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Psychedelic-Assisted Psychotherapy In The Treatment Of Post-Traumatic Stress Disorder In Brazil: A Critical Review.

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Running title : Psychedelic-Assisted Psychotherapy for PTSD in Brazil

Abstract

Objective: Post-Traumatic Stress Disorder (PTSD) is a pervasive but often overlooked public health issue in Brazil, a country characterized by deep social inequalities that perpetuate high exposure to traumatic events. Despite its prevalence, PTSD remains vastly underdiagnosed. Even when identified, current treatment modalities - both pharmacological and psychotherapeutic - frequently fail to provide complete remission, leading to the chronicity of the disorder and imposing significant individual, social, and economic burdens. This study aims to compile existing research on PTSD within the Brazilian context, assess the limitations of current treatment strategies, and explore the potential of psychedelic-assisted therapies, particularly 3,4-methylenedioxymethamphetamine (MDMA), as a viable alternative.
Method: As a literature review, special attention is given to the challenges of integrating these emerging therapies in the Brazilian context. Addressing the substantial gaps in diagnosis is a key step toward improving outcomes.
Results: Early evidence suggests that MDMA-assisted psychotherapy may significantly reduce PTSD symptoms below the diagnostic threshold, offering a promising avenue for future treatment.
Conclusion: Pending further research on its safety profile, it could be applicable within Brazil's public healthcare system (SUS).

Keywords : Post-Traumatic Stress Disorder, MDMA, Psychedelics, Brazil.

INTRODUCTION

Post-traumatic Stress Disorder (PTSD) is a debilitating mental health condition that occurs in some individuals after experiencing or witnessing a concrete episode of actual or threatened death, serious injury or sexual violence[1]. It is characterized by four symptom clusters which persist for over a month: intrusive re-experiencing of the traumatic event, such as through flashbacks or nightmares; avoidance of trauma-related stimuli; heightened arousal and reactivity, manifested through hypervigilance, irritability and/or destructive behavior; and negative cognitive alterations. The latter may present as peritraumatic amnesia, negative affect towards oneself and the world and/or feelings of isolation. Additionally, it may produce dissociative symptoms, and be further classified into the depersonalization or derealization subtypes.

Although valuable understanding of PTSD has been achieved through research conducted on war-related stressors, this predominance[2] is symptomatic and acts as a reinforcer of the misconceptions about the causes and prevalence of the disorder. The incidence of trauma exposure is globally high, albeit unequally distributed, and future research must take into account the differential PTSD risk across trauma types[3]. In fact, the burden of PTSD (trauma prevalence multiplied by trauma-specific PTSD risk and persistence) is highest for traumas of interpersonal nature, such as sexual violence and unexpected death of a loved one. Though the former is less prevalent than the latter, the category of intimate partner sexual violence accounts for 42,7% of all person-years with PTSD. Therefore, the war-centric understanding of the disorder perpetuates an underestimation of its significance and limits public policies' efforts in preventing, identifying and addressing PTSD across the world.

To date, established psychotherapeutic and pharmacological treatments have proven insufficient, as they primarily

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alleviate symptoms without achieving a cure, leaving most patients still above the diagnostic threshold[4,5]. Additionally, untreated PTSD carries substantial social costs beyond the individual, with an economic burden through higher rates of comorbid conditions, medical service utilization, lost productivity and unemployment, disability payment, premature mortality, and more[6]. As a result, long-term PTSD places a strain on welfare and health resources, which further underscores the importance of new treatment options with higher effectiveness.

For this purpose, promising research on the use of psychedelics for PTSD treatment has been done, and its therapeutic potential has increasingly gained recognition, including breakthrough designations by the FDA, particularly 3,4-methylenedioxymethamphetamine-assisted psychotherapy (MDMA-AP). However, most research has been conducted in the Global North, with extremely limited reach in Brazil, despite encompassing a population with higher exposure to interpersonal violence, which is associated with a higher conditional risk of PTSD development[7]. To our knowledge, only one study of MDMA-AP for the treatment of PTSD has been done in Brazil, following the same methodology as established by recent trials. It sheds light on the importance of novel approaches given the high incidence of interpersonal violence, and shows clinical improvement in symptoms consistent with previous research, concluding that MDMA-AP could become a viable treatment in Brazil[8]. So far, these findings prompt the need to carry out additional clinical trials in hopes of developing much needed treatment alternatives to the currently adopted directives. Nevertheless, ongoing research on non conventional treatments and Psychedelic-Assisted Psychotherapy (PAP) still warrants discussion and investigation on its safety for patients, its therapeutic potential and mechanism, as well as on the specificities that must be considered for its applicability in Brazil, such as ethnoracial factors, knowledge of PTSD amongst healthcare workers and more. This study proposes to gather previous research on these topics, in order for the development of novel therapeutic approaches to PTSD to commence in Brazil.

PTSD IN THE BRAZILIAN CONTEXT

Globally, the prevalence of PTSD varies significantly based on cultural, socioeconomic, historical and environmental factors. In Brazil, a country marked by a late urbanization and political instability, these factors present in an intensified manner, as the high rates of urban violence, domestic abuse and socio-economic disparities grow greater every decade. While existing literature has highlighted some aspects of PTSD in Brazil, such as its estimated prevalence for some capitals and great urban centers, its dynamics in this continent-like territory are complex and under-researched. PTSD's impact extends far beyond the immediate emotional and psychological suffering as it has long-term effects on the untreated patient. The profound social inequality in Brazil exacerbates the vulnerability of certain populations, since the living conditions generate unequal access to mental health care[7]. Moreover, there is a long-term consequence associated with the economic burden of PTSD, since the lack of treatment could lead to an irreversible impairment of the patients' ability to work and productivity, which further aggravates the stress, thereby contributing to a cycle of mental health issues.

Additionally, the cultural contexts in which trauma occurs play a critical role in how the individual may experience and respond to the traumatic event[7]. The cultural narrative around mental health in Brazil is often one of stigma and denial, possibly as a result of a normalization of chronic exposure to violence, where PTSD may be perceived as a sign of weakness. This can prevent individuals from seeking help and acknowledging the impact of trauma, which highlights the importance of culturally sensitive approaches to PTSD treatment and the need for mental health services that are attuned to the cultural contexts of the population they're inserted in and whom they serve[9].

Current research overlooks how the intricacies of socioeconomic and cultural factors differ across populations, and affect exposure to traumatic events in lower income countries. In Brazil, domestic violence is among the leading causes of morbidity and mortality[10]. In its two largest cities, exposure to traumatic events reaches a staggering 86% of the population, especially through urban violence[7]. While the conditional risk of developing PTSD secondary to any trauma type is 11,1%, the high prevalence of traumatic events stresses the non-negligible nature of these numbers, and allows for an estimate of over 1.680.000 individuals suffering from PTSD in the general population of São Paulo and Rio de Janeiro in 2022.

Moreover, trauma types caused by interpersonal violence have the highest conditional risk of PTSD development[7]. Underreporting notwithstanding, the country's high endemic rates of interpersonal, especially sexual, and urban violence, including that perpetrated by the police, deemed unreliable and untrustworthy[10], brings into question the lack of epidemiological studies on this subject. The Brazilian population's susceptibility to PTSD urges for the acknowledgement of the disorder as a significant public health issue, in order for primary and secondary PTSD prevention to gain effectiveness by means of public safety policies, improvement in treatment options and access.

PTSD and its underdiagnosis in Brazil

Despite the likely high prevalence of PTSD in Brazil, there is a significant underdiagnosis of the disorder. A study conducted at a Brazilian university hospital found that 20.5% of 200

outpatients had PTSD, yet 97.6% of these cases had not been previously diagnosed[11]. This can be attributed, in part, to the frequent co-occurrence of other psychiatric disorders, as PTSD often presents with comorbidities that lead to misdiagnoses, in turn impacting the efficiency of treatment[12]. Additionally, access barriers to psychiatric services and a shortage of adequately trained mental health professionals in Brazil's public health system (SUS) further contribute to the underreporting of PTSD, as few have shown themselves to be capable of identifying the condition[9,13]. There is a resistance to the use of diagnostic tools outside of the theoretical context, stemming from the normalization of chronic exposure to traumatic events in vulnerable communities, which reportedly perpetuates the false belief that individuals from these communities do not develop the disorder[9]. Contrary to this belief, chronic trauma is strongly associated with a higher likelihood of developing PTSD, particularly in its complex form (cPTSD), characterized by more severe psychopathology and qualitative differences to non-complex trauma[14]. A qualitative study into the mental health challenges of sexual and gender minorities in Brazil (SGMs) was recently released and highlighted the prevalence of specific traumas within these communities that have been ignored by society. The study revealed that almost 40% of the participants screened positive for PTSD, a number that illustrates how societal exclusion, compounded by institutional discrimination, can create a specific trauma profil[15].

It has been shown that healthcare workers often lack the knowledge needed to identify these complex presentations, hence the significant diagnostic gap[9]. It should be noted that the resulting lack of epidemiological data further restricts access to treatment, and therefore exacerbates the gravity of its social and economic cost. This underscores the need for improved training in the identification of PTSD among Brazilian healthcare providers.

The latest Brazilian guideline regarding PTSD16 failed to address the most recent scientific discoveries on alternative therapies on the disorder, and focused largely on PTSD within the police force. This narrow perspective reinforces a fundamental misunderstanding regarding the condition, perpetuating a stagnant approach to its treatment. There is an urgent need for public policies in Brazil to evolve their understanding of the PTSD, allowing for much needed change and more effective interventions.

The cost and consequence of untreated PTSD

Due to its debilitating nature, left untreated, the disorder produces profound suffering, which, in turn, impacts social relations, executive function and productivity, as well as physical health. In Recife, women who developed PTSD symptoms associated with intimate partner violence (IPV) were five times likelier to attempt suicide than those asymptomatic after exposure to the same trauma type[17]. PTSD is also associated with higher likelihood of incarceration[18] .Diagnostic criteria are met in 40,3% of incarcerated women in Rio de Janeiro, among whom illicit stimulant drug consumption is higher than in PTSD-negative individuals[19]. Comorbidity of other mental health conditions reached 67% of individuals diagnosed with PTSD in São Paulo and Rio de Janeiro[20]. Evidently, the disorder presents with high morbidity and social cost, and standard treatment should screen for substance dependence, high-risk behaviors, depression, sleep disturbances, suicidality, and other associated health conditions that co-occur in the vast majority of PTSD patients[21].

Lastly, inadequately treated PTSD may contribute to the patient's permanence in retraumatizing situations, due to the difficulty faced by many individuals suffering from the disorder in sustaining living conditions, such as social relations and financial stability. It has been argued that distance from retraumatizing situations are likely a result, rather than a precondition, of successful therapeutic interventions[13]. Thus, untreated PTSD puts the afflicted individual at risk of exposure to recurring traumatizing events, thereby aggravating their condition.

Regarding psychosomatic symptoms, PTSD has been shown to impact general health and life quality[22], lead to poorer health functioning and higher rates of medical service utilization[23]. In survivors of intimate partner violence (IPV), over 75% of whom sought medical treatment within 9 months, PTSD avoidance uniquely predicts neuromuscular, stress, gynecologic and sleep symptoms[24]. Additionally, PTSD is associated with graver symptom intensity in reported cardiovascular health status[25]. Thus, to prevent psychological and general health degradation, social suffering and to reduce the economic burden on the health system, it is essential to improve PTSD awareness and develop effective public policies. These should aim to improve diagnostic sensitivity by means of better professional training, robust epidemiological data on the disorder, and reducing access barriers to health services.

The neurobiology of PTSD and cPTSD: Understanding the treatment options

The neurobiology of PTSD is complex, as it involves multiple neural circuits and various biochemical processes which are yet to be completely elucidated. Recent models, such as the "Dual Pathology Model" and the "Triple Network Model" propose that PTSD arises from a wide circuit-based disruption in the connectivity and activity of different interconnected brain regions such as the Salience, Central Executive and Default Mode Network regions. These areas are related to vigilance, sensitivity to stimuli, fear management, executive functioning, dissociation and avoidance, all areas of cognition commonly affected in PTSD and cPTSD[26]. It is observed that the traumatic event and the stress response it evokes

comprise the triggering factors for the development of the condition, and it is influenced by genetics, the psychological stage of development of the patient, aspects of the traumatic stressor itself and the social context in which they are inserted following the traumatizing event[27, 28]. A brazilian cross-sectional study analyzed the prevalence of PTSD among adolescents in a low-resource city of the state of Rio de Janeiro, and found an important cross-link between the age of the patient during the exposure to traumatic events and the number of exposures, especially between 16 to 20 years of age. This phenomenon suggests that the cumulative trauma during this developmental window presents a "building block" effect, composing one of the greatest factors to the deepening of vulnerability and gravity of the disorder[28].

Emerging research in neuroimaging revealed neurochemical and structural alterations in the amygdala, prefrontal cortex (PFC), and hippocampus, central brain regions involved in emotional processing, fear response, and memory consolidation, which are consistently implicated in PTSD[29, 30]. Studies found several alterations in plasma proteins, such as BDNF (Brain-Derived Neurotrophic Factors), tau protein, NCAN (Neurocan) and CTSS (Cathepsin S) to be involved in neuroinflammation and synaptic function that could also be related to a greater risk of cognitive impairment development in PTSD patients that have been described in literature[31, 32]. These disrupt normal neuronal activity and synaptic plasticity, lead to a state of impairment of fear response extinction, consequently resulting in the establishment of PTSD[29, 33]. Common symptoms of PTSD are theorized to stem from hyperactivity in the amygdala and dorsal anterior cingulate, potentially caused by a loss of regulatory control from a hypoactive PFC[33, 31]. This imbalance, which becomes chronic over time, is not unique to PTSD, being also observed in various anxiety-related disorders[27]. In the case of complex PTSD (cPTSD), repeated activation of the amygdala due to chronic exposure to stressors may result in more profound alterations in the brain's physiological and structural circuits, contributing to the disorder's more severe symptomatology.

Current PTSD treatment

Currently, standard PTSD treatment consists of trauma-focused psychotherapy, with a primary component of exposure or cognitive restructuring to achieve fear extinction, rather than pharmacological approaches[21]. The latter, comprised of Selective Serotonin Reuptake Inhibitors (SSRIs) such as sertraline and paroxetine, is typically reserved for cases where engagement with or access to psychotherapy is hindered. These medications increase serotonin levels in emotional regulation circuits, helping to modulate the fear response and provide symptomatic relief[34]. However, despite symptom attenuation through SSRI-assisted psychotherapy, 60-72% of patients remain above the diagnostic threshold following treatment, which displays the unsatisfactory clinical effectiveness of this approach[4, 5]. Therefore, the intervention reach is limited, treatment options have stagnated in subpar efficacy, and are consequently accompanied by significant non-response and dropout rates. Thus, PTSD upholds its status as a chronic condition[35] and urgently requires new approaches in the search of remission in treatment-resistant cases.

Advances in our understanding of PTSD's neurobiology have underscored the limitations of SSRIs, paving the way for the reevaluation of both existing and novel treatments that target different facets of the disorder. By addressing neuroplasticity and neuroinflammation, emerging psychotropic drugs show promise not only for rapid symptom relief but also for promoting long-term recovery by repairing neural circuits and reorganizing brain networks. These treatments offer a new, hopeful pathway towards a more effective and sustained recovery.

Psychedelic-Assisted Psychotherapy

Psychedelic-assisted Psychotherapy (PAP) is at the forefront of scientific advancement in the treatment of refractory PTSD. In this review, we will refer to PAP with a broader definition of compounds, including classic psychedelics (Ayahuasca, Psilocybin and LSD), entactogens (MDMA) and other psychoactive substances (ketamine and cannabinoids). Though different compounds are associated with specific benefits, the therapeutic rationale behind their use for the treatment of PTSD is based on their catalytic effect upon psychotherapy[35] and their increase of receptiveness to engaging in deep therapeutic processing. This is believed to be due to their ability to attenuate symptoms through neural modulation and plasticity, to facilitate resilience, which influences the duration of PTSD[16], and to produce changes in the mental state. Furthermore, the complex nature of psychedelics' mechanism of action acts on several targets, providing perhaps a response more at par with this equally complex condition than single-target SSRIs.

Classic Psychedelics

Classic psychedelics act as agonists to serotonin receptor 5HT2A, facilitating psychological and neurobiological changes. This mechanism is believed to lead to an increased ability to process traumatic memories and to promote an attenuation of PTSD symptoms[35]. Notably, the key aspect of investigating the use of psychedelics is their capacity to promote cognitive restructuring, which may disrupt the psychological and neurobiological foundations of PTSD.

Current research has demonstrated promising results in the use of psychedelics for an array of mental health conditions. For instance, Ayahuasca has shown promising results for the treatment of grief, depression, eating disorders and substance

use disorders (SUDs), while Psilocybin has been recognized for its success in addressing treatment-resistant depression, for which it has earned breakthrough therapy designations. However, the use of these psychedelics in the treatment of PTSD remains largely unexplored[36], notwithstanding the fact that Psilocybin and Lysergic Acid Diethylamide (LSD) showed successful treatment of formerly called "Concentration Camp Syndrome" prior to their criminalization[35].

Nevertheless, despite the limited focus on PTSD, these substances offer valuable insights, particularly through their intersection between indigenous and western knowledge systems, on the crucial role of the ceremonial setting for the therapeutic process[36]. This highlights the importance of a guided approach, as an isolated pharmacological treatment is shown to be less likely to suffice. The beneficial properties of these psychedelics, adjunct to the native Amazonian understanding of their medicinal use, also call for a lens shift through which to define adverse effects: Ayahuasca induces vomiting in 59,9% of patients, a response that is culturally understood as an integral part of the therapeutic process. Therein lies a lesson for researchers worldwide in re-classifying adverse reactions associated with PAP.

Entactogens: MDMA-based treatment

The entactogen 3,4-methylenedioxymethamphetamine (MDMA) is a monoaminergic release agent, well understood by the literature, that promotes empathy and compassion towards oneself and others through the release of various agents, among which are serotonin, norepinephrine and dopamine. The most interesting characteristic of the MDMA-based treatment is the drug's capacity to work in synergy with psychotherapy. It is hypothesized by recent studies that its empathogenic effect allows the patient to form an improved alliance with the therapist, while reducing the fear response in the recall of traumatic memories[35], thereby augmenting the efficiency of the psychotherapeutic treatment.

The pilot study of MDMA-AP for PTSD demonstrated its safety and efficacy for patients refractory to other treatments, and paved the way for the current growing body of knowledge on this therapeutic modality[34]. Significant evidence of MDMA demonstrating a sustained reduction of PTSD symptoms when integrated as a catalyst for the psychotherapeutic approach has been attained[36]. After MDMA-assisted psychotherapy (MDMA-AP), 83% of patients no longer met the diagnostic criteria for the disorder. MDMA-AP was shown to be more efficient than SSRIs conventionally used for PTSD treatment, and also leads to lower dropout rates[35]. The former was proven to achieve clinical response after 3-5 days of treatment, whereas the latter demonstrates any detectable improvement only after 2-12 weeks of treatment. Furthermore, efficacy after 12 months is yet to be demonstrated for SSRIs, which raises into question whether they only address mood and depressive symptoms that co-occur in PTSD, rather than the disorder as a whole. The same does not hold true for MDMA-AP, since patients notably remained in remission 3,5 years later, showing signs of posttraumatic growth[38].

To date, systematic reviews indicate similar impact outcomes of MDMA-AP and cognitive therapy (CT), but a comparative study is yet to be done[39]. However, the reduction in symptoms has so far been shown to exceed that of control psychotherapy[40]. Furthermore, it is worth noting that the CT extends through a much greater treatment period, which could argue in favour of a sped up healing process through PAP. Although some adverse effects may be present during and in the aftermath of the limited number of MDMA-administered sessions, such as jaw clenching and anorexia, paroxetine and sertraline are associated with more side effects due to their prolonged treatment period[35]. Similarly, discontinuation of SSRIs is accompanied by adverse effects, contrasting to a lack thereof in MDMA-AP. Nevertheless, further investigation remains of utmost importance, since existing clinical trials have had limitations yet to be resolved in order to confirm the safety profile of this novel approach[41].

Finally, there is some risk of bias in clinical trials performed so far[41]. Indeed, the body of evidence was largely produced by the same research team. The reduced heterogeneity of the sample, comprising more than 76% white participants, also needs addressing in order to evaluate the drug globally. The control bias can be addressed in future studies by means of low-dose MDMA for active control, to verify existing significance in comparison to psychotherapy alone[39], and significant symptom attenuation has already been reproduced with such blinding[42].

Other psychoactive substances: Ketamine and Cannabinoids

Ketamine, on the other hand, does not target serotonin receptors, acting as a NMDA-R antagonist[36]. Recently, an increasing body of evidence suggests its indication in the treatment of SUDs, depression and suicidality. The compound also acts as a modulator of the glutamatergic system, prompting rapid synaptic plasticity, restoring the normal function in the amygdala-PFC circuit. This property is believed to underlie the rapid, albeit temporary, reduction of PTSD and comorbid depressive symptoms as seen in clinical trials. The effect on Glutamate pathways is hypothesized to aid in memory processing as well.

Finally, cannabinoids act on the endocannabinoid system through cannabidiol (CBD) and Δ9-tetrahydrocannabinol (THC) in a dose-dependent manner. This system is downregulated in PTSD, so that attenuation of characteristic symptoms, such as hyperarousal and exacerbated stress response[43], may be achieved through neuromodulation, especially in patients with trauma types unrelated to sexual violence[26].

Recent advances in the acceptance and legalization of the medicinal use of Cannabis sativa in Brazil have expanded our understanding of its potential in treating several health conditions. Since 2022, its commercialization for medical purposes has been regulated by ANVISA, paving the way for broader research and clinical applications.

The latest systematic review on the safety and efficacy of cannabinoids for anxiety-related disorders demonstrates that CBD not only alleviates anxiety associated with PTSD but also presents fewer side effects compared to commonly prescribed medications, suggesting a potentially safer and more effective profile for cannabinoids. Current research further indicates that CBD is well-tolerated, relieving symptoms without impairing physical performance or cognitive abilities. Additionally, it carries a significantly lower risk of dangerous interactions with other substances and is less prone to misuse and overuse compared to benzodiazepines[26, 43]. These findings raise the possibility of partially replacing existing medications with cannabinoids in patient care, particularly benefiting senior patients or those with concurrent substance use issues[43].

However, optimal dosing is critical for CBD's therapeutic success and must be tailored to the specific subtype of the disorder. For instance, a Brazilian study on PTSD patients who were survivors of sexual violence found that a single 300mg dose of CBD could reduce cognitive impairment triggered by recalling the traumatic event. Future research should focus on crosslinking the potential risks associated with CBD use, comparing the effects of single versus continuous dosing[43].

Viability and potential bias in PTSD studies

Despite its designation as a breakthrough therapy, MDMA-AP has not yet been massively used among psychiatrists and neurologists since its safety is still in question. Still, there has been a widespread repercussion in the scientific community and in society at large concerning its potential use as a new treatment for PTSD. Public perception about psychedelics has been set by culturally conservative agents, and it has been argued that resistance to investigating their therapeutic value in spite of their potential benefits stems from sociopolitical, rather than scientific reasons[44]. Thus, in light of the apparent advantage demonstrated by recent studies in comparison to current treatment options, MDMA-AP warrants further research to address existing questions, concerns and obstacles, some of which will be discussed next.

The first major concern refers to the safety profile of MDMA. The latest systematic review[41] on its efficacy and safety concluded that existing evidence does not yet suffice to clarify the risk-reward ratio of this treatment. However, said risk is significantly informed by previous research done on long-term deleterious effects of recreational ecstasy, which contains several adulterants and is often ingested by polydrug users in uncontrolled environments, consequently constituting a risk estimate that is not scientifically sound[35]. Additionally, MDMA-AP has shown fewer side effects and, when compared to SSRIs, did not indicate high abuse liability due to its isolated and supervised administration, constituting a favorable safety profile.

Another cause for concern is the certainty of evidence. Despite promising results regarding symptom improvement, response and remission rates reported by meta-analyses, the high risk of bias, indirectness and imprecision in assessed studies must be addressed in order to determine their credibility. Moreover, the short follow-up periods on the trials is still one of the greatests gaps to attest the safety and efficacy of treatment[45].

In parallel, the uncertainty of its therapeutic safety combined with the euphoria of a potentially innovative and effective treatment for a chronic condition produces a critical point, as seen by the growing reports of independent use in psychiatric practices. These could further worsen the public view of PAP, if applied before scientifically established. This reality, in which professionals are led to seek better treatment for their patients in the absence of sufficient directives on the topic, highlights the urgency with which more data should be attained to better understand MDMA-AP. Given the indications of its possible contributions in improving PTSD treatment, an impediment thereof could constitute as a violation of the human right to access its possible health benefits[44].

THERAPEUTIC POSSIBILITIES IN THE BRAZILIAN CONTEXT

Lastly, the question of its applicability in the Brazilian healthcare system (SUS) must be addressed. The MDMA-AP sessions are distributed over several weeks, and encompass the preparatory, medication and integration types, requiring at least two experienced therapists[36]. The unmedicated sessions are 90 minutes long, and the three[39] medicated sessions last 6 to 8 hours each. Evidently, its implementation would require adequately trained professionals and their availability over several hours, which could rapidly become costly. However, PAP has so far demonstrated to attain symptom improvement even below the diagnostic threshold within a much shorter period of time, with a higher efficiency than conventional treatments[35]. Consequently, though time-consuming, MDMA-AP would require fewer sessions, the benefits of which would be long-standing, mitigating future healthcare costs[43]. Moreover, the inadequacy of the latter due to its high non-response and dropout rates allows for the condition to go untreated, whereby comorbidities have a higher likelihood of developing[12, 20, 23]. Whether due to its open-ended nature or to its inefficacy, current PTSD treatment confers, in its sustained chronicity, an economic burden on the healthcare system

that would prove to be much larger long-term than the short-term costs entailed in MDMA-AP.

Conversely, research has been done on the applicability of another treatment approach for PTSD in the SUS[43]. Narrative Exposure Therapy (NET) is a psychotherapeutic approach under investigation for its use as treatment for PTSD in the context of life-long, ongoing trauma exposure. It typically requires 8 to 12 sessions, with each session lasting about 60 to 90 minutes, and requires appropriate training of the professionals. NET is structured in a more similar way to PAP than to conventional psychotherapy, and was shown to be applicable in advanced care services in the SUS. Although MDMA-AP would require the conduction of its own trial runs, the experience with NET is informative of its feasibility within healthcare structures.

CONCLUSION

Post-Traumatic Stress Disorder (PTSD) is a significant public health issue in Brazil, and must be urgently recognized as such, since the disorder's significant underdiagnosing exacerbates both individual and societal impacts, and imposes a considerable economic burden on the country. Current treatment options fail at addressing it appropriately, maintaining PTSD's status as a chronic condition.

In this context, Psychedelic-Assisted Psychotherapy (PAP) emerges as an innovative approach, with MDMA-Assisted Psychotherapy (MDMA-AP) showing particular promise. It has demonstrated the ability to reduce clinical symptoms below the diagnostic threshold - a feat not achieved by conventional pharmacological treatments. While these results are encouraging, this approach warrants further research to establish the safety profile and clinical applicability of MDMA-AP, including ethnically diverse participants, larger sample sizes and a more thorough questioning of adverse effects.

In conclusion, the true obstacles faced by PAP as a potential novel treatment for PTSD are the pre-existing access barriers that result from the lack of epidemiological data on the disorder in Brazil, and from the profound underreporting it undergoes. Nevertheless, its therapeutic potential for PTSD must be investigated. Should its efficacy be further confirmed, MDMA-AP could be integrated into Brazil's public healthcare system, following pilot trials and large-scale validation. Additionally, to significantly improve PTSD treatment in Brazil, efforts must be made to reduce the stigma surrounding the disorder, to better train healthcare professionals for diagnosis, and expand access to mental healthcare services. Only then can more effective treatments, such as MDMA-AP, be widely implemented.

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