disorder saw an improved antidepressant effect when compared to those who had a negative family history (Niciu et al., 2014). This remarkable result indicates that familial histories are essential to be reviewed when developing treatment strategies.

Moghaddam (2021) further adds to existing knowledge related to the pharmacology of ketamine, the myriad uses, and the neuroscience that is implicated. The author also describes how ketamine has uses as a rapid acting antidepressant, while further exploring the mechanisms of action behind it (Moghaddam, 2021). With the novel introduction of Esketamine, an enantiomer (or mirror image) of ketamine, further understandings of the NMDA agonism and lack of psychedelic response is also presented in the research (Moghaddam, 2021). This compendium of information deepens the current and recent literature in providing a fundamental understanding to the community at large.

Ketamine and Psychotherapy

As the only psychedelic medicine that is currently available for the treatment of depression, ketamine does show potential in psychiatric settings, but one that may be improved through the access of psychological therapies (Dore et al., 2019). Ketamine-Assisted Psychotherapy is a novel approach to continuing the expansion of efficacy with the use of ketamine as a moderator (Dore et al., 2019); however, durability and efficacy studies do appear to be lacking in the research. The premise of Dore, et al. (2019) was the understanding of how ketamine is used to onset trance states which leads to psychological transformation. They posit that it allows patients time away from their lives, away from their overall mind state, decreases negative views, and opens them up to their inner thoughts and feelings, resulting in a suggestive mindset for the receptiveness of therapeutic intervention while under the effects of ketamine and after administration (Dore et al., 2019). They also note that this type of work can be beneficial to a practitioner's perspective on this form of treatment due to the outcomes that are observed with KAP (Dore et al., 2019).

The team reviewed cases from 235 participants to determine effectiveness of ketamine through two regional clinics located in Northern California and Austin, Texas (Dore et al., 2019). Most of the sample were college educated individuals with a mean age of 42.7 years old, and were 48.9% female (Dore et al., 2019). Most appeared to be prescribed approximately three medications for treatment of their various diagnoses and fell within a moderate range of depression and moderate levels of anxiety prior to ketamine treatment (Dore et al., 2019). The results suggested that clinically significant decreases ($p < .01$) were observed in both anxiety and depression scales that were measured after the completion of the series, resulting in overall

improvements for the sample, and participants with more severe pathologies (i.e., history of psychiatric inpatient treatment, suicidal thoughts or actions over the past year, those with higher Adverse Childhood Experiences (ACE) scores) were seen to reflect higher levels of overall improvement, to include the amelioration of suicidal ideations (Dore et al., 2019).

The amelioration of acute suicidal ideations does appear to have been well established in the literature (Burger et al., 2016; Soleimani & Murrough, 2015; Reinstatler & Youssef, 2015; Wilkinson et al., 2017). Burger and colleagues (2016) had an extremely small sample size (n = 3) who were given ketamine while comparing outcomes to a control group (n = 7) that received a placebo. Due to record-keeping difficulties, the study was terminated early; however, showed some successes in the amelioration of suicidality and benefited depressive symptoms (Burger et al., 2016). Soleimani and Murrough (2015) performed a post-hoc analysis related to ketamine and suicidal ideation where they found relief of acute suicidal ideation for a period of up to two weeks among a nine-patient sample size along with citing two other studies that also showed a persistent decrease in suicidal thinking. Reinstatler and Youssef (2015) reviewed nine publications related to sub-anesthetic ketamine administration for the treatment of acute suicidal ideation and cited that each study demonstrated the significant reduction in suicidal thinking among a total of 137 patients. Wilkinson et al. (2017) also reviewed 10 studies that had controls with placebo or midazolam when compared to ketamine treatment and found a rapid decrease in suicidal ideation within 24 hours and up to seven days. It is suggested that these various findings support the hypothesis that ketamine provides replicable and predictable effects on suicidal ideation and ameliorating them in almost all instances.

Limitations of Ketamine

Because of these psychomimetic responses, ketamine is not suggested for individuals who experience organic psychosis, specifically related to schizophrenia spectrum disorders, as it may result in an onset of a psychotic episode, though there is not believed to be any long-lasting complications related to the onset of psychosis in individuals who are not susceptible to it (Krupitsky et al., 2002).

Another potential concern is related to negative experiences and how it may affect patient outcomes. A study by Sklar et al. (1981) discussed how patients may feel some form of anticipation from the intoxication effects; however, these feelings were mitigated with psychoeducation of the effects of the drug and minimized patient's negative opinions. Conversely, it can produce negative effects if proper information is not present, as patients feel as if they are hallucinating versus experiencing the effects of the drug, leading to unpredictable outcomes associated with the intoxicative effects (Sklar et al., 1981). Some patients have reported nightmare-like, frightening experiences; however, it is suggested that these occur more infrequently, but are known to occur (Fine & Firestone, 1973).

Synthesis of the Research Findings

It appears that many of the burgeoning studies related to ketamine's effects meet the same expectations and reflect there are durable, noteworthy effects on treatment of mental health conditions when it comes to depression (Akinfiresoye & Tizabi, 2013; Aleksandrova et al., 2017; Salvadore & Singh, 2013), PTSD (Feder et al., 2021), and anxiety (Aleksandrova et al., 2017; Meldrum, 2000). Further studies do appear to show promise related to the treatment of obsessive-compulsive disorder, and substance use disorders (Mathew & Zarate, 2016;

Moghaddam, 2021). While the research implies there are some understandings of these mechanisms, there are more questions related to the exact mechanism of these effects; however, the observable outcomes appear palpable as illustrated by the continued emergence of new research in the past several years over several approaches to treatment (Aleksandrova et al., 2017; Abdallah et al., 2019; Aust et al., 2019; Krystal et al., 2019). It is suggested that this methodology of ketamine treatment for depression does produce the anticipated effects in most patients (Kennedy, 2009; Mathew & Zarate, 2016; Salvadore & Singh, 2013; Soleimani & Murrough, 2015). Further, the safety and addiction potential profiles of ketamine appear to be well within acceptable limits (Perry et al., 2007).

Some of the key benefits of ketamine appear to be a significant diminishing of active suicidal ideation and active depressive symptoms (Burger et al., 2016). As these are primary reasons for individuals to seek treatment, an observable improvement does indicate the beneficial nature of ketamine treatment. It also reflects how durability of these effects, without the need for continual administration, can result in remarkable and sustainable improvement over time (Zorumski et al., 2016). While the durability of ketamine is not permanent and does require ongoing maintenance, the short-term benefit appears to be around adjusting a negative outlook (Mathew & Zarate, 2016). It is considered that, during this short timeframe, therapeutic intervention can assist in maintaining a longer-term effect (Dore et al., 2019).

The observable outcomes appear to be documented regarding durability and efficacy of an infusion, when considered with treatment of PTSD, in as little as a single dose to show beneficial effects (Abdallah et al., 2019; Feder et al., 2014). This is a significant and useful finding to members of the military who have experienced long-term traumatic effects from

wartime engagement (McGhee et al., 2008).

McGhee et al. (2008) deepened an understanding of how the utilization of ketamine as a wartime anesthetic could affect the onset of posttraumatic stress disorder (PTSD). The analysis reviewed cases between 2002 and 2007 where soldiers who were injured in wartime theater were given ketamine as a surgical medication for anesthesia (McGhee et al., 2008). The findings suggested that of the 119 out of 147 patients who received ketamine during a surgical procedure showed a 27% prevalence of PTSD versus a 46% prevalence of those who were not administered ketamine (McGhee et al., 2008). The study concluded that those who received ketamine had a lower incidence of developing PTSD when compared to those who did not receive it, even with more severe injuries or surgical procedures (McGhee et al., 2008). It is a point of consideration that if a single dose can produce these levels of effect, could an infusion series with a mental health provider who is trained in KAP-I could be considered a more effective form of treatment?

Further effects related to treatment-resistant depression, noted as those who have failed with multiple medications or other interventions, do show significant promise with ketamine treatments (Aust et al., 2019). This also is compounded with ketamine's ability to rapidly reduce acute suicidality in over 95% of patients who receive it during these periods of self-harm thought patterns (Burger et al., 2016). With these types of outcomes, ketamine can be considered a worthwhile adjunct treatment method with meaningful outcomes for those who seek it.

Critique of Existing Research

The rate of depression that is currently being addressed in the United States is thought to be at approximately 7% in the adult population (American Psychiatric Association, 2013). Continuing to understand the impact of treatment-resistant depression and the therapeutic

responses also suggests this is a widening problem with efficacious limitations (Dore et al., 2019). While some research suggests that efficacy among antidepressant medications reflects an effectiveness of approximately 80%, these effects can come with numerous short- and long-term side effects (Kennedy, 2009).

It is suggested that the use of ketamine in myriad fashions shows the utility and usefulness of the drug (Sanacora et al., 2017; Soleimani & Murrough, 2015; Wolfson, 2014; Zarate et al., 2012). These various uses that improve lives through medical application are a testament to pharmacological research and application. While there are new avenues to be discovered in various treatment strategies, very few are related to mental health treatment with the inclusion of therapeutic intervention. It is uncertain if this is due to a lack of desirable research opportunities or a void of understanding of these applications that may be worthy of being published.

One of the major critiques that Salvadore & Singh present to the body of research that is already existing is related to the administration methodology when measuring ketamine's psychomimetic properties versus the antidepressant effect and note that these meaningful differences come in the difference of a rapid method delivery via bolus versus a more elongated process, such as an infusion, to provide relief from depressive symptoms (2013). This is a remarkable difference that likely leads to limited understanding of how ketamine works in different applications.

Further concerns come with the documented treatment strategies around psychedelic medicine and its applications (Dore et al, 2019). Few clinicians have created works around utilization of psychedelics and their benefit to the human mind due to assumed fears and

professional liabilities. Dr. Wolfson is considered an exception and has pioneered the field of ketamine treatments and has compiled a collection of treatments with other clinicians as well since his work began in the 1970s in San Francisco (Wolfson & Hartelius, 2016). However, he and his colleagues have not produced works related to delivering therapeutic intervention with infusion experiences. It is suggested this has opened a door for this dissertation to be written to continue to build upon his work and to establish meaningful guidelines.

Summary

Since its inception, ketamine has shown significant promise as a beneficial medication and tool for treatment of medical uses and mental health treatment (Dorandeu, 2013; Kennedy, 2009; Perry et al., 2007)). Only since the early 2010s have researchers and clinicians began to integrate these practices into new medical procedures to help patients overcome concerns related to efficacy, addiction potential, and long-term outcomes (Dore et al, 2019; Niciu et al., 2014). These concerns are mostly limited to efficacy and abuse potential (Krupitsky et al., 2002). While the efficacy of ketamine is not 100%, it does appear to have a remarkable benefit that is durable for a reasonable duration of approximately two weeks (Mathew & Zarate, 2016).

It should be considered that patients who do pursue ketamine treatment will require monitoring for drug seeking behaviors throughout the treatment protocol and after completion to ensure that they do not seek ketamine as a panacea for escaping emotional experiences (Ago et al., 2019). This growing application and use are rife for further development and creation of worthwhile boundaries of practice and guidelines to assist new clinicians in applying these strategies. After establishing an understanding of what ketamine is and what its effects are, clinicians will be able to approach treatment strategies and applications in actual situations. This

chapter is believed to be a basic primer of necessary knowledge to be able to integrate these guidelines into practice.

CHAPTER 3. PROGRAM DEVELOPMENT PROCESS

Purpose of the Program

Throughout the exploration of the processes of psychedelic medicine, there do not appear to be any easily obtainable or even identifiable guidelines for practice. Consequently, clinicians have historically been left to approach emerging treatment modalities with a *trial-and-error* approach due to a lack of clearly defined or delineated processes. To prevent this, some of the methods that have been attempted in practice and have shown benefit are presented with the purpose of assisting others who have not been in this scenario with understanding on how to best proceed in times of unprompted outcries by patients under the effects of ketamine, how to appropriately go about planning delivery of therapeutic intervention with a ketamine facilitator, and how to assist those who are experiencing uncomfortable emotional states during an infusion. These experiences can be difficult to navigate, and even jarring, without proper experience and education. This program design endeavors to address these unexpected situations from causing the patient harm during an infusion by integrating information from the research and implementing them into the program design.

Needs Assessment Process

As ketamine has grown in popularity and availability, it seems prudent for mental health professionals to understand the necessity for training in delivering psychedelic-assisted treatment in at least one modality. Because there are not many training programs available that are specific to ketamine, this program was born out of necessity; however, this program is meant to be a reasonable starting point for further development of these strategies as the field grows. It is understood that this program is to be seen as a primer to familiarize clinicians with the realities

of delivering treatment to patients who are under the influence of a dissociative drug and the challenges that can present themselves.

Prior methods that have been performed were based on limited samples (Krupitsky et al., 2002), but have since expanded to recent practice in a medical model (Dore et al., 2019). Research related to established literature along with interviews with medical providers (Bonnett, 2018; Foster, 2021) have led to the development of this process. Consequently, it became necessary to ensure that mental health clinicians would have access to quality training from professionals who have been in the field doing this type of work. It is also reflective of the determination of developing these frameworks while also enhancing techniques which ultimately led to the creation of this program.

Further, this program is to help already trained and licensed providers to add expanded tools to their toolbox. It assumes that clinicians who are endeavoring to learn these approaches have an interest in delivering psychedelic-oriented treatment to a population of individuals who are seeking it out as a method of intervention. As the accessibility to this treatment grows in an increasing number of states, it will be prudent for clinicians to be prepared in delivering this service as another provider modality.

It is noted that this approach is not for every clinician due to the necessity to be familiar and comfortable with psychedelics and psychopharmacology. Because of the negative views on ketamine that exist, it will require that clinicians interested in performing this will have to perform a deep dive into the benefits of ketamine while also understanding the potential effects and side effects of administration. This is not to suggest that ketamine is a panacea, and should not be treated as such, but instead it is a facilitator that has robust research and documentation in

over 60 years of use as discussed in Chapter 2.

As ketamine clinics continue to open and expand their presence, along with moves by groups around governmental approval for the integration of psychedelics into the emergence of alternative mental health treatment options, and a review of the current literature, it is clear there are few options for training in this area. Therefore, it became incumbent on creating reasonable guidelines related to mental health treatment in conjunction with medical professionals to learn how these guidelines can be beneficial in producing a different style of relationship with clients to ensure that their outcomes can be augmented into their ongoing care. These needs were established in interviews with medical providers who lent their insight into what would improve ketamine delivery and psychotherapy in conjunction with each other providers (Bonnett, 2018; Foster, 2021). This broadening of a relationship seems somewhat counterintuitive to typical established training methodologies for mental health professions, though, by creating a new pathway and delivery model, clinicians can be highly beneficial in an already emerging practice. Further studies may be necessary to replicate findings to establish the evidence base for this type of treatment option.

Program Design Process

The primary purpose of this dissertation is to establish useful and tangible training related to how to augment ketamine experiences with suitable therapeutic guidance. In learning how to provide this type of treatment, it became clear that several different strategies began to emerge with more patient contact when they are under the influence of ketamine (Dore et al., 2017; Mathew & Zarate, 2016). These strategies then aligned into a simple overall strategy to utilize and implement to improve patient outcomes. This method that has been created by this

dissertation has been deemed the *STAR Method* which breaks down the approach into four steps: strategize, teach, amplify, and resolve. It is this method that has appeared to help patients plan their experiences without putting a large onus on them to create their own treatment path or response to the intoxication effects of ketamine. This is because it has been observed in some settings that patients can enter the treatment experience without any form of guidance related to addressing the overall needs versus a specific idea around treatment (though some do see benefit without any such guidance); however, it does appear that others are unable to benefit from the infusion alone and require some form of intervention in understanding how to gain significant insight and benefit (Bonnett, 2018; Foster, 2021).

As mindfulness and other cognitive approaches are shown to be beneficial in therapeutic interactions (Hawley et al., 2017), it is considered that these guidelines will be beneficial in performing KAP-I. Mindfulness as a practice is meant to empower the patient to manage their own symptoms by their awareness of how they onset into a depressive episode while attempting to prevent a significant episode from onsetting (Segal et al., 2010, as referenced in Hawley et al., 2017). It is a core aspect of cognitive behavioral therapy (Hawley et al., 2017).

It is suggested that when clinicians begin integrating the steps related to mindfulness along with other cognitive processing procedures, patients will be able to be in touch with identifying their chief concerns and can guide their approach while working through their concerns that have led them to pursue this treatment (Rosa et al., 2022). A thoughtful treatment plan can alleviate their apprehension, normalize their feelings, and prepare them for their experience in a planned approach. Prior to infusions initiating, providing psychoeducation around dissociation effects, the half-life of ketamine, and relaxation techniques are also

considered to be highly beneficial as it can give patients useful knowledge before their engagement into the experience. As some patients can remain rather lucid, others may have sedation-like experiences where verbalizing becomes difficult or even impossible, while some may have negative experiences. It is important to educate patients that every session may be vastly different from each other; therefore, strategizing prior to the infusion is key to reaching desired outcomes.

It should also be noted that patients are extremely suggestable during the infusion session (Sklar et al., 1981) or that they can experience negative vivid imagery (Fine & Firestone, 1973). This can be both beneficial and detrimental, as unskilled medical professionals can leave artifacts of negative experiences in the subconscious (Rosa et al., 2022). This is the primary reason why it is considered beneficial for mental health professionals to be trained specifically in ketamine treatments to alleviate stressors, provide psychoeducation related to the experience, and to assist in bringing patients back into reality if they should become activated during the session, and to assist in redirecting them to face and address the stressors that may be affecting their experience.

One method of helping patients feel more comfortable when they get too excited is to engage in *Box Breathing*, a method where a patient breathes in for four seconds, holds for four seconds, exhales for four seconds, and holds for four seconds. In times of overwhelming feelings, even outside the ketamine infusion, this technique helps patients reorient around a more calmed feeling (Norelli et al., 2021). In ketamine infusions, it is considered crucial, as some patients may engage in shallow breathing, often causing them to experience a mild feeling of panic (Mathew & Zarate, 2016). By engaging in this technique, they can re-center and feel more comfortable during the infusion session. This technique is best in a guided approach, requiring

the provider to count out loud for the patient to reorient their attention on their breathing without having to consider how long they are breathing for (Norelli et al., 2021). A suggested model is saying to the patient, “Breathe in, two, three four, hold, two three four, breathe out, two three four, and hold, two, three, four” in a calm, deliberate tone.

Finally, it should be amply noted that ketamine can act as a bladder stimulant for patients. Ensuring that patients use the restroom prior to the infusion is necessary and critical. It becomes problematic when patients are near panicking when they must urinate due to this stimulating effect, therefore, it is highly suggested that patients urinate prior to their infusion (Bonnett, 2018; Foster, 2021). While a pump can be stopped to allow the patient to urinate, it creates issues as they tend to be unable to independently ambulate and will likely require assistance (Foster, 2021). Unfortunately, patients have also been known to soil themselves during an infusion which may cause them to feel shame. This cannot always be mitigated, but it should be a part of best practices to try to prevent it.

A typical process for the ketamine infusion series is based on a six-session model. It is suggested that the model be focused on the pre-infusion meeting, typically taking place prior to the infusion session, the infusion session itself, and a post-session where the processing occurs. This model repeats based on the completion of the infusions and should build throughout the delivery of treatment. Depending on how the series is scheduled will dictate how the follow up session will take place. It is recommended that infusions should take place two to three times per week, and that follow up sessions should occur within 24 to 48 hours, as necessary. However, there is no single way to schedule and perform follow ups and is left to both the mental health clinician’s, ketamine facility, and patient’s availability depending on need.

It should be expressed that this level of treatment can be considered cost prohibitive for some patients. Ketamine treatment is typically not covered by insurance companies due to it being an *off-label* therapy (Mathew & Zarate, 2016). While some clinics have had success in billing various insurance companies for the treatment (Bonnett, 2018), others have not been as successful (Foster, 2021). As such, ketamine infusion series can vary in cost, but are approximately $2,500 or more for a six-infusion series. How the mental health provider and the patient determine the costs for all touch points delineated in this dissertation is up to the provider, but as the infusions can take the provider out of the office, considerations of that business impact are left to the mental health provider to negotiate with their patients.

A review of the STAR method will assist clinicians to become familiar with the approach though an explanation of the four-prong strategy.

Strategize

Strategizing around these experiences is the primary goal of this treatment style, as patients who go into an infusion with no plan of how to address things leads to looser experiences where addressing issues becomes secondary and the experience of the intoxication effect are primary. It is suggested that while this is not considered detrimental, it can elongate a therapeutic process response with somewhat less beneficial outcomes because of a lack of guidance. By determining what is the primary focus of the session to be entered upon, patients can have ideas primed into their consciousness without having to bring them forward during their experience. In essence, having these ideas in the forefront of their consciousness can allow patients to focus on them more easily without needing to spend two or three infusions exploring their own minds. This is the purpose of the guidance being lent by the mental health provider to

the patient.

Secondly, having a tangible treatment goal determined prior to engaging in ketamine treatment can accelerate the understanding gained in their experience. This can usually be accomplished by having the patient journal or write out their primary concerns the night before the first infusion session (or subsequent infusion, should the patient be referred after beginning their treatment plan). By doing so, patients will essentially prime their minds to orient towards the problem they are attempting to face. On the day of their infusion in a brief meeting prior to the infusion, the clinician and patient should discuss those plans so that all parties are on board with the plan. This will allow the clinician to keep the patient moving towards that focus instead of going outwards into the depths of their mind. If this happens, simple redirection does tend to bring the patient back to the topic at hand. Further recalibration related to dosing can be necessary should these issues continue to rise. A simple metaphor that has been useful is the submersed feelings around intoxication (i.e., imagine being at the bank of a body of water and feeling like toes are barely wet versus being wholly submerged).

Teach

The main concept behind teach is related to ongoing psychoeducation throughout the intervention process with the patient. By normalizing and naming their feelings that can be elicited while they are under the influence, certain apprehensions, tension, and fears can be alleviated prior to the infusion to minimize these concerns. The overall strategy is to prepare the patient for uncomfortable or negative experiences that may occur, so that they may redirect their minds to something more pleasant or less negative. This can occur when patients go too deep into a trauma that may trigger a panic or anxiety attack. As in situations where the patient is

sober, redirecting them to a more at-ease place can help the attack pass. The main difference in these situations is for the mental health clinician to not react to a patient's reaction in a panicked manner, but more of a therapeutic calming from breathing exercises to mindfulness. By teaching them these prevention strategies, patient reactions may be more manageable should they arise during an infusion.

Amplify

One of the most beneficial outcomes of ketamine intoxication is *ego dissolution*. During this process, the patient's ego is effectively diminished to the point where its protection is suspended during the time of intoxication and briefly after the infusion completes, approximately twenty minutes post-infusion (Nour et al., 2016; Mathew & Zarate, 2016; Abdallah et al., 2019). The benefit of this process is patients do not have access to the resistance of facing difficult topics and truths that have been plaguing them in daily life, resulting in their pursuing treatment. As a treatment method, this can provide an opportunity for patients to come face to face with an experience, memory, or trauma that has prevented them from moving forward in their lives. Cases where patients have a significant trauma, especially one in childhood, can result in deeply ingrained protections that can prevent individuals from recalling or exploring. It is believed that this inability can cause patients to be deemed *treatment resistant* due to their unwillingness to explore or overcome these situations and cause them to block out these influences and experiences.

The purpose of amplify is to empower patients to overcome their barriers by giving them the mental fortitude and strength to face these unpleasant memories and overcome their deeply ingrained resistance to do so. It gives them the opportunity to see through the suspension of their

own ego that their lives do not have to be maintained in their current state and that they have the power to overcome these setbacks and limitations. As patients who are in this position are typically referred to as *stuck*, the idea of amplifying their own abilities is to relieve these limitations and put them in a better direction of healing that occurs throughout the infusion process, therapeutic intervention, and post-infusion processing sessions. Overall, ensuring a patient's perspective of empowerment is key for this step to permeate.

Resolve

As with most therapeutic processes, the goal of resolution for patients should be primary in treatment goals. Because this modality is no different, the final stage of KAP-I revolves around resolving the presenting issues. This is typically done during the post-infusion session that would accompany the infusion process. It is that part of the session that yields the best time to process through not only the experience, but also the topics that may have come up during the infusion. Ketamine has a distinct effect on making people comfortable and open to discussing even their deepest regrets, decisions, failures, and traumas. This can be an extremely emotional piece of the puzzle and requires a clinician who is open to listening intently without judgment or even feedback. It is considered that silence is the best approach during this time, as allowing patients to sit in their emotions, feelings, and thoughts, is the most important step in resolution. Feedback during this time should be minimal and done at a later time after the session is complete.

A final step in assisting in this phase is having the patient go home and write as much as they can recall about the experience, to include feelings, memories, visual stimuli, and the emotions that were brought up. If the patient cannot recall specifics during the infusion,

discussions around the latter part of the infusion can also be helpful. While some patients may want to nap after an infusion (a completely understandable and foreseeable reaction), it is beneficial to advise them that the sooner they can get to this task, the better. It has been shown to assist in the mnemonic processes that occur post-infusion. By writing out their experiences, especially by hand, they are solidifying those processes for long-term potentiation.

Program Evaluation Process

As ketamine infusion series are a structured protocol that have been developed by medical professionals, this evaluation process will follow that protocol of an infusion series of six infusion sessions. At this interval schedule, there are times between sessions to assess patient functioning, determine updated goals, and process through sessions. While some patients may not adhere to this model for various reasons, this model will be considered a best practice for ongoing treatment strategies, and should be considered aspirational, not a requirement for every patient. The purpose of establishing this level of care is to ensure wraparound services are included in the intervention.

At the onset of pursuing a ketamine treatment protocol, some basic data collection should be performed. Ideally, the assessment battery should be consisted of a variation of assessments from the following selections: the Personality Assessment Inventory (PAI), or the Minnesota Multiphasic Personality Inventory – Third Edition (MMPI-3). The Beck Anxiety Inventory (BAI), the Beck Depression Inventory – Second Edition (BDI-II), the Beck Helplessness Scale (BHS), and/or the PTSD Checklist for DSM-5 (PCL-5) are useful, brief assessments that can produce limited, specific results related to the presence of depression, anxiety, and PTSD-related symptoms, respectively. Appropriate levels of graduate-level training are required for

administration of some of these measures and should be within the competencies of the delivering clinician. Utilizing measures related to psychopathology, substance use, and trauma-related symptom assessment is highly suggested for a robust and complete profile but should also be considered the minimal information necessary for a comprehensive treatment strategy for ketamine infusions.

The PAI is a 344-item assessment that requires the patient to have a 4th grade reading level, and produces 22 scales of personality related to neuroticism, psychosis, and behavioral dysregulations (Morey, 2007). The assessment is self-administered and produces an objective personality profile related to the presence of clinical disorders (Morey, 2007). The scales produced consist of 4 validity scales, 11 clinical scales, 5 treatment scales, and 2 interpersonal scales (Morey, 2007). An overall understanding related to this assessment, and the related psychometrics, along with the produced scales should be part of the clinical training already held by the assessor and within their professional competencies.

The MMPI-3 is a 335-item assessment that requires the patient to have a 5th grade reading level, and produces 52 scales related to validity that explore emotional, thought and behavioral dysfunction (known as the higher-order (H-O) scales); clinical scales that measure myriad areas related to overall functioning and self-concept (known as the restructured clinical (RC) scales); problems related to overall health and neurological concerns, eating problems and memory issues (known as the specific problems (SP) scales and somatic/cognitive scales); internalizing issues related to suicidality, helplessness, self-doubt, and other areas (known as the internalizing scales); problems within the family structure, substance abuse, impulsivity and other externalized behaviors (known as the externalizing scales); scales related to interpersonal issues (known as

the interpersonal scales); and the Personality Psychopathology Five (PSY-5) Scales (University of Minnesota, n.d.). It is suggested that the MMPI-3 will produce a robust level of data for the consideration of the treatment strategy.

By administering these measures before and after the infusion series, clinicians will be able to establish a baseline for comparison of pre- and post-treatment effects of the therapeutic intervention, as collecting a repeated measure after the completion of the infusion series should be used as a secondary data point. It will also create a basis of comparison for the patient to review after the treatment is completed to see how their scores have changed over the course of the treatment. If some of the presenting concerns revolve around substance use, a measure related to substance abuse treatment is recommended, such as a Substance Abuse Subtle Screening Inventory – Fourth Edition (SASSI-4). The SASSI-4 is an empirically validated, standardized screening tool for the potential of substance abuse and is highly effective as an aid in treatment planning (The SASSI Institute, 2016). After twenty-five years of research, the resultant instrument is highly accurate, correctly classifying substance dependent people in approximately 93 percent of all cases (The SASSI Institute, 2016). Additionally, the SASSI-4 subscales provide clinically useful information regarding the client's attitude toward the assessment, defensiveness, emotional pain, ability to acknowledge problems, and risk of legal problems (The SASSI Institute, 2016).

A further measure will be subjective ratings using a Subjective Units of Distress Scale (SUDS) that inventories the patient’s overall functioning and emotional state prior to the infusion. That rating is then documented to follow up after completion of the session to determine any observable change in emotional functioning throughout the infusion process. This

will assist in documenting patient functioning and help to intervene with patients who are in a bad mental space prior to the infusion. Assisting in relaxation techniques, mindfulness exercises, and focusing on being present can assist in keeping patients grounded and in an appropriate headspace before and during their treatments. This process is similar to that of Eye Movement Desensitization and Reprocessing (EMDR) in that these subjective ratings can help patients understand their tolerances to these negative feelings to continue to become desensitized to their negative effects (Shapiro, 2018).

As some facilities may capture and monitor Blood Pressure readings, it is good practice to view these readings along with respiration rates and pulse oximetry (pulse-ox) levels to be aware of patients physiological functioning and for potential intervention with medical professionals. As some patients can experience diminished breathing, giving them a gentle reminder to breathe is a prudent tool in keeping them calm during ketamine intoxication. Ketamine is also known to elevate Blood Pressure as a side effect; therefore, monitoring elevations can prevent emergency scenarios that can be jarring while a patient is under the influence. While this is the primary job of infusionists, collaborating with caregivers can create a team-oriented approach for client comfort. It should also be noted that patients who have diagnosed cardiological concerns should not pursue ketamine as a treatment, but these determinations should be left to medical professionals for ensuring patient safety.

Program Development Logic Model

Table 1 describes the logic model for the incorporation of training for KAP-I while also outlining short, intermediate, and long-term outcomes. The purpose is to identify and establish the primary goals and to outline potential outcomes related to the implementing of this concept.

The desired results are to create a program where mental health professionals are given the training to appropriately deliver KAP-I and alleviate the patient's presenting concerns that have led them to pursuing ketamine treatment, while also helping them overcome their traumas or causes for long-term depression.

The goals for this logic model are threefold: 1.) Provide an outlined program to deliver treatment that will enhance patient outcomes with ketamine treatment; 2.) Reduce patient concerns by delivering high quality psychoeducation regarding ketamine, treatment, and expected outcomes; and 3.) Create a strategy throughout their treatment with ketamine to obtain those outcomes by the end of the treatment protocol.

Table 1: Logic Model for KAP-I Project

KAP-I Program Project Logic Model

Desired Result	The purpose of this model is to create a program where mental health professionals are trained to appropriately deliver Ketamine Assisted Psychotherapy for Infusions to alleviate patient concerns, manage negative experiences, and help them overcome prior traumas or long-term depression that has led them to treatment.
Goals	**Goal 1**: To provide an outline for treatment to enhance patient outcomes with Ketamine treatment. **Goal 2:** To reduce patient concerns with Ketamine as a treatment option by providing psychoeducation throughout the process. **Goal 3:** Help patients to strategize their treatment plan to formulate outcomes more effectively with Ketamine treatment.

Inputs →	Activities →	Outputs →	Outcomes		
			Short-term	**Intermediate**	**Long-term**
• Provide targeted care with patients who are seeking Ketamine treatment for ongoing mental health concerns, such as PTSD, Anxiety, or Depression • Work with Ketamine treatment centers to normalize mental health providers being present with their patients during infusions to improve patient outcomes. • Expand training to mental health providers who are interested in providing therapy in conjunction with psychedelic-oriented treatment for patients.	• Hold trainings for mental health and, potentially, medical providers to understand the STAR method of KAP-I to improve patient outcomes. • Create opportunities for providers to improve their understanding of Ketamine and potential side effects while also assisting patients through negative experiences and outcomes. • Dispel disinformation about Ketamine in a clinical setting versus street use and the inherent differences between them.	• Provide high-level information to a fragile population to improve perspectives around this form of treatment to improve their overall functioning. • Create pathways to healing by integrating this treatment method to reflect the benefits of engagement while also spurring change and effective resolution. • Improve awareness in the medical industry around the benefits of Ketamine without having to be a tertiary or quaternary option.	• Introduce new and novel treatment approaches for depression, anxiety, and posttraumatic stress disorder. • Train mental health providers in basic Ketamine-oriented treatment plans, courses of treatment, and necessary knowledge to augment outcomes and facilitate best practices.	• Establish documentation of proven methodology with determined and demonstrable results that reflect the benefit of ketamine-assisted psychotherapy. • Establish ongoing research related to KAP-I to examine methods to improve outcomes and measures. • Widen the delivery method to other psychedelic treatment modalities that show promise for treatment of these disorders.	• Obtain longitudinal data from recovered patients to reflect durability of treatment and benefit of the intervention to illustrate the positive outcomes without the burden of addiction potential or side-effects that are detrimental to patient outcomes. • Continue to expand treatment options to improve KAP-I while also innovating new approaches with proven methodologies.

Inputs

The main concern with KAP-I is to overcome patient apprehension due to a lack of information. Patients who have struggled with issues related to trauma, depression, or uncontrolled anxiety may have found negligible benefit from other medications, leading them to feel they are out of options. This targeted approach can empower patients to explore non-traditional outlets to better manage their own care.

Secondly, as mental health providers are not able to provide this level of medical treatment, engagement with medical providers is also necessary to augment their own methodologies of treatment. Medical providers who facilitate ketamine treatments all have a wide variety of philosophies when it comes to the application of the treatment itself, as there are no specific protocols outside of the NIH recommended dosage schedule (Aleksandrova et al., 2017; Dore et al., 2019; Rosenbaum et al., 2022) which are loosely adhered to in the field based on the comfort of the providers who come from various backgrounds in medicine. This interdisciplinary approach also does not consider mental health applications unless the medical provider is a psychiatrist.

Because physicians are required to hold a medical license to provide ketamine as a treatment option, several disciplines within medicine have emerged as the most likely treatment providers: ER physicians, Anesthesiologists, and Psychiatrists. As two of the three are likely not used to working with mental health providers outside a hospital system, access to mental health providers who are knowledgeable in KAP in general can be rare to nonexistent. Therefore, it becomes prudent for mental health providers to reach out to local clinics to provide their input and expertise to augment patient treatment plans with an adjunct of KAP-I.

Finally, workshops around national, state, and local mental health organizations can assist in disseminating information to clinicians who desire to learn more about how to best practice KAP-I. This can be delivered through online methods, in-person trainings, and through archived sessions for the purpose of continuing education. In this manner, clinicians can obtain crucial information and continuing education in this emerging field to be up to date regarding best practices. It is also considered that clinicians should be oriented in psychedelics and their effects, though it is not a strict requirement. Basic understandings of both pharmacology and psychopharmacology are also beneficial, but not a requirement, as better insight into these two domains will help in educating patients regarding risks and side-effects.

Activities

Many of the necessary components of this program revolve around mental health providers trainings. Because this novel approach will include providing this information to mental health providers, the activities that will be needed will center around the delivery of these trainings. Both medical and mental health providers should be up to date on the information that is referred to in this project related to ketamine's therapeutic effects, potential side-effects, and duration as the most basic understanding prior to sitting with patients who will undergo this treatment.

The benefit of understanding these effects can be crucial to assisting patients who experience adverse or overwhelming effects. Because these effects can occur in even relatively small doses, even less than the NIH standard of 0.5mg/kg in some patients (Kohrs & Durieux, 1998), normalizing experiences can assist in calming and soothing patients who experience increased anxiety or panic during intoxication. Keeping patients calm and present oriented will

ensure that they are receiving full benefit from the treatment. There are also medical methods which can assist with these concerns, such as slowing or stopping the IV pump (Foster, 2021). In the case of slowing the pump, it should be done for the duration of the session (Foster, 2021). This will allow for absorption and metabolizing ketamine to pass into metabolites which are less psychoactive (Acevado-Diaz et al., 2020). These considerations should be determined by medical staff but may be suggested by mental health providers who are observing the patient's comfort level.

Stopping the pump temporarily can also assist in reorienting the patient to a comfort level that the session can be resumed (Foster, 2021). In some cases, the necessity to discontinue the session should be considered when the effects are causing more harm than good (i.e., the physiological effects create a significant concern, such as increased blood pressure, tachycardia, significantly decreased respirations, or the patient turns aggressive) (Foster, 2021). This is a time where the mental health provider can assist in calming exercises, reminding the patient to breathe. Reorienting is more possible without the influence of the effects and can put patients back into a receptive mindset to continue treatments. However, if the session does require a discontinuation, considerations around continuing an infusion series should be discussed with medical providers and the patient.

Finally, in preparing patients for an infusion series, it seems prudent to discuss the addiction potential of ketamine. Because ketamine's primary mechanisms of action specifically target Glutamate, NMDA, AMPA, and the Opioid-$\boldsymbol{\mu}$ receptor (Ago et al., 2019; Aleksandrova et al., 2017; Zorumski et al., 2016), its addiction profile is not like that of other drugs which target Serotonin or Dopamine. In street form, ketamine is often blended with other substances that do

affect Serotonergic and Dopaminergic receptors, which increase the likelihood of addiction potential. However, in clinical use, ketamine by itself does not seem to have any physical addiction properties, per se, but can be a substance that assists in avoidance of facing emotional difficulties or experiences, causing a more psychological dependence (Mathew & Zarate, 2016). Therefore, close monitoring of patient responses should be considered throughout and after the infusion series.

Outputs

In delivery of these informational trainings to providers, the goal is to assist individuals in deciding to pursue this treatment method or giving them options in treatment with a clearer understanding of how this treatment may affect them and how plans to mitigate the potential side effects can alleviate their stress or apprehension. As the adage *information is power* is considered, empowerment for patients to determine their own treatment path can be emboldening and may assist in their overall benefits.

As empowerment is a primary goal in certain therapeutic treatment styles such as music therapy, community psychology, feminist psychology, and even within sociological applications (Rolvsjord, 2006), it is believed to have the power to lend itself to significant benefits in ketamine treatments. This is considered to come from the orientation of helping patients take control of their treatment and thereby taking control of their ongoing struggles. Therefore, it is believed that this approach will better assist in positive outcomes that focus on patient-centered controls and engagement. It can also assist patients in collaborating with medical providers to drive their own treatment and comfort in their experiences.

Outcomes

There are several outcomes that are anticipated through implementation of these activities and are delineated through short-term, intermediate, and long-term expectations around the produced outcomes.

Short-term Outcomes

In the implementing of this strategy, it will take time to disseminate throughout the therapy zeitgeist. Acceptance of new models to treatment take time, and it is considered that others will read these guidelines and gain some useful knowledge around KAP-I, but also delivery of psychedelic-oriented treatment as a sub-specialty. However, the purpose of this is to foster conversation around how to appropriately deliver this style of treatment, but this in no way is considered the only authority on how to do so. It is only considered a primer to better understand how this treatment can be used in a beneficial and practical manner.

Further, it can be of use to treatment plans in considering these approaches for those who are open to exploring it. Therapeutic toolboxes are often comprised of multimodal treatment options, and this approach is considered another tool in the toolbox. Blended applications through Cognitive-Behavioral Therapy, Dialectical-Behavioral Therapy, and other treatment modalities are believed to be applicable to the delivering clinician and their areas of expertise. By adding this model to their consideration, clinicians can be better equipped to develop appropriate treatment plans and courses of action for patient benefit.

Intermediate Outcomes

As this model grows in application, it is hoped that clinicians will notify the author of their findings in field application. Through these experiences, a compendium of outcomes is

hoped to be established to document how this methodology can be shown to improve patient outcomes and the benefit of including KAP-I as an adjunct to treatment. It is also the goal of this project to establish ongoing research related to KAP-I to validate the approach, but also to continue to develop it as an overall strategy while making improvements when needed. Further considerations will be based on reported instances when they occur in the treatment space and will help formulate better approaches to this therapy style. Finally, with other psychedelics being considered for implementation in the therapy space such as psilocybin and MDMA, some of these approaches can be applied to these interventions with the specific understandings that the facilitators produce (i.e., half-life, expected experience, etc.). It is also important to understand what side-effects are produced by the specific substances being applied; however, these considerations can be applied to those settings as well.

Long-Term Outcomes

While durability studies have been shown to exhibit the benefits of ketamine in stand-alone application, it is considered prudent for the longitudinal data collection post infusion-series to examine how patients exhibit durability of these outcomes and benefits with the inclusion of KAP-I. As there will likely be negative or indeterminable outcomes experienced by some patients, it is important to understand that the outlined program within this dissertation and its approaches will not have 100% benefit or efficacy for all patients in all circumstances. Therefore, examining treatment failures can help in developing improved applications and treatment outcomes to innovate better performing intervention.

Another consideration is in expanding the boundaries of what is understood in psychedelic-oriented treatment for individuals who suffer from severe mental illness and

potential outcomes that can foster improvement while engaged in treatment, but also after completion of treatment. Basing the measure of success around the amelioration of symptoms can be a short-sighted goal in the long-term outcomes of patient experiences; however, are considered ideal in the overall treatment of patient concerns.

Ethical Considerations

Reportable Offenses

As ego dissolution is a primary byproduct of psychedelic treatment, it does bring up potential ethical concerns that may be complicated by the patient's intoxication. This concern leads to an assumption that bounds of confidentiality may be pressed. There are certain reportable situations that vary state to state, but the major offenses (i.e., child and elderly abuse, suicidality, and homicidality) are seemingly standard throughout the country, while obligations like The Tarasoff Rule may or may not exist in every state (e.g., Texas does not follow The Tarasoff Rule). In cases where patients may process through a triggering memory can result in them admitting to engaging in or being the victim of reportable behavior, this can present unique challenges. It is advisable to be aware of local governing laws related to admissions of reportable offenses if the person who is making these admissions is under the influence of a substance like ketamine, which should be reviewed in the informed consent phase of treatment.

It is highly recommended that group or multiple individual administrations should not be attempted in the case of KAP-I, and only individual, one-on-one sessions should be engaged in. It is not uncommon for ketamine facilities to have spaces where multiple administrations occur simultaneously. These settings would be an incongruent space for KAP-I to occur, as issues related to confidentiality are presented. Therefore, private spaces are the only acceptable location

to provide direct services.

Side Effects

As previously discussed, side effects are a significant consideration when managing patients who are under the influence. While medical staff may be present during an administration, they are not always comfortable in managing patients who are having panic or anxiety-like symptoms. Therefore, it becomes necessary to intervene when patients are having uncomfortable experiences that result in negative emotional states to maintain benefit. While these side effects are rare, they do happen, and being prepared for them to happen is considered best practice. Some instances require medical intervention, and this should be determined in the moment, as some reactions are more serious than others. These instances can occur when patients have extreme reactions, such as loss of reality contact, resulting in panic attacks. In these cases, IV pumps should be paused for a long enough duration for the patient to regain reality contact, while also having their anxiety or panic directly attended to by the mental health provider, with intervention methods such as box breathing or guided meditation.

Another significant concern with individual dosing has to do with responses to the medication. Medical providers can have anticipated effects with higher dosing (i.e., 1.5-2.0mg/kg or more) in what has been coined a Psychotherapeutic Response (PTR) (Bonnett, 2018; Foster, 2021). This is a direct response to the medication that is commonly referred to as a *K-Hole*. There are philosophical differences that exist whether this effect is beneficial or not. This author prefers a different labeling approach that is an allusion to wading into a body of water. The main objective is to feel submerged in the body of water and not standing at the banks of the water or even having patient's feet in the water. The immersion allusion tends to relate

well to patients with a fair subjective gauge of their experience. This submersion allegory is not necessarily consistent with better outcomes; however, does provide a point for patients to understand where they are in their treatment and to determine their toleration of ketamine.

Ultimately, mental health providers do not determine dosing schedules; however, they are certainly able to make recommendations for assisting patients in exploring the bounds of their own minds through this process. It can also be beneficial for clinicians to explore the profound effects of moderately increased dosages, but this should be done with caution. Collaborating with medical providers to see what their comfort levels are can be integral in their patient's outcomes and can help patients feel they are getting the most out of their experience. But because ketamine can act as an anesthetic at higher doses, high-dose ranges (i.e., 3.0mg/kg and above) are not recommended for this type and style of treatment (Dore et al., 2019).

Patients who have extreme reactions to ketamine are minimal; however, they can occur. Patients should be medically cleared by their primary care physician or specialist if there are any significant health concerns present (Foster, 2021). Ultimate medical eligibility is left to the determination of medical staff at the ketamine clinic and should be referred for assessment if necessary (Foster, 2021). If lack of patient suitability due to health concerns is determined to occur after beginning the series, further medical clearance may be required, or the treatment should be discontinued (Dore et al., 2019; Foster, 2021; Mathew & Zarate, 2016). All these considerations should be left to medical providers to determine.

Ineligible Patients

Because of the psychotomimetic properties of ketamine, there are certain diagnoses that are considered incompatible with ketamine, or at least, strongly advised against. First and

foremost is Schizophrenia. Some historical research (Lahti et al., 1995; Lahti et al., 2001) shows an increase in positive symptoms in individuals with schizophrenia that may lead to a subsequent psychotic break. Due to this risk, it is highly advisable to not engage in ketamine treatments with individuals who have had prior psychotic episodes.

European researchers, however, found that there can be some benefit in treatment of acute depression and suicidality that may be useful for individuals with Schizophrenia. Bartova, et al. (2018), found that a patient who had been treated with ketamine after a psychotic episode who was experiencing significant depressive and suicidal concerns and was treated with ketamine with no impact or recurrence of psychotic symptoms. This case report does appear to have some interesting implications, as there may be patients who are able to tolerate an increase in positive symptoms without a psychotic break; however, determinations of who is appropriate and who are ineligible is not clearly defined. Therefore, it may be considered best practices to not engage in this form of treatment with this population.

Finally, a consideration is made for Bipolar individuals with acute manic symptomology. An observed consensus among medical providers is the same with individuals with Schizophrenia, in that it may cause positive psychotic symptoms to manifest, leading to a psychotic episode, and may worsen outcomes (Mathew & Zarate, 2016). It has been the findings of these providers that allowing the episode to pass is best for engagement in or continuation of treatment. As it can be difficult to engage in psychotherapy in general in these individuals, it appears prudent to allow the episode to pass and continue treatment afterward the episode has resolved.

Abuse Potential

It is also believed to be prudent to discuss abuse potential regarding patients who may have higher affinity towards obtaining ketamine outside of clinical settings. As ketamine is growing in popularity in the zeitgeist, it is also growing in popularity as a street drug. Access in substance using circles does present concerns about how patients may augment or alter treatment using illicitly obtained ketamine. While a patient's substance use history should always be a consideration of their eligibility, it is important to establish a patient's history that may indicate the misusing of medication or illicit drugs. Attempts to dissuade patients from use outside of clinical experience is key to ensuring beneficial outcomes in controlled settings. It may be best approached in identifying the differences between clinical-grade and street-grade, whereas clinical-grade is tested and known for the contents versus street grade that may be mixed with another drug that can cause more of a concern related to significant abuse potential.

Provider Relations

As with all professional relationships that occur outside of the space of normal practice, it is critical to have good relations with the medical provider and staff. Because infusionists can be paramedics, phlebotomists, or other levels of expertise within the medical field, it may be a difficult adjustment to have them present during infusions. While the operation of the infusion center or clinic is best left to the medical provider's discretion, it does seem that a modicum of leeway can be established with them within the bounds of professional relationships. Some providers choose to have open areas for infusions, while others have individual infusion rooms. It is important to discuss these potential ethical limitations with patients prior to the session to ensure confidentiality and to minimize exposure to sensitive topics in the presence of other

medical professionals. It is strongly encouraged that engagement in KAP-I should be limited to private rooms with the minimum amount of people necessary for client safety.

In some instances, the presence of infusionists can be bothersome to the relationship between a mental health provider and patient during a highly vulnerable moment or experience. Professional judgment should dictate how to best address these concerns, should they arise, and discussing any potential problem with the medical provider is strenuously important. Ultimately, it is all done in consideration for patient experiences and to maintain good relations with medical providers and their staff.

Finally, it is prudent to have a Release of Confidential Information on file for the medical provider's center to include staff. Because confidential information will be exchanged during the infusion series, proper documentation is necessary to ensure the maintaining of confidentiality. Establishing an agreement with medical providers is essential and should be done in compliance with federal and state law and with the boundaries of the ethical code of the provider's professional affiliation.

Expected Outcomes

It is considered that the main benefit of this approach is to engage in patient trauma, depression, or anxiety, to determine the root of these problems with the assistance of a facilitator like ketamine. As it has been shown to work as a stand-alone treatment, the augmentation can be profound through a guided experience that KAP-I can provide. While both forms of treatment as standalones can have benefit, the synergy of these two treatment models does seem to show excellent promise in overcoming patient's presenting concerns. As valuable insight into internal processes progresses, patients can gain much needed and valued perspective to overcome the

cumbersome issues that have caused them such concern prior to receiving treatment. With these benefits, it does appear that KAP-I does indeed show promise and anticipated assistance for most patients.

CHAPTER 4. PROGRAM DESIGN

Introduction

Throughout this project, the aim has been to document what to do in certain circumstances along with how to address scenarios that may arise during the infusion itself. The project will now be laid out in a manner conducive with a six-infusion series with aligned KAP-I therapeutic intervention. While this project does not endeavor to be nor is it considered a manualization, it is considered a process-oriented flowchart and guideline to allow clinicians to establish their own approach for how to best implement this process with their patients and in conjunction with medical providers. This is because these interventions are highly tailored to each patient due to time constraints, financial ability, and any other factor that may impact the patient's ability to fully integrate into their schedules.

While some patients (and clinicians, for that matter) may be able to make time for three infusions and two sessions per week, that availability does not seem feasible for most clinicians. If, however, it does work out for both, then there does not seem to be any rationale while it could not be implemented in this manner. Therefore, the outline itself will simply be laid out in a manner of individual sessions and infusions. Ultimately, it is up to clinicians to determine what works best with their patients, along with scheduling to best fit.

Regardless of how the overall sequence is scheduled, it is suggested that the infusion series not be extended to longer than six weeks, if possible. While ketamine does not need a titration effect to see best benefit, it does appear to have some benefit for continuity. This means that there should be at least one infusion per week over the course of six weeks, if not shorter. It is also suggested that regular talk-therapy should be completed as soon as possible, preferably

the day after to assist in solidifying the outcomes of the session. It is also considered that all these scheduling assumptions are made on behalf of the medical providers as well; therefore, it is suggested that coordinating with these practices to ensure continuity of the series is best. In the case that the practice is scheduling for the patient, ensuring that there is some collaboration for the inclusion of KAP-I is also worthwhile.

Context for New Program

This program has been borne out of necessity, as access to this information does not readily exist in the literature or within the public domain and is minimally emerging from continuing education programming. Perhaps it is due to the small number of clinicians who have been engaged in this work up until recently. It may also be that there are new protocols being developed within the medical community that are being more widely accepted, therefore new strategies for mental health providers are needed to follow these protocols. Now that the access to ketamine appears to be growing, it was determined that these basic approaches should be documented, reviewed, and implemented to assist providers and the community at large in establishing guidelines to best integrate and model themselves after to not start from scratch.

It was also deemed a necessity to help reticent clinicians become educated in this field that is currently still considered to be in its infancy. Having access to quality trainings does not readily exist, and it is hoped that access to them becomes more widely available as the emergence of psychedelic treatments continue to grow. Finally, documenting real-world experience and patient outcomes has helped develop this model to be able to empower clinicians to create suitable treatment plans, set patient expectations, and how to best work with local resources. By ensuring these approaches are met, clinicians can thoughtfully navigate patient

treatment while not overly complicating their own need to understand how to best do so, thereby alleviating potential stressors to delivering the intervention.

Finally, a consideration to addressing the recent increase in Treatment-Resistant Depression (TRD) is also notable. This relatively new nomenclature has been met with various approaches to help patients overcome their long-term battles. As there has been significant developments around finding efficacy in treatment of TRD with ketamine, assessing evidence-based approaches that combine the delivery of psychotherapy with medically oriented treatment strategies also appear to be poorly documented. Therefore, this program is also considered to be a useful tool in providing new options that may have more beneficial outcomes in treating these patients than with standard monotherapies or polypharmacy, especially with individuals who feel that medications and/or traditional talk therapy did not help them. This project can be a new option to consider with a brighter outlook than traditional means.

Program Description

Appendix A shows a suggested process flow related to the planning stages of an infusion series from beginning to end. It begins with initial diagnostic interviews for eligibility and assessment and diagnosis. It then flows into treatment planning, scheduling with providers, pre-infusion strategizing meetings, infusion sessions, and post-infusion processing sessions. It finally ends with reassessment and maintenance phases that will occur upon completion of the series.

Intake and Determination of Eligibility

As with any traditional therapy client, all patients should start with an intake interview. Determination related to exclusion criteria can be performed with any validated measure which may assist in diagnosing organic brain dysfunction disorders, such as schizophrenia or an acute

manic episode. A brief list of these measures has been covered in Chapter 3 and can be found in the Assessments and Diagnostics section of this chapter. Psychometrically validated measures are preferred; however, are also limited to the amount of training that the provider is appropriately capable to perform. Therefore, it is up to the individual provider to make appropriate determinations that are within their competency.

Table 2 includes a simple questionnaire that was created by this author to determine several aspects of a potential patient's understanding of ketamine and levels of current functioning that are directly attributed to the known effects of ketamine (i.e., treatment for treatment-resistant depression and abatement of suicidality). The survey is comprised of 11 questions and is broken down into domains of ketamine awareness (questions 1-5), acute PTSD symptoms (6 & 8), acute depressive symptoms (7 & 9), and acute suicidal ideation (10 &11). Items 2, 3, and 4, are reverse scored to combat response acquiescence.

The survey is built on a Likert scale. Cutoff scores are more indicative of treatment approaches with ketamine for the purpose of establishing potential avenues to discuss information related to treatment options. Therefore, each question should be analyzed for appropriateness versus adding the individual scores for a comprehensive outcome.

Note: It is understood that this scale has not been analyzed for reliability and validity. Its purpose is meant to be utilized as a screening instrument, and not a diagnostic one. It is strenuously stated that eligibility for treatment cannot be determined on this scale alone. It is also hoped that future research into this program will examine the validity and reliability of this instrument. It is hoped that a more thorough assessment will be completed by the clinician who

is providing KAP-I, or by other qualified professionals to determine the eligibility for this treatment style.

Table 2: Ketamine Questionnaire

	Strongly Disagree	Somewhat Disagree	Neutral	Somewhat Agree	Strongly Agree
1. I am familiar with Ketamine and its uses in treatment	1	2	3	4	5
2. I would not consider using a drug for treatment if it had a high abuse potential.	1	2	3	4	5
3. The idea of using hallucinogens scares me.	1	2	3	4	5
4. The idea of not being in control is not a pleasant thought for me.	1	2	3	4	5
5. I have a hard time letting go of things that have happened in my past.	1	2	3	4	5
6. I am having difficulty letting go of an event from my past.	1	2	3	4	5
7. I have recently had more bad days than good.	1	2	3	4	5
8. I have been awoken by nightmares recently.	1	2	3	4	5
9. I often think about death or dying.	1	2	3	4	5
10. I have previously made a plan to end my life.	1	2	3	4	5
11. My problems are overwhelming my ability to want to continue living.	1	2	3	4	5

Assessment and Diagnostics

The purpose of this step is to make clinical judgments that are relegated to mental health providers to identify whether ketamine treatment is a viable option for the patient. While medical eligibility is determined by the medical provider, the providers may rely on mental health professionals' judgment to determine if the patient is a good candidate for treatment. It also establishes a baseline for the purpose of documenting pre-treatment severity of symptoms, which can be useful in identifying the work to be completed (i.e., trauma, depressive etiology, etc.). These steps are included to assist in the decision-making process for all providers involved.

Therefore, joint efforts in making determinations can assist in ensuring patient safety and appropriateness for treatment.

Potential instruments that can be utilized to determine baseline symptomology are the Personality Assessment Inventory (PAI), The Minnesota Multiphasic Personality Inventory – Third Edition (MMPI-3), the Beck Anxiety Inventory (BAI), the Beck Depression Inventory – Second Edition (BDI-II), The Beck Helplessness Scale (BHS), and/or the PTSD Checklist for DSM-5 (PCL-5). Information related to these assessment instruments and their utility are discussed in Chapter 3. The overall purpose of these assessments is to provide a quantifiable baseline at the beginning of the infusion series and to establish a treatment effect after the completion of the series.

While the Alcohol Use Disorders Identification Test (AUDIT) and Patient Health Questionnaire (PHQ-9) are useful screeners and may be used to determine substance use and brief screening of mental health concerns, respectively, it is considered that there are more precise instruments that should be utilized by those who are not medical providers, and instead by those who are extensively trained in psychometrics and assessment to better determine a more specific level of severity and duration of symptoms as described in the section labeled Intake and Determination of Eligibility.

Treatment Planning and Scheduling

As with any suitable treatment process, a plan and treatment schedule need to be established with the patient and an estimate of how long the process will take from beginning to reasonable end should be disclosed (Dore et al., 2019; Mathew & Zarate, 2016). The process should encapsulate the entire infusion series and the supporting sessions around the infusions, to

include pre- and post-infusion planning and processing sessions, thereby making the infusion series a total of 18 distinct sessions throughout the process, though these sessions only occur around the pre-session planning, which is to be done at a different day and time prior to the infusion and should be a standard therapy hour. These sessions can be included with the six infusion sessions with three touch points per visit (pre-session planning session, and a post-session processing occurring directly after the infusion, and a separate post-infusion session to be completed several days after the infusion itself). To clarify, if a patient is engaged in an infusion series, (1) a planning session should be completed on a different day prior to the infusion, (2) a small strategizing meeting can occur immediately before the infusion followed by the therapeutic intervention during the infusion and a post-infusion processing session that takes place directly after the infusion, and the post-infusion session (3) should be done several days after the infusion session. The suggested timeframe for the infusion and immediate post-infusion session is a two hour session.

It is acknowledged that this may be difficult to manage from both a patient and provider perspective which is why, if necessary, this can be shortened to a brief planning session prior to the infusion and a post-infusion session directly afterward the infusion to process what had occurred. Should the process be broken up into three separate sessions, that can be discussed between the provider and patient for what may work best. Whatever setup is the simplest for both parties, these three components should be included throughout the series and time should be made to engage in all three.

Post-Infusion Series Activities

Upon successful completion of the entire infusion series, a post-series diagnostic re-assessment should be completed to document any potential treatment effect. This can be done by readministering a testing battery that is chosen and comparing results. It is important to document the change in symptom severity, but also to assess the overall functioning of the patient post-series to accurately determine their experience throughout and to identify their progress when it is still being processed by them. These steps are best done in a separate session after the completion of the series with a document to present the results and any necessary interpretation of them. This step will also assist in establishing any necessary maintenance phase, where booster sessions can be discussed, and any ongoing therapeutic intervention can be determined.

Lack of Patient Success

As with any therapeutic intervention, there will be patients who do not respond to treatment. While this treatment is considered to have a high level of efficacy, it is not 100% effective for all participants. A meta-analysis performed by Han, et al. (2016) showed that there are remarkable effects for at least one week post infusion in approximately half of participants who were monitored through a variety of placebo-controlled, double-blind experiments. The subjects in this study were only reviewed for short-term benefits (Han et al., 2016) and were not given repeated administrations. It should be discussed with patients that there is a potential that they may not overcome their issues, and that this is a possible outcome. However, ketamine has been shown to work independently, without therapeutic intervention, and a patient's failure to meet their ultimate treatment goals should not be regarded as a complete failure (Niciu et al.,

2014). Reorienting their perception around amelioration or diminishment of symptoms is considered a benefit and should be seen as such. As a part of the patient's informed consent, lack of success should be at least briefly discussed.

Program Details

The program details will outline patient interaction and the process that they will experience from initial consultation to the end of the ketamine protocol. This program will focus on patients who are seeking KAP-I as their treatment strategy without a medical provider already selected. It is crucial to understand that many patients who are seeking ketamine as a treatment option have likely explored other treatment options, and this program will focus on this type of patient. The following patient is fictional and does not reflect any experience with an actual patient. The initial steps look like any intake for treatment by providers and consist of initial contact and intake and assessment. It is also noted that the treatment process that is illustrated below is not indicative of all ketamine patient interactions but is meant to illustrate the included sessions of pre-infusion meetings and post-infusion sessions separate from the infusion itself and reviews the nature of this type of treatment strategy. This fictitious client is built on a three-appointment time per week meeting with one infusion per week. The pre-planning meeting is to take place the day before the infusion (i.e., a Monday), the infusion will happen the next day (i.e., Tuesday) while the follow up meeting is scheduled for one to two days after the infusion (i.e., Thursday). It is stressed that the frequency of these meetings, along with infusion sessions, should be dictated by the individual treatment plan that is determined for the patient after the initial consultation and results are presented.

Initial Contact

A married 32-year-old patient contacts a psychologist as a potential treatment provider. They disclose that they have been diagnosed with Major Depressive Disorder and Posttraumatic Stress Disorder in the past and had been taking medications for several years but had not found them to be helpful in the long-term. They state that they are interested in learning about ketamine treatment, as they read about it on social media as well as had a friend who had completed an infusion series with beneficial results.

Intake and Assessment

The patient sets their first session on a Wednesday, and during the diagnostic assessment, it is learned that their primary care provider has told them that they were not certain that the medication regimen they had been on is working as expected and has identified them as "treatment resistant" due to their lack of response over the past several years with various medications. Due to this diagnosis, their medical provider has referred them to a psychologist for further assessment and treatment planning. The psychologist then performed an assessment with several instruments to determine their current levels of severity: a PAI, SASSI-4, PCL-5, and the Beck instruments. Screening for suicidal behaviors or risks was also completed.

The psychologist determines, based on the findings of these instruments, that the patient does not show any significant signs of Bipolar Disorder, Schizophrenia, or current Substance Use Disorders related to illicit substances, but does show a significant level of alcohol use. The BDI-II shows a Severe level of depression, as was also reflected in the PAI results. The PCL-5 also shows significant levels of trauma that does appear to support a maintained diagnosis of PTSD which becomes the working diagnosis to build the treatment strategy upon.

The psychologist then uses the ketamine survey to determine the patient's awareness around this treatment option. The patient's results suggest that they are neutral on the use of ketamine in treatment, is not worried about abuse potential, is unafraid of hallucinogens, has some issues around being in control, cannot let go of events from the past for which they are struggling, feels that they are having more bad days than good, endorses nightmares, does somewhat think about death often, denied having a suicide plan and had no prior attempt, but does feel that their problems are overwhelming them, suggesting that this trauma has not been resolved and is continuing to be problematic for them. This component is considered the genesis point of the patient's ongoing concerns that the treatment will attempt to alleviate.

During the diagnostic interview, the psychologist learns that the patient had used some psychedelics while in college, notably psilocybin mushrooms on several occasions, but had no further use afterwards and denied any other hallucinogen use. It was also learned the patient had experienced a trauma where their sibling was killed in an automobile accident during which the patient was also a passenger, and this occurred when they were 27 years old. The patient suggests that they had experienced problems letting this trauma go and has experienced guilt around surviving. They suggested that they had tried some counseling in the past to deal with the loss of their sibling but did not focus on their own experiences. After feeling they had moved past their grief, they discontinued therapeutic services.

The patient also disclosed that they did not sustain any significant injuries from the accident but had some moderate anxiety around being a passenger in a car. They indicated that they were generally in good health and were not taking any medications for medical concerns. They also note that their alcohol use had increased after the accident, suggesting that they would

often drink to go to sleep and to try to stave off nightmares related to the incident. They also noted using marijuana in the past, occasionally, but did not like the anxiety it would induce, and denied that they would rely on it.

These findings appear to suggest that the patient would be a suitable candidate for treatment based on the overall physical health of the patient, the duration of the symptoms, lack of efficacy with other modalities, and the results of the assessed measures of functioning (Hyde, 2015). The acuity of the event, along with the recurrence of nightmares and attempted self-medicating with alcohol do reflect how the patient is attempting to overcome the issues themself but was failing to do so by not addressing the underlying issue. There do not appear to be any health issues that would be concerning to proceed (Hyde, 2015).

During the presentation of the results to the patient, the psychologist identifies the onset of the anxiety and the trauma response from the accident to better address the client's needs and how to overcome the resistance that they may be experiencing. The psychologist then proposes a six-infusion series during which therapy would be interwoven to work through the issues that the patient had presented. The patient agrees, and the psychologist works with the medical provider to schedule the initial session.

Pre-Infusion Education and Strategizing

Two weeks after the initial assessment, the psychologist provides their report to the patient and details the treatment plan. The psychologist and patient sit down in the psychologist's office to discuss the upcoming infusion treatment strategy, what to expect from the experience, and several coping skills that the patient can use to help them relax in times they may feel overwhelmed. The psychologist explains that ketamine may make them feel like they are outside

of their body or that it may produce visual stimuli, and that this is a normal effect of the drug. The psychologist also notes that they may feel like their breathing feels shallow and informs them of a technique where the psychologist will remind them to breathe. It is explained in a *Box Breathing* fashion, where in four second increments, they are told to breathe in, hold it, breathe out, and hold again. The purpose of this is to help the patient slow down their thoughts and reorient themselves with their body. The psychologist notes to the patient that dissociation can be a difficult experience for people to prepare for, and that by giving patients an awareness of this idea is considered crucial.

It is also explained that during the initial infusion, the psychologist will predominantly be observing and not be doing any meaningful intervention. The infusion room is also discussed, where the patient will be placed in a comfortable reclining chair, facing a television with visual stimuli, an infusion IV pump attended by an infusionist, and an infusionist who will set up the IV line and start the infusion. It is explained that the infusionists are typically paramedics or registered nurses, and sometimes even a medical doctor. A nurse practitioner is typically on site to oversee the procedure and monitor any concerns that may arise during the infusion. It is also explained that the patient may not ever interface with the medical doctor who runs the facility during the actual infusion.

It is important to see how the patient responds to the medication from an objective observation of any changes to their mental status, which is expected and should be recorded, but is also monitored by the medical team. This allows the patient to better understand their response to the intoxication effects of ketamine while also experiencing their own responses to ego dissolution and dissociation. It is decided that the patient would like to recall the events of the

accident and the immediate outcomes from it. The patient is then told that the psychologist will be closely monitoring their verbalizations during the experience with several points of checking in with the patient should they fall into a non-verbal state.

An intervention is discussed around patient comfort, whereby it is noted that if a patient begins to feel panicked, the medical staff from the ketamine facility (i.e., the infusionist) can slow down the infusion pump or discontinue the infusion to allow the patient to resolve back to a baseline perception as they can be in the room during the entirety of the infusion. This is done in cases where patients can feel overwhelmed, are fearing a loss of reality, or are inconsolable and are unable to be redirected. While these effects rarely occur, they can and do occur, and it is important to discuss them with the patient prior to beginning the series. There is also a need to have a discussion around physiological effects of ketamine outside of breathing, having to do with blood pressure. Because blood pressure can spike during an infusion, informing the patient of this is also necessary prior to the series. Caution should be taken with individuals who have a history of hypertension, and it is important to discuss this with the medical staff prior to the infusion series to allow the staff to make a more informed decision about patient suitability and eligibility.

A marginal time is spent discussing the infusion process and noises the pump may make to minimize any concerns that may arise during the infusion. Familiarity with infusion pumps is typically outside the scope of mental health training, therefore, it is incumbent on the mental health provider to become familiar with the equipment used at the medical provider's facility. Infusions can last anywhere from 45 minutes to an hour, depending on the practice of the medical provider. Being aware of infusion times is important to discuss with patients. Also, most

infusion pumps sound alarms at the 10-minute mark to indicate the infusion is almost complete. It will typically sound again at the end of the infusion cycle. Monitoring of the pump is suggested to be aware of the amount of time left in the infusion.

Finally, discussions around the psychedelic experience are discussed. Because patient and infusion experiences can be wildly different, and can change from infusion to infusion, it is considered beneficial to discuss the experience in broader terms, as there is no predictable experience, just predictable effects. These effects can include visual hallucinations, perceptual miscues, and other psychotomimetic effects. The duration of the effects is also worthy of discussion, and they typically resolve within 10 to 15 minutes after the infusion has completed. Because these experiences can be peculiar or odd, normalizing the onset of these experiences is a practical piece of information.

After discussing all the necessary components of the infusion and all questions that may arise are answered, the psychologist and patient will later meet at the infusion center to engage in the first infusion. The treatment plan calls for 6 infusions, with pre-infusion strategy sessions to take place. They also agree that there will be a post-infusion brief session to process, with a session to occur after the infusion in the psychologist's office to explore the patient's thoughts that occurred after the session.

Infusion 1

Upon arriving at the infusion center on a Tuesday, the patient meets with the psychologist and reports being rather anxious about the experience. They note that they did not sleep well and that their appetite had somewhat been decreased leading up to the infusion. The psychologist advises the patient that when entering any new experience where there are unknown outcomes,

anticipatory anxiety is a normal emotional response and eases their mind, reminding them that they are in a controlled environment with medical providers on hand to ensure their safety. The psychologist also reminds the patient to use the restroom to ensure that their bladder is as empty as possible to prevent an accident.

They enter the infusion room, and the infusionist then prepares to place the IV line while the psychologist and patient are getting comfortable. It is suggested that it is a good idea to distract the patient while they are getting the IV placed, thereby attempting to alleviate the anticipation of getting stuck and attempt to minimize any vasovagal response that may occur. The facility's nurse practitioner discusses the medical side of the experience with the patient and does some subjective ratings with the patient regarding anxiety and depression, which the psychologist notes for their records. The patient noted that their anxiety was an 8 out of 10, and their level of depression was a 7 out of 10.

After the nurse practitioner leaves and the infusionist begins the session, the patient tells the psychologist of the writing they had done in preparation for the infusion and identify that they wanted to address the loss of their sibling and the impact on the family. At the onset of the infusion, the psychologist notes the initial blood pressure reading, with the purpose to monitor any fluctuations as an indication of how the client is tolerating the infusion. The patient then starts discussing the realities of the loss of their sibling and how it had affected the entire family. This led to them discussing how they blamed themselves for the death of their sibling and feels intensely that they could have done more. The therapeutic process continues with the psychologist helping the patient come to terms with the idea that the outcome could not have been easily changed and guides them towards acceptance. Within 10 minutes, the patient began

showing signs of intoxication and drifting in and out of consciousness. Their earnest efforts to discuss all the familial response to the accident would then be diminished as a notable effect of the ketamine. The patient then closed their eyes and begin to mumble phrases. The psychologist notated these mumblings to identify any possible themes that may reveal themselves throughout the session to discuss afterwards.

As the session continues, the patient's eyes continue to open and close, but they look to be comfortable. At times, the mumblings continue, mostly around missing their sibling, but mostly they are quiet and in their thoughts. The patient's breathing becomes noticeably shallow, and the psychologist prompts them to take a deep breath. The patient does so and draws in breath very quickly. The psychologist then reminds them to take another breath, but more slowly this time, prompting them to engage in box breathing, and counting out loud while the patient draws their breath and exhales over a repeated pattern of three or four breath cycles to bring down their excitement. The patient responds well to the prompts and continues to be peaceful.

After the patient has been quiet for some time, the 10-minute alarm sounds on the infusion pump. The patient has been in their own thoughts for much of the session and appears mildly catatonic. The psychologist asks them how they are doing, and the patient gives a thumbs up. After the infusion completes, they remain mildly catatonic for a few minutes. Approximately ten minutes after the completion of the session, the patient opens their eyes, and the psychologist tells them "welcome back." The patient smiles and says thank you.

At the end of the infusion and after the patient had been disconnected from the infusion pump and had their IV removed, the psychologist begins to unpack the session by asking what the patient's experience was like, citing others often feel as if they had left the room or were just

deep in thought. The patient notes that they felt they left the room but not to anywhere scary or unfamiliar; just that they had some flashbacks to life prior to the accident. They indicate that they felt like they were dreaming, but it left them with a good feeling. The infusionist then removes the IV after asking if the patient had any signs of a headache or nausea. The patient says no, is then disconnected from the pump, and the infusionist gives the two the room to continue processing.

In the brief period after the infusion, the patient begins to come back to their usual baseline. The nurse practitioner comes back in the room after 20 minutes and asks the patient some usual medical questions. The patient indicated that they did need to go to the bathroom and was assisted. After they returned on their own, the patient and psychologist began to discuss the infusion experience with a clearer level of lucidity. They noted that the thoughts regarding the accident were still fresh in their mind, but felt they were not intrusive, just present. The psychologist continues to process through these feelings with the patient and normalizes their response. The psychologist then re-checks the subjective units of anxiety and depression. The patient states that the anxiety had gone down to a 2 out of 10, and that their level of depression was at a 4 out of 10. After they complete the post-infusion session, the psychologist gives the patient homework to return home, take a nap, and write out everything that they can remember, and reminds them of their next appointment time.

Post-Infusion Processing Session 1

The post-infusion session was scheduled for two days after the initial infusion (it is suggested that the follow up session be scheduled within a standard 24-to-48-hour timeframe). In that time, the patient reported having some mild anxiety after the infusion but slept for

approximately four hours after returning home from the session. The psychologist suggested that these two experiences were considered were typical and began to process through the experience (See *Side Effects* in Chapter 3 for guidance related to severe reactions). The patient noted they were able to write everything they remembered about the infusion and suggested that a lot of things were difficult to explain. The patient then noted that they could recall the images easily but could not put them into words. The psychologist tells the patient that this is also a typical response and to try their best to do what they could to verbalize it as clearly as they could. They discuss the patient's thoughts through the sessions related to their sibling and the accident, using some somatic processing techniques around recalling information and minimizing the activation that occurs in their body, identifying where they felt these feelings, and helping the patient sit in those feelings to continue to lower their impact by implementing and pairing the experiences with ongoing breathing strategies.

The psychologist then asks the patient about how their current family relationships are going. The patient acknowledges that the family strife issues had to do with their own perceptions of the current state of things that occurred after the death of their sibling. The patient suggests that they have tried to keep themself away, often not responding to messages or phone calls, and attempting to avoid the communication from their family. The psychologist then attempts to give the patient support in overcoming these impositions by reorganizing them into their own ideas of what happened. Suggestions around processing and resolving these thoughts are the primary focus of these meetings post infusion, therefore, the psychologist is intent on helping the patient make these realizations to assist in overcoming the limits of the patient's ego state prior to the start of infusions. The psychologist and patient continue to explore the patient's

feelings around family relations and to support the patient in creating acceptance around these issues and to discontinue using avoidance and resistance when these themes present themselves.

At the conclusion of the session, the patient is given more homework related to exploring their familial relationships that are currently seen as problematic. The patient indicated that the strain on their family relationships have started impacting their marriage and their desire to get close to those around themself, furthering their feelings of isolation and withdrawal. The patient also notes that they continue to experience nightmares that center around the trauma. The psychologist suggests the patient continue journaling and working through the trauma. They agree to meet the day prior to the next infusion to strategize and see where the patient has gotten related to their perceptions and relationships.

Review of STAR Techniques Through Session 1

Throughout the first infusion session and pre- and post-session meetings, the psychologist has focused their approach on implementing the STAR method. The (S)trategizing portion occurs throughout the initial session and through the infusion session in forms of tuning the patient's awareness around confronting issues along with identifying the specific trauma the patient wanted to work through that had prevented them from experiencing their life in the way they wanted. The psychologist has also continued (T)eaching the patient around feelings that are associated with the ketamine intoxication, how to work through somatic concerns, while also affording strategies to overcome these feelings. The (A)mplify portion was addressed during processing feelings of newly realized emotions and impacts on those relationships to help bring them to the forefront of the patient's experiences and emotional processing. Finally, the (R)esolve portion began developing around normalizing these feelings, reorienting patient

expectations of improvements, and how to better integrate these findings throughout the process.

Pre-Infusion Session 2

The pre-infusion session was scheduled for the following Monday. At the onset of the session, the patient reports that they had reached out to their parents in the interim since their last session. The patient noted that their mother told them that she missed talking with them and seeing them and their spouse, especially because their parents lived close by to the patient and their spouse. This was a significant trigger for the patient, and they became emotional thinking about lost time and how they felt guilty for losing that time. The patient indicates that it felt good to talk with their family and that they had been missing those connections for a while. The psychologist continues to probe the feelings around that missed time and suggests that the patient focus on their family relationships during the upcoming infusion. It was also suggested that the patient write down feelings they could relay to their late sibling. The patient feels this is a good and necessary step.

Because of the emotional response elicited from the patient talking to their mother, the psychologist feels it is appropriate for them to focus on one aspect of the trauma versus the entirety of it, thereby keeping a more specific intent over an overwhelming sense of connection. This way, the patient is not focusing on a five-year gap of lost time, but more on the most beneficial outcome that they would want for themself. It is decided that their relationship with their spouse was the most important focus for the next session because of the proximity of their current symptoms that affect their spouse the most. The patient notes that their spouse has been very supportive of them through this time, but the patient feels that their emotional distance has taken a toll on their spouse and continues to strain their marriage. By having the psychologist

reorient the patient to address the relationships of those closest to the patient, it places the onus on the patient to focus on their own home first with the person who is the most supportive, their spouse. Plans are made to meet at the infusion center with the goal of navigating through their relationship with their spouse.

Infusion 2

The next day, the patient and psychologist meet at the infusion center. The medical team performs their pre-infusion steps. As the patient began to get connected to the infusion, the psychologist begins to explore the relationship with their spouse and the impact that this event has had on their marriage. The nurse practitioner came in and performed her pre-infusion checklist, reviewing the patient's current symptoms, which the patient noted was a 4 out of 10 for anxiety, and a 6 out of 10 for depression. The patient noted they felt somewhat better since their last session.

As the infusion began, the patient began talking about how they had been married for the past nine years, and that prior to the accident, the couple had been very social people, often hosting dinner parties or attending social functions; however, this had all changed dramatically after the accident. The patient noted that they would often experience issues with feelings of needing to escape social situations and having a sudden onset of panic symptoms. The patient also believed that due to these ongoing feelings, they did not like leaving the house out of fear of embarrassment, citing they would often feel weak if anyone observed these feelings wash over them. The psychologist reminded the patient that these reactions, while remarkable, are typical after a trauma, continuing to normalize the experiences for them.

As the ketamine began to take effect, the patient became more talkative about their

spouse and relationship, saying things like “I’m so grateful for my spouse,” and “I am lucky to have them” while they began drifting in and out of awareness. The psychologist kept the patient talking about their spouse, roughly 25 minutes into the session, at which point the patient became non-verbal and internalized their thoughts. The patient continued to mumble some of their appreciation of others, and the psychologist noted these mumblings for continued exploration.

At the end of the infusion, the patient sat and had a pleasant look on their face while sitting quietly for approximately 15 minutes. When the patient opened their eyes, they appeared to have an expression of hopefulness. The psychologist asked how they were doing, and the patient endorsed an overall sense of relief. They noted that their anxiety had dissipated and that their mood had improved. The patient reported improved subjective ratings and expressed that they wanted to hold on to this feeling of improvement. The psychologist reiterated that idea to help engrain that belief into the patient’s memory about the experience.

The patient then stated that they wanted to continue to improve their relationship with their spouse, because that was the most important person to them, and they had unfortunately deprioritized their spouse. The patient began to recognize that this was a grievous error and wanted to correct it as soon as they could. Ultimately, the patient realized this was one of the easier problems to overcome and felt emboldened to do so. Prior to this, the patient noted that they had not considered how much their mood was impacting their marriage and this realization gave them clarity in how their ongoing concerns were impacting more than just themself. The patient decided they were going to go home and talk to their spouse about how determined they were to repair their relationship.

Post-Infusion Session 2

During the post-infusion session that took place two days later, the patient reported that they experienced several moments of clarity and had an epiphany. They recalled that they had started feeling disconnected from people shortly after the accident because they wanted to prevent the feelings associated with losing anyone again. This had compounded into strained and surface-level connections with many around the patient due to their reticence in establishing deep, meaningful relationships that could cause them distress in the long-term, should something occur to those they were close with. Consequently, they had begun alienating friends and family to not open themselves to that potential outcome, creating a buffer from getting too close. The patient realized that they had missed those connections without realizing it out of fear. They also determined that this was greatly affecting their overall sense of happiness, realizing that they were much sadder than they had considered with the lack of intimate connections with those around them. The patient determined that they would really like to have those connections again and wanted to ensure that they were open to those experiences again.

Review of STAR Techniques Through Session 2

Throughout this session, the patient is made to focus on a more acute area of the trauma to meet their goals, focusing on how it had impacted social relationships, including intimate and familial relationships. Part of the (S)trategizing occurs through the more intent focus on those impacts through the examination of the trauma. (T)eaching lent itself to focusing on how those issues should be pulled apart into one piece at a time, while also normalizing the response to the trauma itself. The psychologist then (A)mplifies the message of how the patient's beneficial relationships required time and focus while also echoing the sentiments of improvement in the

post-session meeting. These approaches help to guide the patient into further developing these senses for themselves. The aim of (R)esolve phase in these early sessions may be premature while continuing to enable the patient to face their reality through the process.

Pre-Infusion Session 3

The following Monday, the realities of the patient's lost opportunities that they had since the loss of their sibling began to become clearer to them. The patient reported that they had come clean with their spouse about the strains they felt relating their intimacy and apologized to them for the years of grief that they had experienced along with the pain that they had caused their spouse. The patient noted their spouse understood, and that the apology was unnecessary, but felt it was a beneficial step for them to make these apologies. The patient felt their relationship had become stronger than before, citing that their spouse was much more a part of their daily life. The patient also indicated that they realized how much they missed their friends.

This realization led to the patient reaching out to several friends whom they had considered close but had not spoken with in some time. The patient stated these calls reminded them that people cared about them and were anxious to see them. The patient indicated that their friends remarked how much "lighter" they sounded, as if the patient had alleviated themselves from the years of turmoil they had been experiencing. These remarks appeared to be internalized by the patient, as they began to believe what others were telling them. The patient also felt that they needed to begin the process of forgiving themselves for feeling this way for so long. The psychologist again normalized these feelings and suggested that the re-establishment of connections can be tedious, but beneficial for long-term success in creating adequate social support.

Together, the patient and psychologist endeavored to work through intimate connections with others while continuing to engage in the healing process. It also became a strategy to bring forward these concerns while engaged in the ketamine infusion to begin to reorient these feelings and alleviate the patient from them. The patient identified their best friend as someone they had regrettably pushed aside throughout the period they had been grieving and that was the next relationship to improve. The psychologist gave the patient a homework assignment to write a letter to their best friend and to detail their feelings along with creating a narrative detailing how they intended to improve their relationship for the next infusion. The patient also noted that they felt that they should apologize to their best friend.

Infusion 3

At the onset of the infusion the next day, the patient remarked their overall sense of improvement was noticeable and persistent. The pre-infusion steps were taken, the patient began to get connected to the infusion, and the psychologist begins to explore the relationship with the patient's best friend and the lack of connectedness that had made the patient feel worse. The nurse practitioner came in and performed her pre-infusion checklist, reviewing the patient's current symptoms, which the patient noted was a 3 out of 10 for anxiety, and a 5 out of 10 for depression.

The patient then began talking about the relationship with their best friend. They had met at university during a football tailgate. The patient noted that they loved attending football games at their university and was proud to have those experiences with a large group of friends. They also indicated that they missed those days, even with being relatively close to their alma mater. As the ketamine took hold, the patient began reliving those days, suggesting how optimistic they

were for the future and how they felt sad that they no longer had that youthful optimism, instead facing the realities of adulthood. The patient talked about how the two had plans to make it big as business magnates, and how they never let their dreams have limits. The patient seemed to brighten up when talking about their experiences of youthful exuberance and how much things had changed since those times.

The patient also recalled being in their best friend's wedding in a position of honor and how they were the one who convinced their best friend to talk to their future spouse when the two met. The patient appeared somewhat dismayed that they were no longer that person, instead changing in their life for the realities of adulthood and limits. The patient also began to feel that they could get some of those feelings back regarding excitement and hopefulness for the future, and for the first time, realized these were within reach. The psychologist continued to guide the patient through the reorientation of hopefulness versus dread and encouraged the patient to realize these possibilities for the positive benefit instead of the negative associations they had with them.

The patient also realized that they had similar feelings towards their sibling, noting that they would often discuss the future and their retirement plans with a lake house or boat they could purchase together. The patient then began to understand how these plans they had made had begun to unravel after the loss of their sibling. The patient also began to realize how much they had limited their own potential, because they did not want to outgrow those goals they had with their sibling. These moments of clarity continued until they became non-verbal through the end of the infusion. The patient then appeared comfortable and in a positive headspace through the rest of the session.

Upon completion of the infusion, the patient again recalled how grateful they were for the experience. They suggested that their subjective views on anxiety and depression were minimal and felt better than they did when they arrived at the facility. Their spouse, who was also at the session, remarked that they had noticed the patient was sleeping better without the panicked responses during sleep. The patient's spouse also noted that they were more confident that the process was working for the patient. The psychologist gave the patient homework around reaching out to their best friend and rekindling their friendship along with journaling their experience.

Post-Infusion 3 Session

As the session began two days after the infusion, the psychologist sees that the patient's affect is remarkably improved. The patient notes that their sleep has improved, their appetite has returned to normal, that they do not feel as anxious as they had been feeling and how they feel relieved from a good amount of the self-imposed burden that they had placed on themselves. Instead, they began to feel like they should be feeling. The patient states that they have been in touch with their best friend and had recently talked to catch up on life and where things were at. The patient appeared to mildly punish themself for allowing the friendship to become so distant but noted that their best friend had forgiven them as they understood the impact that the patient's sibling's loss had on them. This had been a relief for the patient, as they felt that all their actions had impacted people in ways that were unforgivable, resulting in the distancing from others.

The psychologist clarified how trauma impacts even the closest relationships and advises that the patient's progress is remarkable when it relates to their insights, improvements, and evolving goals related to their treatment. It was discussed that the patient's ability to resolve

these issues was one of the most significant goals in treatment, as they had been avoiding facing these realities, along with avoiding others in the fear of losing them. Throughout the patient's ketamine series, the patient became more aware of how their friendship was meaningful to others, and how their contributions and presence in their lives were important to everyone. The patient concluded that their self-pity and depression had prevented them from living their life to the fullest and vowed to change the approach going forward. The psychologist commended the patient for their adherence to the desire to continue towards improvement and suggested that the patient make earnest efforts to continue to reach out to those whom they had let go of.

Review of STAR Techniques Through Session 3

Throughout these sessions, the psychologist has remained focused on the patient's goal of improving their relationships, while also continuing to normalize their responses to trauma and how to integrate the improvements they are making into their everyday lives. These (S)trategizing sessions are reflected in reiterating the importance of these social connections, especially around important relationships. (T)eaching the patient to understand that while tedious, relationships take work and intervention to improve them overall, and to reflect on the idea that life does not stop when changes in plans occur. The psychologist also (A)mplifies the idea that reinforcing these ideas can be applied to other sentiments, such as how plans change over time, but does not prevent people from making new plans. Finally, the patient is helped in (R)esolving feelings of how relationships are necessary in helping people face improvement while also seeing how the future can proceed with making new goals. Friendships, at times, can be fixed with effort, but taking the time and energy to do so can be tedious. Ultimately, the patient is in a better position to repair these relationships with a better outlook on why they are

important.

Pre-Infusion Session 4

When the patient arrives for the planning session the next Monday, they note that they were uncertain what to set as a goal. They noted that they continued to see improvements, had been more outgoing, had contacted old friends, felt a rekindled relationship with their family and spouse, and felt much better overall. This was welcomed news to the psychologist who remarked about their improvement and how to continue to maintain these benefits. The patient then stated that they had been experiencing some issues related to sexual intimacy and that they wanted to improve was their sex life with their spouse.

The patient recalled that after the accident, intimacy was very difficult for them to become aroused and to engage in sexual activity, including masturbation. They recalled that prior to the accident, the couple's sex life was easy and enjoyable, but afterward, became a seldom occasion. The patient stated they had continued to re-establish their intimate emotional connection with their spouse, but that they were continuing to have apprehensions around re-sparking their sex life, though they did want to try.

The patient also noted that the couple had wanted to have a child, something that the patient noted was completely unthinkable to them after their sibling's death. However, now, the patient decided that they were in a much-improved place mentally to make the attempt and move forward with trying to conceive. The psychologist began to help the patient continue to develop and realize these feelings around intimacy, sexuality, and taking on the responsibility of being a parent, further defining the things that would likely change in the couple's life. The patient then exhibited a remarkable hope for their future and what it could look like.

Infusion 4

At the onset of the infusion the following day, the patient remarked they were continuing to see benefit. The pre-infusion steps are taken, and the patient began to get connected to the infusion pump. The nurse practitioner enters and performs her pre-infusion checklist, reviewing current symptoms, which the patient noted was a 2 out of 10 for anxiety, and a 2 out of 10 for depression. The patient further remarked how they were amazed at their progress and felt that the last infusion was very beneficial.

After the infusion begins and the infusionist has left the room, the psychologist begins to explore the ongoing concerns with sexual intimacy. The patient states that fear had been the primary concern as the patient did not want to the couple to get pregnant, because they did not feel they could deal with any potential loss by a miscarriage or sudden infant death syndrome. The patient explained that they had convinced themselves that something would invariably go wrong with the pregnancy, or even after birth. The patient had created a reality where no matter what, they would have to face another devastating loss and how that loss would impact them.

During that moment, the patient realized that these catastrophized outcomes were all made up in their head and realized that taking chances required a certain level of risk. While having children was a risk they would not have previously imagined, the patient was much more willing to take a chance on it now because of their improved outlook on the future. The patient discussed how they had told their mother about wanting to try to have children and their mother was overjoyed, telling the patient that she would love that, and that the patient appeared to be in a much better place to have children than they were previously. The patient agreed and told their spouse that the time had come for them to try, which their spouse agreed to.

At this point in the treatment, the psychologist realized they had very little to do with the patient's ongoing intervention, as the patient was redefining their own empowerment through the updating of their goals. The psychologist notes that the patient had begun to take charge of their own life, their decisions, and had taken control of their future without hinderance or encumbrance and how things were much more hopeful in these regards while overcoming these self-imposed limitations. This was welcomed news for the patient, as the session ended.

Post-Infusion 4 Session

At the beginning of the post-infusion session two days later, the patient notes how much clarity they had regained since the onset of the series. While they endorsed that their sleep continues to be improved, their appetite has been better, their connections are feeling more restored, and their relationship with their spouse is better than it has been in years, the patient continues to feel a sense of mild anticipation regarding being concerned that something could invariably go wrong. The psychologist discusses the realities of resiliency, whereby the patient can deal with situations through the lens of a newfound optimism while still having the endurance to navigate situations that are unforeseen and troublesome. The patient acknowledges that they can see themselves more easily adapting to new challenges as they arise and felt that they were more capable of facing these situations than they would have been in the past.

The patient notes that they would previously stay in bed, often letting problems compound until they felt insurmountable, leading to the patient feeling as if they were unable to solve their own problems, let alone those of anyone else. The patient acknowledged that these feelings have dissipated, and that they are ready to face challenges that have yet to present themselves. The psychologist again reframes the concerns related to the patient being incapable

of facing problems by detailing how many problems had been solved since the beginning of the treatment protocol and how the patient now realizes that their overall ability to deal with new problems was significantly improved than before. By engaging in deeper thoughts of how the patient had been limiting their abilities, the patient was able to resolve the conflicting ideas that were in their mind related to problem solving.

Review of STAR Techniques Through Session 4

As these later sessions continued to spurn growth, the patient has become much more aware of their own ability to engage in problem-solving while also taking control back in their life. The psychologist's approach then becomes around strategizing ongoing benefits that are obtained through the sessions and infusions while also allowing the patient to welcome positive outcomes. The teaching phase comes about in helping the patient realize that new beginnings are challenging, and sometimes can be difficult, but are worth the effort and are not impossible. The psychologist also continues to amplify the client's goals in this infusion treatment of family building and hope for the future. It is also important to understand how risks do not come without the potential for negative outcomes but are worth being taken. Also, the idea of empowerment for the patient to overcome their own issues is a powerful lesson by recognizing their own power and to facilitate that hope they can overcome their concerns. The resolution can be aimed at understanding that the patient is in control of making whatever life they want while also closing painful parts of their past.

Pre-Infusion Session 5

On Monday, the patient began the session discussing their inability to be assertive when necessary. The patient explained that they did not have this problem in the past prior to their

sibling's passing but noted that following the accident when they returned to work, they felt a new meekness around their engagement with others. The patient felt that they were unable to take control of situations or tasks that had been given to them and felt that they would never regain this confidence. However, recently, they noticed that they were much more confident in their daily functioning and desired to overcome their lowered sense of assertiveness.

The psychologist explained that through the benefit of regained self-efficacy and empowerment, these senses can be rebounded after a depression had lifted and a trauma had been resolved. The psychologist detailed how a mild adjustment in the patient's thinking could make a significant difference when it becomes prescient. This can lead to re-enabling or re-tuning a previously forgotten ability through giving ourselves permission to restart this process. The patient resolved to give themself permission to take back the ability they felt they lost and allow themselves the authority to regain their assertiveness. The psychologist recommended writing a letter to themselves about the abilities that they had let go of because of their sibling's death and delineate the attributes they had lost that they would like to regain.

Infusion 5

On Tuesday at the facility, the pre-infusion steps are taken, the patient began to get connected to the infusion pump. The nurse practitioner enters and performs her pre-infusion checklist, reviewing the patient's current symptoms, which the patient stated had remained steady, and was a 2 out of 10 for anxiety, and a 2 out of 10 for depression.

After the infusionist left, the patient remarked how their work had become easier and how their mind was clearer. The patient stated they were much more capable of predicting outcomes without the fear they had previously experienced. The patient noted that they were not

worried about answering the phone out of fear that bad news was on the other end. The patient also said how they and their spouse got together with their spouse's best friend and their husband, a task that would have previously been a "no-go" for the patient and how they had such a wonderful time with the other couple. The patient commented how they had realized how much they had been limiting their own life and how they could not even remember how their thinking had changed resulting in this perspective. The patient indicated that they had completed their homework and that they wanted to share the letter with the psychologist at the end of the series, which the psychologist noted as a positive step for their treatment.

The patient also stated that they and their wife were actively trying to get pregnant. The patient bashfully admitted that they felt like a teenager again with their libido, and that their spouse had been happily obliging their newfound prowess. The patient remarked how connected the couple felt, like they were when they were back in college. The patient continued to be in disbelief that they had made such progress, noting that they were grateful to the psychologist and all the processing work they had completed throughout the series. The patient stated they were hopeful that it would all stick after the series was complete, and that they would continue to feel in charge of their own life. The patient made these remarks as the infusion ended.

Post-Infusion 5 Session

Upon the outset of the session two days after their infusion, the patient cited having a nightmare for the first time in a while. The patient noted that it was a visualization of the accident again, except this time, they were the one who perished as their sibling lived on. The patient recalled how this affected them when they woke up, and how grateful they were for being alive. The patient admitted that they felt somewhat selfish in this realization but noticed that a

part of them died in the loss of their sibling and that was something they had never realized before. The patient explained that this thought had seemed to be the piece that was holding them back and that they understood how much guilt and responsibility they had put on themselves for the purpose of memorializing their sibling. The psychologist again normalized these feelings and commended the patient for their strength through overcoming these feelings.

The patient disclosed that they had realized that they had been paying penance for the loss of their sibling over the past five years and that their mourning period had come to an end. The patient reported that they had gone to their sibling's grave to go and talk with them. It was a place that they had not been since the funeral because they could not face the reality of their loss. The noted that they talked out loud to their sibling's grave, something they felt silly for, but as it continued, they began to feel more emboldened by it. The patient cried as they thought about the moment during which they apologized to their sibling for not living their life to its fullest after their loss.

After composing themselves, they stated how they were able to "say goodbye" for the last time and instead reframed the loss to an experience of knowing that their sibling was always with them. The patient noted that they spoke to their spouse, and that if they were to have a child of the same sex, they would name them after their late sibling. The patient felt a peace with this idea and felt it was the best way to honor their sibling and to ensure that their sibling's memory stayed with them for the rest of their life. The psychologist noted that it was a remarkable idea and one that would surely bring them joy.

Review of STAR Techniques Through Session 5

As the series is coming towards completion, it is important to continue to embolden the

patient to continue to engage the empowerment they are feeling. The (S)trategizing does not only encompass the idea of assertiveness the patient is verbalizing, but to continue to feel empowered to live their life. (T)eaching at this point is only around reinforcing this idea for the patient, and the (A)mplification is supporting the patient in making improved judgments and decisions. (R)esolution continues to occur throughout the process as the patient continues to integrate these ideas in everyday life.

Pre-Infusion 6 Session

On Monday, the psychologist asked the patient to reflect on their progress using the STAR model psychotherapy throughout the infusion series and hat had brought them to treatment, while also reviewing how they had overcome their presenting issues. The patient noted that their fear had almost completely abated. The patient recalled that they had recently received a "we need to talk" email from their boss which sent chills down their spine, only to find out that they had recently been awarded a citation for an improvement in productivity for their department. The patient admitted that they had feared for the worst but went into the meeting head on to face whatever the potential situation would bring about. The patient recalled how they would have been completely debilitated by an email like that in the past, but with their newly reclaimed confidence, they had no concerns about facing whatever came their way. The patient felt that they had a new lease on life, finding their ability to honor their sibling without the need to sacrifice their own life as penance. Now, they just felt that completing the protocol was the best way to honor their spouse, their family, and most importantly, their sibling.

The psychologist explained the maintenance phase of treatment, where booster sessions were optional should the patient decide if they should need them. These boosters are set at a two-

month interval and are predicated on the idea of continued support through the end of the entire protocol. It was explained that the door was always open to engage in a booster session should the patient ever need it. The psychologist also encouraged the patient to write one final letter to themself to be opened in a year's time. This letter was to remind the patient of the feeling they are experiencing at this phase in their treatment.

Infusion 6

During the infusion on Tuesday, the pre-infusion steps are taken, the patient had their IV placed and began to get connected to the infusion pump. The nurse practitioner enters and performs her final pre-infusion checklist, reviewing the patient's current symptoms, reviewing the paperwork regarding booster sessions, and reviewing the patient's assessment scores that the facility took at intake. The patient's subjective rating scores had improved to the point of being immeasurable, and the patient rated themselves a 0 out of 10 for anxiety, and a 0 out of 10 for depression, citing they felt no notable concerns with either.

During the final infusion, the patient recalled how much things had changed. They felt that all areas of their life were back in control and that the future seemed hopeful. The patient tended to want to negatively view themselves for causing so much strife in the lives of those who were around them, but also realized this occurred because of their own pain and fear. The patient gleefully reported all of their symptoms were completely gone, and they could not be more enthused about everything that was coming their way. The psychologist reminded the patient that these responses are typical in the face of grief and loss and encouraged the patient not to beat themselves up too much about being susceptible to these outcomes.

The patient states they and their wife are continuing to try to get pregnant and they are

mildly concerned that something may be wrong, but also realizes that they are not aware of anything being wrong, so they should just let things work themselves out. The patient caught themselves in wanting to fear the worst but admonishes themself for thinking negatively and overrides their impulse to be caught in a thought loop. Instead, they let go of the feeling and prepares for whatever is ahead. The psychologist reminds the patient of how much progress they had made in this vein, and how this would have been impossible for the patient at the outset of the protocol. The patient agrees and slips away into a quiet introspection during the rest of the infusion.

After the infusion session, the nurse practitioner and staff congratulate the patient on their progress and completion of the infusion series. They are there to celebrate with the patient in their progress and commend them on remaining vigilant in completing the course. They further expand on the booster sessions and continued support, should the patient need any further support.

Post-Infusion 6 Session

In their final session of the program, the patient reported an overall sense of wellness, calm, and progress. They state that it was too early to announce, but that the couple was pregnant. The rush of emotions that came over the patient were of pride, apprehension, and relief. With these mixed emotions, the patient knew that they were much more prepared to be a parent than they could have anticipated at the outset of this journey and how relieved they were in this improved mindset.

The patient notes that the processing, homework, and sessions were integral to their success, and felt that while the ketamine may have played a role, they thanked the psychologist

for their guidance and input. The patient felt as if the whole process was beneficial in working through their trauma, facing their fears, and overcoming their worries. They noted that through all the work, the structure that was put into place was the piece that made it all make sense.

The psychologist noted that the process itself was a structure that was in place to ensure improved patient outcomes that were as close to success as possible. The psychologist also gave the patient the okay to contact them if needed in the future. The psychologist also thanks the patient for their trust through the program and was grateful for the opportunity to work together.

Review of STAR Techniques Through Session 6

In the final stage of the treatment strategy, the overall sense in progress is to maintain that outcome and to further foster it into fruition. The patient is reminded how they were responsible for their own outcomes, were placed in charge of doing the work, and were the responsible one for the results. It is the job of the psychologist to be there to steer the patient in the right direction and to continue to provide guidance, education, and a resounding of the messages of why the patient's success was brought about. These final sessions reflect how the STAR method can assist in patient outcomes and benefit.

Program Evaluation Plan

One of the most critical points of the pre- and post-infusion sessions is to determine patient treatment efficacy. In this case example, the patient continues to show progress throughout the infusion series. This is not uncommon in this treatment style but should be observed throughout the process to ensure patient success. Obtaining subjective ratings is critical in a pre- and post-infusion setting to determine the patient's awareness around their perceived benefit from the treatment. This perception is suggested to be one of the best ratings related to

ongoing patient outcomes because it challenges the patient's view of the treatment while also producing documentable and measurable changes throughout the infusion series. While these ratings are subjective, they can be utilized to reflect the overall change in the patient's daily functioning.

Another critical data point will be the post-series assessment to determine if the patient continues to meet diagnostic criteria of the disorders that led to the treatment being performed. If the patient shows remarkable change, this should be reflected in the pre- and post-series analysis of validated measures as described in Chapter 3 in a quantifiable measurement-based care model. It is not necessary to create a report of the changes but can be done, if the mental health provider finds it beneficial for the patient's understanding, as well as any other treatment providers who may be concerned with the outcomes. This may also address patient concerns with the extent of the treatment effect that they have experienced.

Finally, tailoring patient priorities with their presenting problems, adjusting as needed throughout the treatment protocol, and documenting pre- and post-treatment effects can help patients understand how their improvement has been ongoing throughout the process. It is suggested that presenting a pre-series and post-series document of findings be part of the patient's chart and ongoing documentation. This can be done within the confines of the treatment plan to reflect treatment effect.

A measure of success for clinicians will be based on the approaches attempted during treatment with the further understanding of how the intervention assisted in improving the patient's outcomes. Supervision or consultation with peers who are well versed in this approach can examine their own techniques and see what was useful and what was not. Because the goal

of these guidelines is tailored to patient outcomes, clinical decision making should be considered throughout the process to identify what patients respond well to versus what is believed to be the best course of action. Because ketamine can put patients into a space of suggestibility, utilizing that timeframe to assist in measuring intervention success should be a significant part of the process throughout the delivery of treatment.

Conclusion

This case is presented to illustrate that ketamine treatment can be utilized to overcome traumas, diminish anxiety and depressive feelings, along with reorienting patient lives to provide them with relief. The conjunction with therapeutic intervention assists in that process, insofar as guiding the patient through their feelings and encumbrances can result in improved outcomes. It is the finding of this project that these guidelines can benefit patient outcomes through a structured plan that addresses these concerns while working in conjunction with medical providers to better patient benefit and treatment goals. Through the approach of the STAR Method and a structured treatment plan, patients can find durable results with measured success.

It is also necessary to ensure that the combination of documenting the findings at the onset of treatment, along with the SUDS that are obtained throughout the infusion series, along with post-series documentation be able to be presented in a digestible manner for patient consumption that illustrates the treatment process and outcomes. By doing so, patients can get a deeper understanding of their journey and measurable results.

CHAPTER 5. DISCUSSION & CONCLUSIONS

Introduction

The process of Ketamine Assisted Psychotherapy for Infusions (KAP-I) is a response to the growing ketamine and psychedelic treatment modalities that are continuing to expand. This dissertation endeavors to bridge a gap in training options for mental health professionals, who are interested in integrating this modality into their treatment options for their patients and to their communities at large. It is the author's hope that this dissertation will provide a useful and understandable primer of information that will lead to further investigation of how to best deliver this treatment to patient populations.

Outside of the presentation of information related to the history of ketamine, along with a review of the current research, this program has illustrated and developed useful strategies related to the implementation of KAP-I into treatment for trauma, depression, and anxiety. As further understandings of these interventions continue to grow, it became necessary to create a process that was directly integrated into a best approach through field experiences and developed practice. Without these experiences, fundamental truths related to ketamine intoxication and client experiences within clinical settings would be difficult to discern without a point of reference. As a result, and through several years of *in vivo* experience, methodologies which have been tried and have succeeded are chronicled in the model herein presented.

Summary of the Process

This program details a case from referral to a maintenance phase of treatment. It has been presented this way to alleviate the necessity of deep diving into basics in psychopharmacology, pharmacology, client intake procedures, and unique therapeutic approaches that mental health

professionals are trained in. By generalizing these procedures, mental health clinicians can infer their necessary approaches and tailor them to their level of comfort and expertise.

Because of the intense amount of interaction between patient and mental health clinician, these steps are given as a check box to complete throughout the intervention. As a typically manualized therapeutic intervention would discuss and determine activities in a session-by-session manner, this program has been developed to simplify the process as much as possible to better understand the numerous steps required in this program. It is also understood that this process may be difficult to implement due to mental health clinician's practice models along with the scheduling availability for the ketamine clinic; therefore, it is left up to the individual mental health clinician to determine if this approach is right for their practice.

The explanation of the process in the program is also predicated on the patient's awareness of ketamine treatment. It is considered that mental health clinicians may be compelled to introduce their patient to the idea of ketamine treatment and that it can be integrated into the process after intake and even beginning therapy. It may also be that a medical provider who is utilizing ketamine has referred a patient for concurrent therapeutic intervention. Whatever the impetus of the patient's engagement into ketamine treatment, the steps related to patient education, strategizing and resolution are still applicable and important steps in the process.

The program is laid out in the model of a six-infusion series but may be adjusted depending on the patient's progress in an infusion series prior to contact with the mental health clinician, if the medical provider deems a different number of infusions throughout the series or depending on clinician availability. If the mental health clinician is unable to meet all during all sessions, it is suggested that contact be made with the patient within 24 hours of the infusion

and/or prior strategizing to assist in developing the path for the infusion. By doing so, client processing can be assisted in both pre- and post-infusion sessions to assist in overcoming their presenting problem(s).

Summary of the Outcome

The expected outcomes with this type of treatment strategy are to help alleviate acute symptoms related to trauma, depression, and anxiety. While there are other applications related to ketamine treatment, it is the focus of this program to address these three issues. It is considered that traditional psychotherapy and ketamine-only treatment strategies are effective in addressing these issues independently, it is believed that the synergy of these two approaches can result in improved outcomes. Therapeutic guidance with ketamine is considered optimal to steer patients into documentable results. Conversely, while therapeutic interventions with evidence-based approaches do show efficacy, the blending of these two approaches can assist in short-term solutions with long-term benefits. While traditional talk therapy has repeatedly been shown to alleviate symptoms, these symptoms can become long-lasting and difficult to overcome.

It is the purpose of this model to suggest that the best approach to determining these outcomes relates to pre- and post-infusion data gathering to document success and/or benefit. As medical providers only have minimal screening instruments to determine efficacy, psychologists and other mental health professionals who are trained in assessment have access to a battery of different measures to better determine patient outcomes. It is suggested that the use of these instruments is critical in observing differences that may change diagnostic impressions and show the alleviation of clinically oriented symptoms. By implementing a before and after analysis, creating a treatment strategy around these symptoms, engaging in psychoeducation, and

integrating change into patients' psyches, demonstrable changes that integrate benefit are expected outcomes through a multi-pronged approach in treatment delivery. Ultimately, a joint effort in helping patients through these difficult times can be considered the best available approach.

Discussion of the Outcome

It is suggested that the presumed outcome of this treatment style can be viewed as positive without therapeutic intervention; however, does have potential to be improved through the guidance provided with this style of treatment, but does come with potential strengths and limitations as discussed below. Comparatively, a review of Dore and colleagues (2019) who reflected significant improvements with patients who experienced depression and anxiety when given ketamine intramuscularly or orally, but do not discuss intravenous delivery. It is considered that this approach would provide similar outcomes with the adjunct of therapeutic intervention and ketamine intoxication that was somewhat more potent due to the bioavailability differences in these methodologies (Mathew & Zarate, 2016). One of the notable differences in measuring these two successful outcomes will be in the post-series assessment to measure outcomes and to reidentify the severity of symptoms upon completion. While Dore and his colleagues utilized brief measures, the difference here is to utilize more robust instruments to establish treatment effects on a broader scale. This change is different from the medical approach of treatment successes as it implements psychometric data from larger instruments.

Strengths and Limitations

Strengths

As previously discussed, ketamine and talk-therapy, independently, do show benefits on

their own (Ballard et al., 2014; Barton & Armstrong, 2019; Burger et al., 2016; Niciu et al., 2014). It is the operating principle of this program that blending these two techniques can offer a more robust treatment outcome that shows prolonged durability. This outcome is considered the strongest option for the treatment of acute stressors related to trauma, depression, and anxiety for those who may have been deemed *treatment resistant* (Abdallah et al., 2019; Acevado-Diaz et al., 2020; Hartberg et al., 2018). Because of durability measures that have been chronicled throughout the current available research, it is believed that continuing to implement strategies around processing techniques in conjunction with ketamine, along with long-term benefits by removing painful stimuli from patients who are suffering can be considered emerging practices that are hoped to be reviewed by others and established in future evidence-based practices.

Limitations

The most significant limitation to this treatment strategy is cost. Because this treatment is an off-label usage of ketamine, insurance companies are not prepared to reimburse medical providers for the infusion series. While this is being explored, it currently does not meet standards for primary medical care and does come with a significant cost component simply for the infusion series itself. Secondly, the cost of clinicians to be out of office can also be a barrier of treatment, as scheduling two-hour sessions out of the office can lead to scheduling limitations for other patients who are in-office. As a result, clinicians may increase costs for hourly rates to supplement lost time in the office due to travelling to various sites.

It is greatly understood that these realities may limit the access to this treatment with a wide range of potential patients who are attempting to get in with ketamine providers for treatment. However, there are patients who are able to access these treatments, as evidenced by

the continued growth of ketamine centers throughout the country. While it may be a barrier for some, it does not seem to be a barrier for all.

Perceived limitations of this form of treatment does also appear around concerns with abuse potential and addiction concerns. While some suggest there is little abuse potential (Salvadore & Singh, 2013) as historical data was reflective of self-reported experiences, others believe that the abuse potential is concerning, but acceptable in practice in the correct settings (Mathew & Zarate, 2016). This is where philosophical differences exist in medical providers and seemingly come from their individual training. This author is hopeful that ketamine will be seen as a more useful treatment option and that the integration of mental health treatment will produce worthwhile effects and beneficial results for patients.

Next Steps

As it is the purpose of this project to create guidelines for practice, the overall process has not been implemented in a randomized control trial for outcome analysis. It is hoped that there can be an institution that may undertake this colossal task to compare outcomes with ketamine-only, psychotherapy-only, and KAP-I to determine the differences in these various approaches and examine which may have the best outcomes. It is the hope of the author that this monumental project can be completed to examine the overall efficacy of KAP-I, in practice, versus traditional techniques.

Another consideration is around the utility of the Ketamine Questionnaire that was created by this author to determine a patient's awareness around ketamine, and to identify important considerations related to PTSD, suicidality, and their understanding of ketamine treatment. It is posited that the questionnaire is primarily a screening tool to be utilized for the

sole purpose of determining and better understanding patient eligibility. Analysis related to reliability, validity, and other important statistical analyses are necessary for the purpose of establishing this screen as psychometrically sound. These analyses are simply outside of the scope of this project. It is the hope of this author that future projects will endeavor to analyze this tool to provide analysis of the screening instrument and determine its utility.

Finally, it is hoped that a ketamine treatment center may utilize this protocol to integrate mental health treatment and medical treatment to establish a more synergistic approach to patient treatment. Because the approach is formulated on an agreement between medical providers and mental health providers, to see a center where the integration is already done in-house could be the best approach in establishing the effectiveness of this treatment strategy.

Conclusion

Ketamine therapy has been growing in popularity for the past several years. Mental health professionals have been interested in trying to integrate a modality of psychotherapy assistance in practice but have had few resources to rely on to establish practices that are useful around this style of treatment. With the years of experience that the author has had in delivering this treatment, it was necessary to share what has been learned along the way. By creating a path forward for other clinicians to learn the realities of providing ketamine treatment, it has presented an opportunity to create a dialogue between mental health providers and medical professionals about improving care among those who are afflicted with trauma, anxiety, and depression. Bringing awareness to the unique nature of ketamine and its healing applications outside of the primary use has been a net benefit for the medical and mental health community at large.

It is also noted that there is no single way to provide this type of treatment. Numerous influences from different theoretical orientations can be applied to this treatment strategy. It is not to say that this program is the only acceptable approach, just a guide to understanding the realities and limitations that have been documented in the literature and in private practice. It is the hope of this author that future applications can validate these findings, or even refute them for better options. Either way, the possibilities around ketamine are clear, and may even be in their infancy regarding what we truly know about them.

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APPENDIX A. KETAMINE TREATMENT CHECKLIST

Ketamine Treatment Checklist

Patient Name:	**DOB:**
Referral Date:	**Referral Source:**

KAP-I Process Flow

Pre-Infusion Series Activities	
Diagnostic Interview/Assessment Completed Date: _____	Diagnoses identified for treatment:
Treatment Plan Review & Results Completed Date: _____	# of Sessions to be completed:
Schedule Series with Medical Provider Initial Infusion Date: _____	Provider information:

Infusion Series Flowchart	
Pre-Infusion Education and Strategizing (to be completed prior to first session) Completed Date: _____	**Pre-Infusion Education and Strategizing Infusion #4** Completed Date: _____
Infusion #1 Completed Date: _____	**Infusion #4** Completed Date: _____
Post-Infusion Processing Session After Infusion #1 (Should be done In Office) Completed Date: _____	**Post-Infusion Processing Session After Infusion #4** Completed Date: _____
Pre-Infusion Education and Strategizing Infusion #2 Completed Date: _____	**Pre-Infusion Education and Strategizing Infusion #5** Completed Date: _____
Infusion #2 Completed Date: _____	**Infusion #5** Completed Date: _____
Post-Infusion Processing Session After Infusion #2 Completed Date: _____	**In-Office Post-Infusion Processing Session After Infusion #5** Completed Date: _____
Pre-Infusion Education and Strategizing Infusion #3 Completed Date: _____	**Pre-Infusion Education and Strategizing Infusion #6** Completed Date: _____
Infusion #3 Completed Date: _____	**Infusion #6** Completed Date: _____
Post-Infusion Processing Session After Infusion #3 Completed Date: _____	**In-Office Post-Infusion Processing Session After Infusion #6** Completed Date: _____

Post-Infusion Series Activities	
Diagnostic Re-Assessment Completed Date: _____	Does patient continue to meet diagnostic criteria?
Re-Assessment Results Completed Date: _____	Unresolved issues?
Schedule Maintenance Series with Medical Provider Initial Booster Session Date: _____	Estimated Booster Sessions: