PSYCHEDELIC-ASSISTED PSYCHOTHERAPY: HOW PSYCHEDELICS COULD CATALYZE CONVENTIONAL THERAPEUTIC APPROACHES FOR TREATING TRAUMA-RELATED CONDITIONS

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Abstract

The use of psychedelics as a therapeutic adjacent to psychotherapy is emerging as a treatment method for various psychiatric conditions. The purpose of this review was to evaluate the safety and efficacy of psychedelic-assisted psychotherapy (PAP) for treating trauma-related conditions such as complex trauma, PTSD, and acute stress disorder. This review evaluated clinical trials assessing the experiences induced by psychedelics such as MDMA, psilocybin, and LSD. Clinical trials evaluating the safety and efficacy of PAP for treatment of various psychiatric conditions, including PTSD, were also assessed. Results indicated the safety and efficacy of PAP in reducing clinical outcomes associated with trauma-related conditions when administered in controlled settings, even for treatment resistant conditions. Common themes reported from qualitative reports included significant decrease in arousal often precipitated by the recall of traumatic memories, increased insight into the self, reduction in resistance to communicate feelings, increased connectedness to others, increased acceptance and processing of emotions, positive changes in worldview, forgiveness, enhanced therapeutic alliance, enhanced selfcompassion and empathy, ego dissolution, and increased motivation and commitment to change. All of these experiences could enhance the efficacy of conventional therapeutic approaches such as cognitive behavioral therapy, prolonged exposure therapy, psychodynamic psychotherapy, and internal family systems psychotherapy in the treatment of trauma related conditions. Psychedelics used in conjunction with conventional therapeutic approaches could potentially aid in the treatment of trauma-related conditions and positively influence clinical outcomes.

PSYCHEDELIC-ASSISTED PSYCHOTHERAPY: HOW PSYCHEDELICS COULD CATALYZE CONVENTIONAL THERAPEUTIC APPROACHES FOR TREATING TRAUMA-RELATED CONDITIONS

Over the past few decades, substantial clinical research has focused on identifying the most effective treatment options for victims of trauma. Trauma is the result of one or more life events that cause an individual overwhelming amounts of stress that exceed their ability to cope or integrate the intense emotions involved. Trauma has a number of lasting adverse effects on an individual's functioning in terms of their physical, social, emotional, and spiritual well-being (SAMHS, 2014).

Sufferers of particularly traumatic events have the potential to develop Post-traumatic Stress Disorder (PTSD). In PTSD, victims experience a variety of symptoms such as reexperiencing the traumatic event as flashbacks, becoming easily aroused or frightened, and feeling an overwhelming amount of guilt or shame. Another form of trauma that is getting increasing attention in the literature is Complex-post Traumatic Stress Disorder also known as Complex trauma. Complex trauma can develop after a person experiences repeated and prolonged abuse at the hands of someone in a position of power in their life. When experienced in childhood, chronic traumatization interrupts the entire course of a child's psychological and neurological development. The developmental and psychological consequences of chronic exposure to trauma can become embedded into who the person believes themselves to be. Many victims have difficulty controlling, comprehending, and even experiencing their emotions. Difficulties with emotion regulation is a hallmark challenge for sufferers of this disorder. Other symptoms include distortion in the perception of their abuser/s and themselves, interruptions in

consciousness that can range from completely forgetting traumatic events to forgetting large gaps of time, and difficulty with relationships (Cook et al., 2017).

Felitti and colleagues (1998) assessed the frequency of traumatic childhood experiences. They found that the average prevalence rate for physical abuse is 30% among men and 27% among women, and the average prevalence rate for sexual abuse is nearly 25% among women and 16% among men (Felitti et al., 1998). These traumatic experiences are the origins of PTSD and complex trauma. PTSD and complex trauma are extremely debilitating and severely negatively affect an individual's quality of life. These disorders often result in difficulties with relationships, depression, decreased daily functioning, severe anxiety, diminished cognitive and psychosocial functioning, substance abuse and negative self-perception (Feduccia et al., 2019).

There are more than fifty different therapeutic approaches aimed at assisting individuals work through trauma (Rauch, 2016). Medications and trauma-focused psychotherapies including prolonged exposure therapy, cognitive behavioral therapy, psychodynamic psychotherapy, and internal family systems are the most commonly used.

Cognitive behavioral therapy or CBT is used to understand and treat psychological problems by looking at the relationship between traumatic events and stimuli, and an individual's thoughts, feelings, and behaviors. The core principles of CBT include the belief that psychological problems are based, in part, on faulty or maladaptive ways of thinking and behaving and that individuals suffering from psychological problems are capable of learning better ways of coping with said problems (American Psychological Association, 2017).

Prolonged Exposure Therapy is commonly used in conjunction with or separately from CBT in order to guide individuals to gradually approach trauma-related memories, feelings, and

situations. This treatment includes gradually exposing the individual to the trauma memories that have been avoided so they can experience the trauma-related memories and cues as no longer dangerous, and do not need to be avoided (Hembree et al., 2003).

Psychodynamic psychotherapy helps individuals to understand that their behaviors and emotions are affected by unresolved issues and unconscious conflicts or feelings caused by traumatic events. By making these unconscious psychological processes conscious, patients can begin to recognize recurring patterns, see how they avoid distress or develop maladaptive coping mechanisms (defense mechanisms), and therefore begin changing those patterns. This approach aims to address the foundation and formation of psychological processes (Leichsenring et al., 2006).

The Internal family systems model seeks to identify and address alternate representations of oneself or "parts" within an individual's internal system. These parts represent the individual's internalized family relationships, each part has its own role in the individual's family system. These parts work amongst one another to create a system that provides resources for the individual. Some parts serve to protect the individual from vulnerable feelings that may feel threatening to the core self. These parts often present as difficult emotions, thoughts, feelings, images, and more. The patient and therapist work together to identify and understand each of the patient's parts, thus addressing the patient's suppressed feelings and conflicts. This approach seeks to free parts from their extreme protective roles, harmonize the self and various parts, and restore trust to the core self (Schwartz, 2013).

The psychoactive medicines known as Selective Serotonin Reuptake Inhibitors (SSRIs) are commonly used to treat trauma-related conditions. These drugs inhibit the reuptake of serotonin in serotonin-containing presynaptic neurons in the central nervous system (Artigas et

al., 2002). In this process, serotonin neurotransmission is increased, which can result in improved regulation of mood and cognition.

Although the treatment strategies of conventional therapeutic approaches are effective for the treatment of trauma-related conditions, these strategies alone often lack the ability to fully engage the patient in the treatment, and as explained below, have the potential to cause more harm than good. Psychedelics have been reported to facilitate feasible access to traumatic memories, decrease hyperarousal and heighten the capacity to confront traumatic memories (Passie et al., 2008; Roseman et al., 2014; Sessa et al., 2019), induce deep introspection and openness (Katz et al., 1968; McGlothlin, 1962; Savage, 1955), and enhance therapist-patient relationships(Carhart-Harris et al., 2014; Chandler & Hartman, 1960), hastening the deconstruction of the habitual maladaptive ways of thinking and behavior often precipitated by trauma. This treatment method utilizes the profound psychological effects induced by the psychedelics in conjunction with psychotherapies designed to treat trauma-related conditions to facilitate the confrontation, processing, and integration of traumatic memories. PAP allows those suffering from trauma-related conditions to feasibly confront, process, and work through these traumatic memories enabling them to heal.

I will first present the literature on the effects that psychological trauma has on an individual's behavior, mood, cognition, and development. Next, a few substances used in psychedelic-assisted therapies will be presented in terms of the effects each psychedelic substance has on mood, behavior, cognition, brain activity, and neurotransmission. Then, a deeper exploration of each traditional therapeutic approach, their effectiveness on treating symptoms of trauma, and their limitations will be conducted. I will then explain why these drugs, used along with psychotherapy, are effective in treating symptoms of trauma. I will then compare

the effectiveness of psychedelic-assisted therapy and each traditional therapeutic approach in treating symptoms of trauma. Finally, the limitations and implications of psychedelic-assisted psychotherapy will be discussed.

The Psychological and Neurobiological Effects of Trauma

For several years, clinicians and researchers have sought to understand the impact that traumatic events have on the lives of children and adolescents. Every year, researchers are increasingly uncovering how pervasive and detrimental the effects of these traumatic events can be on the functioning of an individual. These events can affect far more neurobiological and psychological systems than ever anticipated. Eth and Pynoos (1985) define psychological trauma as an occurrence in which an individual is exposed to an overwhelming event that leaves them helpless in the face of intolerable danger, anxiety, and instinctual arousal. A review conducted by Armsworth and Holaday (1993) summarized the findings of the cognitive, affective, behavioral, and somatic physiological effects of trauma.

Cognitive Effects

Traumatized individuals often experience intrusive thoughts or images; these traumatized individuals often consciously try and suppress their memories of the event(s) while avoiding specific situations, people, or things that remind them of the event(s). Various defenses are often developed against traumatic thoughts and memories often to avoid thinking about, gain mastery of, or gain control over the traumatic event. (Pynoos et al., 1987; Terr, 1984; Van der Kolk, 1987a).

Eth and Pynoos (1985) emphasized that there are distinct observable differences in the effect that trauma can have on children and adolescents. Psychological trauma is most detrimental to a child since their central nervous system and cognitive functions are not yet fully matured. Thus, trauma experienced in childhood can have profound effects on their development. Mowbray (1988) highlighted that a child's stage of cognitive development played a major role in understanding how the child would make sense of traumatic experiences. Piaget's conception of egocentrism predicts that children view their world from their own perspective and only their perspective, which plays a major role in how a child translates the causation of events (Piaget, J., 1936; 1952). Consequently, children are likely to blame themselves for the distressing events and for their victimization. This internalized blame can often result in the child feeling inappropriate amounts of guilt and/or shame, negatively impacting on their self-concept (Holaday et al. 1992; Mowbray, 1988; Terr, 1983; Zimrin 1986). Conceptualizing the event(s) in this way results in negative emotional effects.

Emotional Effects

Many studies have documented the changes in self-perception among traumatized children and adolescents. A lack of self-confidence, low self-esteem, poor self-concept, and body image are frequently documented (Kinard, 1980; Oates, Forrest, & Peacock, 1985; Tong, Oates, & McDowell, 1987). Traumatized children may also be extraordinarily critical of themselves or their behavior often judging themselves as worthless and deserving of the traumatic event (Doyle & Bauer, 1988; Terr 1988; Zimrin, 1986). Several studies have reported a heightened sense of vulnerability and sensitivity to environment threats among traumatized children; these children tend to re-experience the traumatic events emotionally from both reminders of the events and from intrusive thoughts of the events (Rosenheck & Nathan, 1985; van der Kolk, 1987b).

Traumatized children also had low stress tolerance and felt overwhelmed by life (Armsworth & Holaday, 1993).

There are two traumatic stress reactions exhibited by traumatized children agreed upon by researchers: a hyperresponsive mode with unmodulated anxiety and hyperactivity, and/or a hyporesponsive mode and withdrawal, both socially and emotionally (Horowitz, 1976; van der Kolk, 1988; Zimrin 1986). These reactions, without early intervention, make these children vulnerable to developing psychopathological conditions in adulthood.

Behavioral Effects

There have been several behavior response patterns documented following traumatizing events. Traumatized children are more likely to exhibit aggression towards others and be more self-abusive and self-destructive than their non-traumatized peers (Burke et al., 1982; George & Main, 1979; Green, 1983; Hoffman-Plotkin & Twentyman, 1984; Zimrin, 1986). They also have been shown to exhibit more extreme adjustment difficulties and regressive behaviors, withdraw from social interactions, human caring and nurturance and are more likely to become chemically dependent (Doyle & Bauer, 1988; Hoffman-Plotkin & Twentyman, 1984; Mowbray, 1988; Pynoos et al., 1987).

Physiological-somatic Effects.

Trauma can also cause numerous physiological and neurochemical changes. A study published by Pitman and colleagues (2012) reported an association between PTSD and a number of distinct abnormalities in biological systems including the central and sympathetic nervous systems (SNS), the hypothalamic-pituitary-adrenocortical axis (HPA axis), the endogenous opioid system, and the diurnal sleep cycle. These effects on the SNS and HPA axis suggest over-

responsiveness to stress, effects on opioid systems, which reduce physical and emotional pain, and on the sleep cycle suggest lingering effects of highly stressful over-arousal. A study published by the PTSD Research Quarterly (1990) found that abused children and adolescents had reduced alpha-2 receptor binding, which can precipitate symptoms such as depression and other neurological problems. Traumatized individuals were also found to have higher baseline heart rate, higher blood pressure, and increased acoustic startled eyeblink response, all suggesting chronic hyperarousal.

Consistent with these findings, Pynoos and Eths (1984) found that traumatized individuals experienced exaggerated autonomic arousal and startle responses to other challenging experiences to the same degree as they were during the traumatic event. Terr (1984) reported that kidnapped children experienced startled responses, breathing difficulties in small spaces, distressing physical sensations, and anxiety at stimuli that reminded them of the traumatic event(s) long after the event. Another study investigating the effect of trauma on physiological systems found that the pituitary gland becomes dormant and decreases in hormonal function under severely abusive conditions. The pituitary gland is the master gland of the human body. If dormant, the consequences can be severely detrimental to a child's neurophysiological development. A dormant pituitary gland before puberty will delay its onset, interfering with the child's ability to physically mature at the rate of their peers. This could significantly impact the way that child perceives themselves and how they are perceived by their peers, leading to compromised social relations and negative self-esteem. The growth hormone somatotropin was also not being secreted. Sleep disturbances are also an immediate and long-term effect of trauma, suggesting chronic hyperarousal (Caldwell & Redeker, 2005). Sleep deprivation can lead to poor coordination, irritability, loss of concentration, and severely compromises overall cognitive

functioning, all of one's thinking and cognitive processes, processes essential for effectively navigating one's daily life.

Learning how to cope with adversity is an essential part of healthy development. These adaptive coping skills are required for the child to optimally navigate natural obstacles in life (Romens et al., 2015). When not taught these adaptive ways of coping with natural life stress, combined with a lack of a secure support system, toxic stress can be experienced. Toxic stress is an experience of strong frequent and prolonged adversity with limited or no support. Toxic stress responses occur when an individual has experienced extreme and prolonged adversity; this can result in changes to their baseline state in daily life and can influence the expression of genes. When prolonged toxic stress is experienced, the hypothalamic pituitary and adrenal hormone axis (HPA), the central stress response system, may become overactive and both the immune system and HPA axis cannot develop normally (Romens et al., 2015). Higher levels of cortisol, a steroid hormone that regulates various processes in the body such as helping the body respond to stress, have been found to follow exposure to traumatic stressors (Elzinga et al., 2003). Frequent toxic stress results in high levels of the stress hormone cortisol in the blood, which can have detrimental long-term changes in inflammation and immunity. If toxic stress persists, these systems may not develop in a way that responds appropriately to ordinary levels of stress (Romens et al., 2015). When exposed to ordinary levels of stress in the future, these systems will automatically respond as if the child or adult were under extreme stress. Although this response is adaptive when faced with a significant threat, it is often not appropriate in the context of normal stress (Peterson, 2018).

Forms of Trauma

Post-traumatic Stress Disorder

Post-traumatic stress disorder (PTSD) develops in response to an event in which a person experiences overriding horror, terror, guilt and/or helplessness. This disorder consists of a number of symptoms including re-experiencing the traumatic event, increased arousal, recurrent, intrusive distressing memories and/or dreams about the traumatic event(s), intense or prolonged psychological distress at exposure to cues associated with the traumatic event, emotional numbing, and negative changes in cognitions and mood associated with the traumatic event(s) (DSM-V; American Psychiatric Association, 2013). It is common to experience some of these symptoms sometime after experiencing unusually stressful or frightening incidents. However, those suffering from this disorder experience all of these symptoms, and thus have difficulty recovering from the trauma. These symptoms must persist for at least one month to meet DSM-V criteria for the disorder, but they can last months or even years after exposure, severely disturbing the individual's ability to function in their daily life. According to research reviewed by the Sidran Institute, about 5% of Americans, more than 13 million people, have PTSD, and of those who experience a traumatic event, 20% will develop PTSD (Sidran Institute, 2018). PTSD is highly comorbid with other psychological disorders especially depression, anxiety disorders, substance abuse, and suicidality. Psychotherapies such as EMDR, CBT, and exposure therapy are commonly used to treat PTSD and typically focus on the symptoms related to a particular trauma.

Complex Post-traumatic Stress Disorder

Complex Post-traumatic Stress disorder (C-PTSD), also known as "complex trauma," occurs when an individual has experienced multiple interpersonal traumas over an extended period of time. These repeated traumatic experiences are inflicted on the individual at the hands of someone who maintains complete power over them, from the individual's point of view. This dynamic of power leaves the person fundamentally powerless to change and is central to the consequences of complex trauma. Many years after the abusive relationship ends, victims report continuing feelings of powerlessness (Peterson, 2018). Alongside the learned helplessness, complex trauma completely deprives people of a sense of will and agency. It destroys their sense of community and often completely deprives them of a sense of self. This cumulative trauma extensively impacts the individual's social and interpersonal functioning, occupational functioning, overall adjustment, and their personality (Herman, 1997; Khan & Masud, 1963). Prolonged childhood emotional, sexual, and/or physical abuse are a few examples of complex trauma.

A consistent, safe, and stable primary caregiver is essential for a child's healthy physical and psychological development. Without this, the child's ability to form secure attachments and develop healthy coping strategies that aide in their daily survival and functioning are compromised (Peterson, 2018). Children who grow up with exploitive, neglectful primary caregivers in unstable or unpredictable environments, in which their needs, wants, and emotions go consistently ignored or unmet, may learn that the world around them is an unsafe, terrible place, other people cannot be trusted or relied on and that they themselves are fundamentally flawed. These children left powerless, are often forced to blame themselves for the abuse rather than recognize the flaws in their neglectful, unreliable, and dangerous caregivers (Peterson,

2018). This leaves the child feeling worthless, despondent, and significantly impacts their self-image. Some of these learned adaptions are essential when physical and/or emotional threats are present but can be counterproductive and severely interfere with one's capacity to live, love, and be loved if these adaptions are consistently present through development and into adulthood. These children grow up struggling to control and express their emotions and may react inappropriately to certain situations. They are more likely to perceive situations as dangerous or stressful and may act guarded in their interactions with others. This inability to identify, express, and manage emotions often leave the person feeling helpless, depressed, angry, and/or anxious (Peterson, 2018).

Our ability to form healthy supportive relationships with others depends solely on the relational references we develop from our first developed relationships, our family. Children who do not have healthy attachments with their primary caregivers often have difficulties in romantic relationships, friendships, and with authority figures (Peterson, 2018). Psychodynamic Psychotherapy is commonly thought to be the most effective treatment for complex trauma because it can target basic emotional processes underlying personality traits that may have developed due to the trauma (Plakun & Shapiro, 2000).

Acute Stress Disorder

Acute Stress Disorder (ASD) develops when feelings of intense fear, helplessness or horror are experienced in response to being confronted with or experiencing an incident involving actual or threatened death, injury, or other threats of physical integrity of the self or others. Although similar to PTSD, this disorder differs in that the reflected disturbance experienced within the individual lasts for a minimum of 2 days and can only be diagnosed up to

a month after the initial stressor. This disorder also is explicitly developed as a dissociative response to trauma (Brewin & Rose, 1999). When encountering an overwhelming or terrifying experience, an individual may cope with a traumatic event by dissociating from it mentally, separating themselves from all aspects of the traumatic memories. This dissociation can take various forms such as feeling detached, a reduced awareness of one's surroundings, feeling as if one's thoughts or emotions do not seem real or they don't belong to them, which all result in emotional numbing. At least three dissociative symptoms are required to meet criteria for this diagnosis. Symptoms of reexperiencing, avoidance, arousal, and impairment are also necessary. This disorder puts individuals at risk for the development of PTSD and is often a predictor of later PTSD (Brewin & Rose, 1999).

Psychedelics

Psychedelics have been used for therapeutic, divinatory, and religious purposes to cause alterations in states of consciousness and induce perceptual changes for thousands of years (Hoffmann, 1980; Metzner, 2004; Stamets, 1996; Wasson, 1980). Current psychedelic-assisted psychotherapy sessions are conducted by licensed professionals, who are trained how to administer the drugs, properly monitor the use of the drugs, how to guide the patients to minimize distress, and how to assist the patient in integrating the experience afterwards (Mithoefer et al., 2016; Wheeler et al., 2020). Current data suggests that the altered consciousness produced by psychedelics provides a deeper healing experience during psychotherapy sessions than traditional therapeutic interventions only (Belser et al., 2017; Bogenschutz et al., 2018; Mithoefer et al., 2011; 2018; Noorani, et al., 2018; Swift et al., 2017; Wagner et al., 2017). A few common themes identified from clinical trials evaluating the effects of psychedelic-assisted psychotherapy for psychiatric conditions, including those suffering from

trauma related conditions, are: "...increased acceptance and processing of emotions, connectedness to others, forgiveness, self-compassion, insights into the self, peak or mystical experiences, ego dissolution, positive changes in worldview, motivation and commitment to change" (Wheeler et al., 2020, p.276). Users of psychedelics have also been found to experience an "afterglow" of improved mood and perceived mental state for days or even weeks after ingestion (Majić et al., 2015). Results from clinical trials indicate that these psychoactive drugs can significantly reduce clinical impairment associated with psychiatric conditions (Wheeler et al., 2020).

These drugs are markedly associated with the experience of self-disintegration, commonly known as ego dissolution (Letheby & Gerrans, 2017). This state can allow the patient a more objective perspective on maladaptive patterns of behavior, thoughts, and emotions, consequently allowing the person to change them (Swanson, 2018; Wheeler et al., 2020). Additionally, psychedelics facilitate access to maladaptive, intense, or unexpressed emotions such as grief and trauma-related psychological pain; this access grants patients the ability to confront and resolve them (Watts, et al., 2017). The substitution or supplementation of psychedelics have been found to provide symptomatic relief for patients who have been resistant to past traditional therapeutic treatment methods (Bouso et al., 2008; Johnson et al., 2014; Ot'alora et al., 2018; Roseman, et al., 2018; Watts et al., 2017).

Despite their efficacy, the supplementation of psychotherapy with psychedelics as a therapeutic adjunct has been debated for years due to safety concerns. Clinical trials assessing the safety of psychedelic-assisted psychotherapy for treatment of various psychiatric conditions often report no drug-related adverse events or neurocognitive effects, safe physiological and psychological responses, and little, if any, physical dependence produced by these drugs

(Carhart-Harris et al., 2016; Grob et al., 2011; McKim, 1991; Mithoefer et al., 2011; Schenberg, 2018; Wheeler et al., 2020; Winkelman, 2014). Among currently published studies of psychedelic-assisted psychotherapy, only about 19% of them pertain to the effect of this therapy on trauma related conditions (Wheeler et al., 2020). Based on its efficacy thus far, the use of psychedelic-assisted psychotherapy to treat trauma related conditions, such as complex trauma, PTSD, and acute stress disorder, may significantly reduce clinical impairment associated with these conditions.

A study conducted by Chandler & Hartman (1960) reported somatic reactions to be commonly produced by psychedelic drugs; Chandler & Hartman understood somatic reactions to be physiological ways of expressing unconscious emotions. The motor side of these reactions can include muscular tensions, twisting, trembling, and even curling up into a fetal-like position. These impulses to motor movement or posturing felt by the patient, if allowed, may bring the fantasy or memory associated with the movement into conscious awareness. Sensory somatic reactions, such as sensations of numbness, throbbing, pain, cold, and warmth, are often felt as well. These sensations are believed to be an expression of dissociated emotion at times associated with the traumatic memories, which frequently can occur as fantasies.

Their study testing the effects of LSD as a therapeutic adjunct to psychodynamic psychotherapy reported a patient who experienced abdominal pain during his session. The patient was encouraged to go along with and experience the pain. As the pain increased in severity, an assumption of the position of a woman in childbirth accompanied it. Eventually, the patient became aware of a clear fantasy of himself as his mother giving birth to his younger sibling. The case study explains that the occurrence of pain usually disappears once the fantasy with which it is associated breaks through into consciousness. When emotional pain does not

subside, from a psychodynamic point of view, it is believed that the pain is representative of unconscious emotions and conflicts; a pain may subside and then return until its deeper meaning has been clarified. This dissociated, psychosomatic pain could be understood as a defense against an emotional memory or fantasy.

Psilocybin

Psilocybin is a naturally occurring serotonin receptor agonist whose principle psychoactive effects are mediated by the serotonin 2A receptor (5-HT 2A). "Psilocybin has a novel pharmacology in the context of currently available antidepressants because selective serotonin reuptake inhibitors are not direct 5-HT receptor agonists" (Carhart-Harris et al., 2016); that is, psilocybin more directly attaches to the receptor site, behaving more like a neurotransmitter than SSRIs, which explains their faster-acting and stronger effects on neurotransmitter systems associated in the involvement of mood regulation and behavior. Animal studies have reported enhanced cognitive flexibility, associative learning, cortical natural plasticity, and antidepressant responses with 5-HT receptor agonism (Carhart-Harris & Nutt, 2017). Human brain imaging studies with psilocybin have showed changes in brain activity suggestive of antidepressant potential. Effective antidepressants have been shown to normalize hyperactivity in the medial prefrontal cortex (Hamani et al., 2011). Reduced blood flow in that same region was observed with intravenous psilocybin (Griffiths et al., 2006). Indeed, psilocybin has been shown to produce significant alterations in perceptual, cognitive, affective, volitional, and somesthetic functions, induce subjective experiences, decrease anxiety, and increase mystical experiences (Griffiths et al., 2006; Isbell 1959; Rosenberg et al. 1964; Wolbach et al. 1962). Thus, psilocybin may help to improve response rates in CBT by lessening defenses and reducing distress associated with confronting traumatic memories.

Antidepressant medications and cognitive behavioral therapy have been shown to be effective for some patients, but not nearly as effective as psychedelics in facilitating recall and the experiencing of traumatic memories. A double-blind study conducted by Griffths, Richards, McCann and colleagues (2006) sought to evaluate the acute and long-term psychological effects of a high dose of psilocybin in comparison to a psychostimulant administered under comfortable and supportive conditions. All participants had no previous experience with hallucinogens, but regularly participated in religious or spiritual activities. Two to three 8-hour drug-assisted psychotherapy sessions were individually conducted at 2-month intervals. Participants received orally administered psilocybin and methylphenidate hydrochloride; a stimulant medication used to treat ADHD. These doses were administered in a counter-balanced order. Methylphenidate was selected for the comparison because it induced subjective effects such as excitability, nervousness and/or increased positive mood, as opposed to those typically induced by psilocybin. Methylphenidate was also selected to demonstrate the contrasting clinical outcomes induced by psilocybin. Participants completed questionnaires assessing drug effects and mystical experiences immediately after and 2 months after sessions. Measures of psychiatric symptoms, mood, personality measures, quality of life, and lifetime mystical experiences were taken at baseline and post-treatment. Psilocybin produced varying subjective experiences and acute perceptual changes. Increased measures of mystical experience were reported. A cumulative 71% of participants rated their psilocybin experience as being either the most spiritually significant experience of their life, or among the top 5 most spiritually significant experiences. 79% of participants also reported that the psilocybin experience increased their current sense of personal well-being. Mystical experiences have been associated with persisting effects, such as

positive changes in behavior, attitudes and values, and an increase in the personality domain of openness (Garcia-Romeu et al., 2014).

As described earlier, trauma-related conditions often precipitate profound emotional and behavioral difficulties (Peterson, 2018). Traumatized individuals often struggle with expressing their emotions and regulating their own behavior, causing them to behave in ways that appear unpredictable or extreme. Similarly, they internalize stress reactions and as a result experience significant depression, anxiety, or anger (Peterson, 2018). Complexly traumatized individuals report feelings of powerless and hopelessness in regard to planning for the future and changing their circumstance, and often perceive positive action as futile (Peterson, 2018). Psilocybin could potentially not only facilitate positive changes in behavior and mood, but also potentially increase individual's openness to themselves and the world around them.

LSD

Derived from a rye fungus, ergot, and commonly known for its induction of perceptual changes, illusion, and pseudo-hallucinations, lysergic acid diethylamide (LSD 25), also known as "acid," has been used to produce profound psychological effects since the early 1940s. This psychoactive drug acts on a number of different receptors in the brain including serotonin (5-HT) and dopamine, producing a number of psychological and sensory effects (Preller et al., 2017). LSD has the capacity to facilitate the retrieval of repressed material, making them conscious, increase insight, and broaden one's spectrum of awareness. LSD also induces euphoria, reduced anxiety, changes of body image and cognitive functions, a sense of spiritual enlightenment and a sense of belonging or interconnectedness with the universe, alterations of time experiences, and synesthesia (Katz et al., 1968; McGlothlin, 1962; Savage, 1955). Unconscious thoughts,

memories, and feelings are more readily experienced, often those that have not been thought about for a long time. LSD broadens the horizons of consciousness, creating openness to memories of trauma (Passie et al., 2008). The facilitation of these processes gives LSD the potential of being a valuable psychotherapeutic tool, especially for trauma-related conditions, which are associated with repressed memories.

A broadened spectrum of awareness not only enables patients to look inwards, but also facilitates greater availability of early typically overwhelming childhood memories, experiences, emotions, and conflicts that were previously repressed. The recall of repressed childhood events, reduction in resistance to communicate feelings, the increased scope of awareness and various adaptive defense mechanisms, a great intensification in a person's level of affectivity, a vividness and reality of memories, all experiences produced by LSD, can be tremendously beneficial therapeutically. LSD allows individuals to direct their attention to their own emotions and projections of their unconscious processes (Chandler & Hartman, 1960; Passie et al., 2008; Schmid & Liechti, 2018; Wolff et al., 2020). Emotions such as embarrassment, distrust, fear of criticism, hostility, and feelings of dependency are reported to be more difficult to conceal when on LSD, enabling patients to be more open with their therapist (Chandler & Hartman, 1960). Patients are able to readily comprehend the therapist's interpretations due to their greater capacity for insight. One study describes the patients as becoming more "flexible" under the influence of LSD due to their greatly increased capacity for spontaneous insight (Chandler & Hartman, 1960). LSD has also aided in "reaching" patients who are unresponsive or resistant to other traditional therapeutic approaches.

Individuals suffering from trauma-related conditions often struggle with expressing, regulating, and making sense of their own emotions and confronting their traumatic memories.

LSD-assisted psychotherapy could facilitate deep introspection and make confronting traumatic memories tolerable by reducing the hyper-arousal and emotional pain typically activated when confronting traumatic memories.

Although profound psychological experiences have been reported with LSD, colloquially known as "good trips," adverse reactions have also been reported. Colloquially known as "bad trips," these potentially traumatic, negative experiences include an array of adverse reactions, such as mood swings, flashbacks, irrational fear, dread, anxiety, and hopelessness; the world can appear ugly, drab, and hostile (McGlothlin, 1962; Strassman, 1984). Generally speaking, these "bad trip" experiences tend to take place in uncontrolled conditions, highlighting the importance of "set and setting," or highly controlled and supportive conditions established by a professional to minimize the risk of a bad trip. The environmental setting is essential for achieving therapeutic benefits with any psychedelic and progressing in psychedelic research (Hartogsohn, 2016, 2018). Under these conditions, LSD experiences more often have lasting positive effects on attitude and personality (CESAR, 2013; Chandler & Hartman, 1960; McGlothlin, 1962; Rogge, 2014).

A review conducted by McGlothlin (1962) assessed the long-lasting effects of LSD on healthy people and its use in psychotherapy. Two studies reported long lasting beneficial effects on participants' quality of life, such as a significantly greater understanding of themselves and others and gaining a sense of new meanings to life, all attributable to their LSD experiences. LSD participants often reported a significantly enhanced ability to view themselves in an unprejudiced and detached position, enabling them to gain important personal insights, and to see clearly the behaviors they use every day to avoid confronting, and therefore reliving, their traumatic memories (McGlothlin, 1962).

In two follow-up questionnaire studies, participants reported feeling a better understanding of themselves and others and having better interpersonal relationships (McGlothlin, 1962). They also reported a higher tolerance of others and their viewpoints and changes of values in several areas. Participants who reported religious or mystical experiences under LSD also reported a high incidence of lasting beneficial effects. The experience is often described as beautiful, pleasant, and integrative, creating a feeling of oneness with the universe.

"For example, a man may be seen as constantly attempting to survive as an individual in an environment where struggle for physical survival is replaced by the seeking of status and possession which will isolate the "I". Then, the picture changes and the desperate need for companionship appears. He realizes that the struggle to create an island about himself results in loneliness and unhappiness, but he nevertheless seems to be irrevocably committed to this course by a stronger evolutionary force. This is a but one of a seemingly infinite variety of universal type insights into the nature or meaning of life that are reported" ((McGlothlin, 1962, p.32).

The participant usually claims that this type of experience was beneficial, regardless of whether they described it as pleasant or unpleasant. Participants often report achievements of personal insights into one's own behavior.

LSD is often reported to tremendously enhance sensitivity of the participant to a wide range of non-verbal cues from those around them. Cohen (1960) reported that their LSD participants could sense the therapist's unspoken feelings with phenomenal accuracy.

Participants reported their amazement at their sudden ability to receive these cues after an LSD session. This phenomenon was retained enough over a few days to account for the claims of

improved social relations (Cohen, 1960). LSD could be potentially valuable for people suffering from trauma-related conditions due to their tendency to be blind to non-verbal cues and others' mental states, given their preoccupation with their own mental state.

MDMA

Since its creation in 1914, Methylenedioxymethamphetamine (MDMA), a psychoactive medicine commonly referred to as and confused with the street drug "ecstasy" or "molly," has been used by psychiatrists and other therapists as an adjunct to psychotherapy (Sessa et al., 2019). A series of uncontrolled case studies conducted in the mid-eighties described the effective use of MDMA for individuals, couples, and groups as treatment for a variety of psychiatric conditions (Greer & Tolbert, 1986, 1998). Gasser (1994) conducted an average of eight MDMA-assisted psychotherapy sessions for individuals and groups. Over 100 people with a wide array of psychiatric conditions participated in this study; over 90% of the participants reported improvements in their symptoms at 19 months follow up (Gasser, 1994). A number of studies report the efficacy of MDMA for the treatment of trauma-related conditions.

MDMA and ecstasy/molly differ in that ecstasy/molly mostly contain adulterants and can, but frequently do not contain MDMA (Saleemi et al., 2017; Togni et al., 2015; Vogels et al., 2009; Vrolijk et al., 2017; Wood et al., 2011). Serious adverse events are very rare with MDMA. The inconsistent terminology used to refer to MDMA has created major confusion about the safety of it (Amoroso, 2016). In recent years, a number of controlled clinical trials have been conducted to test the efficacy and safety of MDMA as a therapeutic adjacent for trauma-related conditions such as PTSD (Feduccia et al., 2019; Mithoefer et al., 2018; Ot'alora G et al., 2018; Schenberg, 2018; Sessa et al., 2019). MDMA is a potent monoamine releaser, a drug that

facilitates the release of a monoamine neurotransmitters, serotonin, noradrenaline, and dopamine, from the presynaptic neuron into the synapse, resulting in an increase in extracellular concentration of the neurotransmitter. MDMA produces experiences of relatedness, oneness, emotional openness and positive mood, empathy towards the self and others, emotional communion, acute euphoria, and most relevantly, users can gain access to and process emotionally traumatic memories (Roseman et al., 2014; Sessa et al., 2019). MDMA acts as a releaser of serotonin (5-HT); activity of 5-HT receptors has been shown to decrease feelings of anxiety and depression (Graeff et al., 1996), reduce fear response, increase levels of selfconfidence, increase feelings of closeness, compassion and empathy for oneself and others (Hysek et al., 2013; Simmler et al., 2013; Verrico et al., 2007; Wel et al., 2012). MDMA's effects at alpha-2 receptors impact its effect on thermoregulation, the ability to internally regulate body temperature; these effects may contribute to a sedation effect beneficial in the context of trauma-induced hypervigilance (Giovannitti et al., 2015). MDMA also acts as a releaser of noradrenaline, and dopamine; increased dopamine and noradrenaline raise levels of awareness and arousal, which can consequently motivate engagement in therapy and promote fear extinction (Hysek et al., 2011; Mueller et al., 2008; Rothman et al., 2001).

The amygdala is a component of the limbic system primarily responsible in the processing of emotional memory and responses (Amunts et al., 2005). MDMA has also been shown to reduce fear-related amygdala activity due to its facilitation of the release of oxytocin, resulting in a decrease in stress response and social anxiety (Domes et al., 2007; Kirsch et al., 2005). A number of animal studies have demonstrated that MDMA increases fear extinction through a mechanism dependent on elevated levels of brain derived neurotrophic factor (BDNF) in the amygdala (Sessa et al., 2019). These findings can explain why MDMA enables patients to

recall painful emotional memories that are typically avoided due to the negative affect the recall of these memories produce (Young et al., 2015, 2017). Increased prosocial effects, enhanced self-compassion and empathy, and improved tolerance for confronting traumatic memories could all aid in establishing a strong therapeutic alliance to effectively process traumatic memories (Carhart-Harris et al., 2014; Kamboj et al., 2015; Kamilar-Britt & Bedi, 2015).

When compared to prolonged exposure therapy (PE) in an independent preliminary metaanalysis, MDMA-assisted psychotherapy was evaluated to be superior by clinician-observed
outcomes, by the patient self-report outcomes, and by the proportion of dropouts, almost 30% in
the PE group versus a little over 12% in the MDMA group. The heightened state of arousal
induced by PE leaves little time to process the traumatic experience in the sessions. Unlike PE,
MDMA-assisted psychotherapy offers a patient-centered approach allowing the patient to
explore other aspects of the trauma that are potentially out of reach in PE. An avoidant nature is
often at the very core of trauma related conditions, which could explain the high dropout rates
for PE, as confronting traumatic memories is typically the last thing that traumatized people want
to do (Amoroso & Workman, 2016), which is why so many of them also avoid treatment.

Mithoefer and colleagues (2011) investigated the effectiveness of MDMA-assisted psychotherapy for suffers of treatment resistant chronic PTSD. These participants were found to be treatment resistant, for an average of 19.5 years, to both psychotherapy and psychopharmacology. Participants were randomly assigned to psychotherapy with a concomitant MDMA and inactive placebo administered for two 8-hour experimental psychotherapy sessions. Both groups received preparatory and follow up nondrug psychotherapy. The CAP PTSD Scale was used as the primary outcome measure 4 days after each experimental session and 2 months after the second session. Results indicated a significantly greater decrease in CAP PTSD scale

scores from baseline for the group receiving MDMA-assisted therapy versus the placebo group, with a 30% reduction in CAPS scores, many participants no longer met criteria for PTSD 2 months following their MDMA-assisted psychotherapy. The rate of clinical response was 10/12 in the MDMA group (83.3%) versus 2/8 (25%) in the placebo group, and no drug-related serious adverse events were reported. MDMA was reported to decrease levels of fear and defensiveness and increase trust between the patient and practitioner. A follow up study conducted 4 years later with the same participants reported a relapse of 2 participants, but on average, an improvement of symptoms was maintained without additional treatments and without inducing drug dependence or abuse. Two sessions alone enabled the majority of participants in the study to achieve long-term remission of their symptoms. MDMA-assisted psychotherapy compared to psychotherapy with an inactive placebo produced clinically and statistically significant improvements in PSTD symptoms. These statistically significant results are very encouraging and indicate the profound effects that this treatment can have on those suffering from traumarelated conditions, even individuals who have been treatment resistant to other approaches for many years.

Other Psychiatric Conditions. Reviews assessing the efficacy of psychedelic-assisted psychotherapy on treating other psychiatric conditions are included in this review because these conditions are relevant to trauma. Trauma-related conditions are highly comorbid with other psychiatric conditions such as depression, substance abuse and dependence, and other anxiety disorders. A number of studies assessing the efficacy and safety of psychedelic-assisted psychotherapy on treating various psychiatric conditions have reported statistically significant improvements in mood, anxiety, and substance misuse (Amoroso & Workman, 2016; Carhart-Harris et al., 2016; Chandler & Hartman, 1960).

MDMA has been found to improve emotional regulation and decrease avoidance through the increasing of ventromedial prefrontal activity and the decreasing of amygdala activity (Roseman et al., 2014; Sessa et al., 2019). It has also been found to increase oxytocin levels and norepinephrine release, which can facilitate emotional processing and engagement, enhance the removal of learned fear associations, decrease stress response and social anxiety, and strengthen the therapeutic alliance (Hysek et al., 2011; Mueller et al., 2008; Rothman et al., 2001). MDMA, when used in conjunction with a psychotherapy, could be effective in helping engage individuals in therapy who are suffering from depressive and anxiety-related conditions and improve depressive mood and anxiety symptoms.

Carhart-Harris and colleagues (2016) conducted an open-label feasibility study investigating the feasibility, safety, and efficacy of psilocybin in patients with unipolar treatment-resistant depression. The therapeutic potential of psilocybin for various conditions including end of life anxiety, OCD, smoking, and alcohol dependence were also assessed. Each participant received 10mg and 25mg of psilocybin 7 days apart in a supportive setting. There was no control group, making this a correlational study. Psychological support was provided during, before, and after each psychotherapy session. The primary outcome measure for feasibility was patient reported intensity of psilocybin effects. Depressive symptoms were assessed with the 16-item Quick Inventory of Depressive Symptoms from 1 week to 3 months after treatment. Psilocybin was well tolerated by all patients and no serious or unexpected adverse events occurred. Depressive symptoms were markedly reduced 1 week and 3 weeks after high dose treatment. Marked and sustained improvements in anxiety and anhedonia were found. This study suggests a correlation between reduction in symptoms of treatment resistant depression and the use of psilocybin- assisted psychotherapy. Due to the lack of a placebo control group in this

study, however, we cannot conclude that psilocybin-assisted psychotherapy caused the reduction in the participants' symptoms.

These limitations were addressed by a double-blind placebo-controlled study conducted by Grob and colleagues (2011), who explored the safety and efficacy of psilocybin in treating patients with advanced stage cancer and reactive anxiety. These patients acted as their own control, used a moderate dose of psilocyn (0.2mg). Safety and subjective experience were monitored before and during the experimental treatment sessions. Follow up data including results from the Beck Depression Inventory, Profile of Mood States and State-Trait Anxiety Inventory were collected unblinded for 6 months after treatment. No adverse events of psilocybin were reported. The State-Trait Anxiety Inventory trait anxiety subscale exhibited a significant reduction in anxiety at 1- and 3-months preceding treatment. The Beck Depression Inventory revealed an improvement of mood that reached statistical significance at 6 months. The Profile of Mood States reported an improvement in mood that approached significance after treatment with psilocybin. The data revealed a positive trend towards improved mood and anxiety suggesting that psilocybin may be effective at treating anxiety. This study established the safety and efficacy of administering moderate doses of psilocybin to patients with anxiety and advanced stage cancer.

Similarly, a meta-analysis conducted by Rucker and colleagues (2016) reviewed the current literature on psychedelic drugs, such as LSD and psilocybin, in the treatment of broadly defined unipolar mood disorders. Of 423 individuals in 19 studies, over 79% showed clinician-judged improvement in depressive symptoms after treatment with psychedelics. Although these results support the efficacy of psychedelic-assisted psychotherapy, many of the studies lacked a control group, and some outcome measures were categorical, forcing the experimenters to group

the results into those who were felt by their clinicians to have 'improved' and those who did not. 'Improvement' could not be further defined.

Psychedelics have also been found to improve symptoms of substance use disorders. A meta-analysis of randomized controlled trials evaluated the literature on the efficacy of LSD in the treatment of alcoholism (Krebs & Johansen, 2012). LSD produced statistically significant short-term benefits in alcohol misuse for participants, for up to a year following their session. A single dose of LSD was found to be associated with a decrease in alcohol misuse in the context of various alcoholism treatment programs. Statistically significant improvements in alcohol abstinence were also shown.

A psychedelic not highlighted in this review, Ibogaine, a psychoactive alkaloid deprived from the plant Tabernanthe iboga, has also been found to be effective in the treatment of drug addiction. Although its mechanisms are not yet completely understood, Ibogaine is effective in blocking opiate withdrawal and reducing drug cravings, providing an alternative treatment for opiate dependent individuals who are treatment resistant to conventional methods (Brown, 2013; Mash et al., 2001).

Traditional Therapeutic Approaches for Treating Symptoms of Trauma

Psychodynamic Psychotherapy

Derived from the theories of Sigmund Freud, psychodynamic psychotherapy seeks to address the foundation and formation of psychological processes, and to fully integrate traumatic memories and emotions into consciousness; "to make the unconscious traumatic memories conscious" (Freud, 1888/1966; Leichsenring et al., 2006). This approach works by using strategic techniques designed to erode maladaptive defenses that may keep painful memories,

emotions, and experiences unconscious – that is, outside of conscious awareness; people are encouraged to speak openly about their emotions, desires, and fears. Psychodynamic therapists believe that speaking freely may help to reveal vulnerable emotions that the person pushed out of their conscious awareness. Supportive interventions such as fostering a therapeutic alliance, empathy, and the strengthening of abilities that may have not been sufficiently developed or are not currently accessible, known in psychodynamic theory as "ego functions," are also foci of this treatment (Leichsenring et al., 2006). The skillful use of empathy, tactful confrontation of defense mechanisms, and full acknowledgement of the traumatized person's emotional experiences are used to bring the unconscious processes to their conscious awareness (Knekt et al., 2008; Leichsenring et al., 2006).

In treatment, the therapist attempts to help the individual recognize patterns in their behavior and thinking, as recognizing these patterns may help individuals to see how they avoid distress, enabling them to begin changing those patterns (Leichsenring et al., 2006).

Psychodynamic psychotherapy has been shown to be empirically effective, and it is the only treatment designed to target defense mechanisms (Brom et al., 1989; Levi et al., 2016; Sachsse et al., 2006; Steinert et al., 2017). Avoidance of any reminder of the trauma, a dissociative defense mechanism, is a primary symptom of trauma related conditions (DSM–V; American Psychiatric Association, 2013; Levi et al., 2016). That is why this approach has been shown to be highly effective for trauma related conditions. Psychodynamic psychotherapy is the most sophisticated approach to addressing defenses. Other therapeutic approaches, such as cognitive behavioral therapy, lack a strategy for defense mechanisms (American Psychological Association, 2017).

Most people who come into treatment have embedded defenses and are deeply conflicted about

confronting their traumatic memories. They often do not want to reexperience the traumatic event or be retraumatized by it.

People have spent years before they attend treatment avoiding all reminders of the trauma and blocking out memories of the trauma. Some people are so defensive and prone to dissociation that they are often resistant to most traditional therapeutic approaches. These people often frequently reinforce their defense mechanisms in an effort to prevent themselves the emotional distress associated with recalling those memories (Brom et al., 1989; Levi et al., 2016; Sachsse et al., 2006; Steinert et al., 2017). Integrating psychedelics with psychodynamic psychotherapy may be effective in this regard; psychedelics have been shown to make it easier for people to access traumatic memories and decrease the severity of their avoidant and dissociative defense mechanisms (Carhart-Harris et al., 2012; Fischman, 2019)

A placebo-controlled study conducted by Carhart-Harris and colleagues (2012) sought to investigate whether psilocybin facilitated access to personal memories and emotions. Healthy participants were given two functional magnetic resonance imaging (fMRI) scans (2mg of intravenous psilocybin v. intravenous saline) separated by 7 days during which they viewed two differing sets of 15 positive autobiographical memory cues. These cues were derived from the personal memories provided by the participants. Each participant viewed each cue for 6 seconds and then closed their eyes for 16 seconds and imagined re-experiencing the event. Activation during this recollection period were compared with an equivalent period of eyes closed rest. The recollection period was split into early phase first 8 s and late phase last 8 s.

Activation of the memories were seen in limbic and striatal regions in the early phase and the medial prefrontal cortex in the late phase in both conditions. There were additional visual and other sensory cortical activations in the late phase under psilocybin that were not present under placebo. Greater late phase sensory activations were observed after psilocybin; late phase parahippocampal activations were positively correlated with how arousing recalling the memories were for the participants. Ratings of visual imagery and memory vividness were significantly higher after psilocybin. There was also a positive correlation between vividness and subject wellbeing at follow up. This evidence suggests that psilocybin enhances autobiographical recollection and suggests that it may be useful in psychotherapy as a tool to facilitate the recall of salient memories or to reverse negative cognitive biases (Carhart-Harris et al., 2012). Psychedelics alongside the tactical psychodynamic approach to defense mechanisms could potentially be especially effective.

Internal Family Systems Therapy

Self-acceptance has been regarded as a key component to psychological and emotional health and serves as an aid when pursuing help for general psychological problems (Macinnes, 2006.; Williams & Lynn, 2010). A lack of self-acceptance is often a major difficulty in individuals who seek out psychotherapy. Often this incapacity to accept themselves acts as an obstacle in their ability to change their unwanted behaviors, emotions, or thoughts. Internal family systems (IFS), a psychotherapy developed by Richard Swartz, uses the model of an internal family system, subpersonalities or "parts" that internally interact like a family. These parts can be experienced in thoughts, feelings, sensations, images, and develop complex systems of interacting together. IFS seeks to foster acceptance of parts in individuals that previously were unacceptable. This acceptance of all parts enables patients to create changes in their emotions, beliefs, and relationships (Schwartz, 2013).

The multiplicity of the mind - the idea that our minds consist of several distinct feeling states, internal selves (Schwartz, 2013), and "self-leadership" are the principal components of IFS therapy. This individual psychotherapy uses "parts" to describe each internalized family representation within a patient; together, these parts make up a family system within the individual each fulfilling different roles. The process of inner focus and dialogue, a central design in IFS, enables patients to learn that the parts of themselves they have ridiculed, feared, hated, or exiled serve as a means to protect themselves; these parts are "frozen in time" (P.1) during earlier traumatic events or attachment injuries. Accessing and beginning to relate to one's turbulent inner experiences, thoughts, and feelings can enable them to accept aspects of themselves they previously struggled with. This approach expands on the "passive-observer" mindfulness attempt often integrated into other psychotherapy practices: encouraging patients to bring awareness to their thoughts and emotions from a place of separation and extended acceptance toward self. Awareness of irrational beliefs has been shown to encourage positives change in behavior (Doblin & Burge, 2014; Szentagotai-Tatar & Jones, 2009; Turner, 2016). Mindful awareness of internal experiences enables patients to further process and make sense of those experiences (Schwartz, 2013).

IFS see internal objects or parts as an innately valuable component of psychological health. These distinct parts with their different talents and perspectives equip an individual with the resources to function well. Trauma forces these internal systems into protective and/or extreme roles that precipitate feelings of distrust in the leadership of the self. The IFS model seeks to assist patients in realizing these selves and the no longer existing threats, their traumatic memories. Patients are taught to connect with natural inner leaders that exist within them that manifests qualities such as compassion, clarity, and acceptance.

Self-cohesion is the idea that gradual recognition of difficulties experienced in oneself pertain to self-esteem regulation and maintenance of a solid sense of self (Kohut, 1971). The mindful awareness of the self contributes to maintaining a solid sense of self and self-esteem. Individuals suffering from trauma related conditions exhibit lower self-esteem, self-confidence, and often a disturbed sense of self. This internal disharmony can often manifest as self-loathing, helplessness, and self-hatred. In IFS, these distressed parts are understood through their interpersonal context and often uncovered through the mindful awareness of an emotion or belief that is interfering with one's life. Patients are encouraged to observe their emotions and beliefs to further understand them as separate from their core self and to accept them. The ability to separate these parts from one's core self enables them to notice their thoughts and emotions as opposed to identifying with them. Similar to psychodynamic psychotherapy, IFS seeks to assist the patient in understanding their defenses. IFS encourages patients to become familiar with these internal coping systems, understanding what role each plays and what they are attempting to protect, which can bring about acceptance and gratitude within the individual.

Psychedelics have the potential to facilitate transpersonal experiences that are profound and generate access to parts of oneself different than the ones we typically operate from.

Transpersonal experiences have the potential to bring to the surface fears, needs, and longing in the individual (Doblin & Burge, 2014). Psychedelics enable us to access our unacknowledged material, deepen our understanding of this material, and increase our capacity to process and integrate the material. Psychedelics ability to increase acceptance of the self and processing of emotions and to decrease hyperarousal, often precipitated in response to the recall of traumatic memories (Hysek et al., 2011; Mueller et al., 2008; Rothman et al., 2001) could enable patients to connect with these traumatized parts of the self-more feasibly. These experiences produced by

psychedelics could potentially be the catalyst that incites compassion for the self and acceptance of the parts previously exiled, hated, or feared by the individual. For example, in a psychotherapy case study, MDMA-assisted IFS psychotherapy was found to increase introspection and awareness of different internal systems and increase compassion and clarity in the exploration of these parts (Mithoefer et al., 2018). "I realize that part of me is not a monster, he's a warrior, a valuable part of me, and he needs healing too" (Doblin & Burge, 2014, P.134).

Cognitive Behavioral Therapy/Prolonged Exposure Therapy

Cognitive behavioral therapy (CBT) is one of the most widely used and researched forms of psychological treatment for various problems by clinicians and researchers. The core principles of this treatment stem from the beliefs that psychological problems are based on maladaptive patterns of behavior and ways of thinking. Thus, those suffering from psychological problems need to learn better ways of coping with them, making skill building a large focus of this treatment (American Psychological Association, 2017). In this treatment, the patient gets the opportunity to learn about the nature of trauma and their disorder, and why their symptoms developed. Recognizing the distortions in their thinking and gaining a better understanding of their own and other's behaviors and motives can help them to build new, more adaptive ways of coping with difficult situations. In this model, the patient and therapist work together to develop a clear understanding of the problems in terms of the relationship between thoughts, feelings, and behavior (Leichsenring et al., 2006).

The goals of CBT are intended to directly target symptoms, reduce distress, help the patient gain practical coping skills, and promote helpful behavioral responses and the reevaluation of thinking. Due to the collaborative nature of this treatment and the support from

the therapist for the patient to tackle their problems by harnessing their own resources, patients learn to attribute improvements to their own efforts (Leichsenring et al., 2006). The goal of a therapist during these sessions is to encourage, guide and teach; the therapist encourages the patient to go against their maladaptive behaviors in their daily life; to utilize their new skills into the handling of their problems, interpersonal relations and to make an effort to react to their environment in an adaptive way (Chandler & Hartman, 1960).

Exposure is an intervention strategy that is typically used in CBT to reduce fear and anxiety by having the patient approach, rather than avoid, the phobic situation. Prolonged Exposure therapy is a type of CBT that teaches individuals to gradually approach, rather than avoid, their traumatic memories. The patient and therapist formulate a series of steps of graduated exposure to the traumatic memories. The patient learns that their traumatic memories and trauma-related cues are not in fact dangerous, and do not need to be avoided. Indeed, not only do the traumatic memories not need to be avoided but approaching them and fully relating them to the therapist, allowing them to enter into consciousness, is the key to coming to terms with them (American Psychological Association, 2017). Despite its gradual approach, prolonged exposure therapy is only effective among people who can tolerate being exposed to their traumatic memories (Zayfert et al., 2005). Recent meta-analyses find that prolonged exposure therapy has relatively high dropout rates (Gunter & Whittal, 2010; Imel et al., 2013; Loerinc et al., 2015), as high as 76% among combat veterans with PTSD, most of whom could not tolerate the treatment due to its hyper-arousing approach. However, those who could tolerate the treatment long enough to complete it have found it to be very effective (Zayfert et al., 2005).

Psychedelics ability to strengthen therapeutic alliance, enhance self-compassion, and empathy, enhance spontaneous insight, and alleviate emotions such as embarrassment, fear of

criticism, and distrust, could enable patients to more readily participate in CBT. (Carhart-Harris et al., 2014; Chandler & Hartman, 1960; Kamilar-Britt & Bedi, 2015; Kamboj et al., 2015). When used in conjunction with CBT, psychedelics could eliminate the hyper-arousal typically precipitated when recalling traumatic memories, enabling patients to tolerate being exposed to them (Carhart-Harris et al., 2014; McGlothlin, 1962; Wheeler et al., 2020). The ability to tolerate confronting traumatic memories, a reduction in resistance to communicate feelings, and a strengthened therapist-patient relationship, all experiences induced by psychedelics, could aid in the confronting, processing, and integration of traumatic memories, and positively influence the patient's ability to gain and utilize the new practical coping skills learned in CBT.

Psychoactive Medications

Psychoactive medicines are typically used to treat a variety of psychiatric syndromes. Many of these drugs are designed to alter the chemistry of the brain, especially the activity of neurotransmitters, in ways that may reduce the symptoms of psychological disorders. The serotonin neurotransmitter system plays an important role in behavioral and emotional regulation (Murrough et al., 2011, p.2). The development of behavioral and emotional regulation systems, systems that regulate or control mood, thinking and associated executive behaviors, are often disrupted in traumatized individuals (Peterson, 2018). A study on the effect of trauma and extreme stress on serotonergic functions reported evidence to suggest that abnormalities in serotonergic functions can be precipitated by exposure to extreme stress and traumatic events (Murrough et al., 2011). Thus, the most commonly prescribed psychoactive drugs are selective serotonin reuptake inhibitors (SSRIs). These drugs function by increasing the level of activity of serotonin by limiting the reuptake of serotonin back into presynaptic neurons (Artigas et al., 2002). Inhibiting reuptake has the effect of increasing the concentration of serotonin available in

the synapse, thereby increasing the likelihood of it binding to receptors, and thus increasing neurotransmission in brain regions that are essential to behavioral and emotional regulation.

Although commonly used to treat symptoms of trauma, the efficacy of these drugs for trauma-related conditions is not well established. A comparative systematic review and meta-analysis on the efficacy and acceptability of pharmaceutical management for adults with PTSD found that SSRIs had significant efficacy on PTSD symptoms only for patients suffering with severe or extremely severe PTSD status; these drugs did no better than placebo for patients with less severe PTSD status (Huang et al., 2020). The same efficacy patterns of SSRIs can be seen for the disorder they are intended to treat, depression. A number of meta-analysis have shown that SSRIs are no more effective than placebo for treating mild to moderate depression (Kirsch et al., 2008,2014); however, SSRIs have been shown to significantly reduce symptoms of severe depression (Kirsch et al., 2008). An open-label continuation phase of a 23-week study reported sustained improvements in PTSD only up to 9 months after treatment with Sertraline (Zoloft), a commonly prescribed SSRI (Londborg et al., 2001).

Traumatized patients who are treatment resistant to SSRIs will then typically be prescribed serotonin and norepinephrine reuptake inhibitors (SNRIs). These drugs (Effexor, Cymbalta) target both the serotonin and norepinephrine systems, inhibiting the reuptake of both neurotransmitters. Since these drugs also effect norepinephrine activity, a neurotransmitter crucial to regulating autonomic arousal, these drugs tend to have stronger effects on arousal than SSRIs. Chronic arousal is often found in traumatized individuals. Jonathan and Davidson (2006) reviewed pharmacologic treatment options for PTSD. They found that SNRIs were shown to improve resilience in PTSD patients and resulted in significant changes from baseline in Connor-Davidson Resilience Scale (CD-RISC).

A study conducted by Feduccia and colleagues (2019) sought to test the effectiveness of 3,4-Methylenedioxymethamphetamine (MDMA), a psychedelic drug, versus two SSRI antidepressant medications, paroxetine hydrochloride (Paxil) and sertraline hydrochloride (Prozac), for treating post-traumatic stress disorder. In this study, MDMA was administered with psychotherapy in up to three monthly 8-hour sessions. The researchers compared MDMA to data used for the approval of paroxetine and sertraline. MDMA-assisted psychotherapy caused a substantial improvement over available psychoactive drugs in terms of safety and efficacy. Results from six MAPS-sponsored phase 2 trials indicated a significant effect of MDMA over the comparator group (p < 0.001) with a large between group effect size (0.9 Cohen's d effect size) that was double the effect size of paroxetine and triple that of sertraline. Mean changes in CAPS total scores when compared were reported. Placebo subtracted scores for sertraline ranged from 6.8-9.8 units, for paroxetine 6-14 units, and for MDMA 26.2 units. Results from MAPS sponsored MP-1 study reported a significant (p = 0.013) difference between MDMA (125 mg) and placebo groups on CAPS-IV total scores 3-5 days after the first experimental session, illustrating the positive clinical response produced after a single MDMA dose. Studies in which MDMA-assisted psychotherapy was administered had lower dropout rates compared to sertraline and paroxetine trials.

The dropout rate for the MDMA-treat subjects was 6.8% or only 5 of the 74 participants; significantly less than the dropout rate among the Paxil treated group, 11.7%, and in the Prozac group, 28%, suggesting that MDMA is better tolerated by individuals suffering from PTSD than SSRIs. The study also found low dropout rates for the control group, 9.7% suggesting some positive effect from the psychotherapy alone. The authors predicted that there was potentially

increased motivation to remain in the study to receive active MDMA during the open-label cross-over segment.

MDMA was found to produce the least number of adverse effects potentially due to the single dosing administered a month apart in a controlled setting as opposed to the chronic daily dosing of Paxil and Prozac. Participants within the Paxil and Prozac trials complained of symptoms such as asthenia, sweating, nausea, dry mouth, diarrhea, fatigue, and several others. Feduccia and colleagues (2019) also noted that the daily self-administered dosing required by SSRIs may be a challenge due to the cognitive and behavioral impairments that can often accompany PTSD. Compliance is not an issue in studies with MDMA due to the clinically supervised administering of the drug. Discontinuation of Paxil and Prozac may also be accompanied by adverse effects potentially caused by neuroadaptations of decreased levels of serotonin transporters in neuronal membranes after the use of SSRIs. Discontinuation of MDMA produced no adverse symptoms although some adverse reactions such as anxiety, dizziness, depressed mood, and others were reported during the 7 days following an MDMA dose. Within 5 days fatigue and anxiety were the only symptoms reported in over 20% of the active dose participants. Fatigue and anxiety were reported equally by the active and control dose participants, these symptoms were mild to moderate in severity and nearly all resolved within 7 days of administering of the drug. Overall, MDMA produced fewer transient side effects, greater compliance, and substantial clinical improvement compared to daily dosing of Paxil and Prozac (Feduccia et al., 2019).

Discussion

Strengths of the Current Research

The studies reviewed produced promising results for psychedelic-assisted psychotherapy (PAP) as a treatment method for trauma and other related conditions. Many studies selected psychedelic native patients, provided multiple psychotherapy sessions before, during, and after the PAP sessions, and attempted to control the set and setting of each session to decrease the possibility of adverse negative reactions. Multiple outcome measures were included in many studies to determine the efficacy, safety, and optimal feasibility of PAP. Psychedelics as an adjunct to psychotherapy have been shown to increase acceptance and processing of emotions, motivate and cause commitment to change, reduce fear response, (Hysek et al., 2011; Mueller et al., 2008; Rothman et al., 2001) increase levels of self-confidence, increase feelings of closeness, compassion and empathy for oneself and others, (Hysek et al., 2013; Passie et al., 2008; Simmler et al., 2013; Verrico et al., 2007; Wel et al., 2012), increase insight and introspection, induce a sense of spiritual enlightenment and a sense of belonging or interconnectedness with the universe (Katz et al., 1968; McGlothlin, 1962; Savage, 1955), facilitate access to maladaptive, intense, or unexpressed emotions, facilitate positive changes in behavior and mood, decrease hypervigilance (Amunts et al., 2005; Giovannitti et al., 2015), reduce resistance to communicating feelings (Chandler & Hartman, 1960; Passie et al., 2008; Schmid & Liechti, 2018; Wolff et al., 2020), and facilitate access to and the processing of emotionally traumatic memories (Passie et al., 2008; Roseman et al., 2014; Sessa et al., 2019). All of these psychological functions could significantly reduce clinical impairment associated with trauma-related and other psychiatric conditions. A study in which other psychoactive drugs, SSRIs, were used in comparison to PAP showed PAP not only to be significantly more effective, but safer for the treatment of trauma

related conditions (Feduccia et al., 2019). The literature suggests that the use of PAP as a treatment for trauma-related conditions, such as complex trauma, PTSD, and acute stress disorder is worth pursuing.

Current Limitations and Directions of Future Research

The goal of IFS, psychodynamic and cognitive behavioral psychotherapy, although executed in very different ways, is to facilitate the recollection and processing of traumatic memories, to experience the trauma-associated emotions, and to integrate and associate the traumatic memories so that they can truly become episodic memories. These traumatic memories are very emotionally painful and lack the quality of an episodic memory; they instead have the quality of a reliving. Intense emotional distress and dysphoric hyperarousal are often experienced when confronting these memories, all of which can be re-traumatizing. For these reasons, sometimes the current treatment methods for trauma-related conditions are often suboptimal and ineffective in reducing clinical impairment. Resistance to confronting traumatic memories in order to avoid the emotional pain associated with those memories and intense anxiety are hallmarks of resistance to treatment of trauma-related conditions. Although psychotherapy may eventually change maladaptive patterns, decrease anxiety, and facilitate the confronting of traumatic memories over time, the last thing those suffering with trauma-related conditions want to do, especially at the start of therapy, is confront their traumatic memories, making traditional therapeutic approaches alone often time-consuming, ineffective, and associated with reported dropout rates as high as 76% (Loerinc, et al., 2015; Gunter & Whittal, 2010). Moreover, the effective components of psychotherapy for treating trauma-related conditions are also the same components that cause traumatized people to avoid this treatment.

These problems can be addressed by the use of psychedelics as a therapeutic adjunct to psychotherapy. Psychedelics can facilitate particular emotional states that allow people to observe and integrate their traumatic memories as opposed to relive them. These drugs make it feasible to recall traumatic memories by reducing hyperarousal and emotional pain, enabling people to experience their traumatic memories without having to fully relive the emotions associated with them, which puts them at risk of being re-traumatized. Psychedelics enable people to communicate their feelings, be introspective, increase their scope of awareness of maladaptive defense mechanisms, and they enable the patient to internalize and comprehend what the therapist is telling them, all of which could be tremendously beneficial therapeutically in treatments focused on the processing of traumatic memories.

Although the findings from these studies are often profound, this re-emerging treatment method should be further investigated in randomized controlled trials (RCT) with traumatized populations for not only PTSD, but other trauma-related conditions, such as Complex Trauma and Acute Stress Disorder. These psychoactive drugs may be more effective for treating other kinds of trauma as opposite to PTSD like complex trauma. Specific RCTs such as placebo-controlled randomized controlled trials in which the psychedelic is used as an adjunct to psychodynamic psychotherapy, Internal family systems therapy, and cognitive behavioral therapy should be conducted. These studies are essential to determining if psychedelics will in fact enhance the process and outcome of treatment. These studies will address whether these drugs facilitate an enhanced capacity to recall early experiences, whether they decrease the dysphoric hyperarousal associated with recalling these memories and if they are more effective at reducing symptoms and maintaining those gains over time.

Additionally, more RCTs comparing the efficacy of SSRIs and PAP should be conducted due to the documented ineffectiveness of SSRIs for treating trauma-related conditions. The studies reviewed here suggest that psychedelics are potentially more effective in terms of how they alter mood and influence the recall of memories. Although SSRIs and psychedelics both alter the activity of neurotransmitters in the brain, psychedelics produce fast-acting, profound mind-altering effects, unlike SSRIs. Psychedelics induce emotional states that enable individuals to confront their traumatic memories more feasibly and thus potentially more readily engage in psychotherapy.

More RCTs comparing various psychotherapies and PAP on traumatized populations is also needed to identify psychotherapies that can effectively be used in conjunction with the various psychedelics. Future research could further investigate the use of internal family systems therapy (IFS) in conjunction with a psychedelic to treat trauma related conditions. Many psychotherapy studies reviewed here failed to specify the specific therapeutic approach used in conjunction with a psychedelic, suggesting that general supportive non-specific approach was used. Future research should include a summary of the type of psychotherapy being used in PAP. In doing so, the efficacy of the psychotherapy being used can be assessed. The demographics from the studies included in this review also indicate a major limitation, with most study samples consisting of mostly, white, young, and highly educated people, limiting the generalizability of these findings to this demographic group (Michaels, Purdon, Collins, & Williams, 2018). Future studies should diversify their patient population and RCTs should be conducted to assess the potential differences in effects across various demographic groups.

Dosing amounts of psychedelics should be further investigated to assess dose-response relationships. Due to the context dependent nature of memory (Hupbach et al., 2008),

maintaining a relatively accessibly state of mind, one that is not too far removed from the person's daily life, may be important for the effectiveness of PAP. Therefore, proper dosing of psychedelics may be essential to optimizing treatment outcomes. If the patient is in a completely different state of mind on the psychedelic than in their normal state of mind, they may not be able to recall the access to the traumatic memories that was achieved and may continue to be subjected to flashbacks and other symptoms. More studies of dose-response relationships are crucial to further understand the effects that manipulating doses of PAP have on mood, cognition, behavior, and the facilitation of memory to ensure effective dosing of patients.

The goals of PAP for trauma-related conditions are to facilitate the recollection of traumatic memories, to integrate them into consciousness, and to decrease arousal in response to recalling those memories. Conducting the future studies describe above is crucial to ensuring the effectiveness of PAP in reaching these goals. We need to understand which psychotherapies can be effectively paired with each psychedelic. Clinicians need to know which dose is most effective for facilitating the recall of memories without inducing a completely altered state of mind, so that the patient does not comes out of the session without being able to recall the memories. Understanding how these substances influence mood, cognition, behavior, and the facilitation of memory are all essential to achieving the aforementioned goals of PAP. Psychedelic-assisted psychotherapy could potentially be the catalyzed psychotherapy that allows those suffering from various trauma-related conditions to process and work through their traumatic memories, enabling them finally to heal and live their lives free of impairment. In summary, the evidence suggests that there is a strong clinical argument for the further investigation of psychedelics in the treatment of trauma-related conditions in controlled clinical trials.

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