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Review Article

Psychoanalytic Formulations in Psychedelic Therapy for Treatment Resistant Depression (TRD)

Carolina Maggio[1,2*], Friederike Meckel Fischer[2], Nadav L Modlin[1,2], James Rucker[1,2]

[1]Department of Psychological Medicine, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK; [2]Maudsley NHS Foundation Trust, Bethlem Royal Hospital, Beckenham,UK;[3]Department of Psychotherapy, Empirical Medicine Registry, Zurich, Switzerland

ABSTRACT

Recent studies have shown promising data regarding the safety and efficacy of psychedelic therapy for Treatment Resistant Depression (TRD), providing initial evidence of rapid and sustained response in this population. Despite lack of rigorous data pertaining to the role of the therapist, historically and in modern trials, the therapeutic alliance is considered a central component in the treatment model, and conceived as inextricable from the drug's subjective effects in achieving therapeutic outcomes. In modern psychedelic research, transpersonal and third-wave cognitive-behavioural psychology have played a primary role in guiding the conceptualisation of the treatment and the chosen interventions of the therapist. However, the intense emotional episodes that may emerge during the psychedelic experience also alludes to the presence of intersubjective dynamics, such as the existence of transference and countertransference in the therapeutic relationship, which psychoanalytic theory may offer insights on and whose scope and significance have not yet been the subject of study.

The current paper explores the role of the therapeutic relationship as a dynamic process within the context of Object Relations (ORT) and Attachment Theory (AT). It postulates that TRD may derive from early years attachment injury, and that the role of the psychedelic therapist has a reparative function due to the reported regressive nature of the psychedelic experience, and its most acute effects relate to a mystical-type experience. The paper also explores the nature of 'non-duality', through a psychoanalytic lens and as seen in the occurrence of ego dissolution in the psychedelic state, as well as in affect. Considering the mysterious nature of the psychedelic experience, this paper conceptualises psychedelic therapy as a fluid and highly interpersonal process; an inter subjective developmental encounter within the therapeutic relationship and between patients and the psychedelic experience. Reporting the experience of two patients undergoing psychedelic therapy with psilocybin for TRD and in combination with therapists' supervision notes, anonymised case studies are presented with the consent of the participants.

Keywords: Psychedelics; Psilocybin therapy; Treatment Resistance Depression (TRD); Major depressive disorders; Psychedelic medicine; Psychoanalysis

INTRODUCTION

Psychedelic research has shown positive results in treating a range of psychiatric conditions when administered under medical supervision and with adequate psychological support [1-5]. With dozens of research programs underway throughout the world, the need for robust measurements of contextual elements in psychedelic therapy is becoming apparent, and so is the importance of developing and refining the current therapeutic framework [6,7]. Drawing attention to the highly relational nature of psychotherapeutic support in psychedelic research, this article explores its function in positive clinical outcomes. Presenting a review of historical and current psychotherapeutic frameworks, the authors postulate that Object Relation Theory (ORT) and its conceptualization of developmental processes are useful models to better understand the role of the therapeutic relationship in Psychedelic Therapy (PT). Considering its complex dynamics within the psychedelic state, the authors propose that careful consideration of the patient's early attachment patterns promotes a genuine sense of trust and safety in the therapeutic dyad [8] in PT, and

Correspondence to: Carolina Maggio, Department of Psychological Medicine, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK, E-mail: carolina.maggio@kcl.ac.uk

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thus related to better therapeutic outcomes [9].

Context

This article will focus specifically on psilocybin for Treatment Resistant Depression (TRD). The choice for this is two-fold: Firstly, the type of theoretical paradigms developed around Phase II trials for psilocybin administration [1] will inform important considerations of therapeutic contexts when designing Phase III trials. Secondly, this article will present case studies based on a current randomised, controlled trial with 25 mg of psilocybin for treatment of TRD, with an optional open label extension [10]. The latter means that the participants who received a single dose of psilocybin 25 mg per oral administration vs. placebo, can opt to take a second dose of the same, independently to whether they have received an active dose or a placebo the first time. This open label extension means a substantial prolongation (an extra 12-week follow-up) of time spent in therapeutic contact with study participants, offering an invaluable opportunity to observe in more depth the usefulness and contraindications of current PT therapeutic models.

Psilocybin is the prodrug of psilocin, a partial agonist of serotonin receptors within the central nervous system [11]. The subjective effect is thought to be almost entirely dependent on stimulation of type 2A serotonin receptors in the cortex, where psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels [12]. Psilocybin occurs naturally in a variety of mushrooms species. It has been part of Central and South America indigenous people's medical and sacramental usages since ancient history [13,14] and since the 1950s has been studied in western clinical settings for its potential for treating psychiatric conditions including depression [5,15-17], anxiety and functional neurological disorder. Having been designated by the U.S. Food and Drug Administration (FDA) as "breakthrough therapy" for treatment-resistant depression, psilocybin has one of the most significant profiles within PT research [18]. When it is administered in conjunction with psychological support that includes preparatory and post-administration therapeutic sessions, psilocybin may catalyse new capacities for change in perspective, facilitate self-discovery and promote emotional breakthrough [19,20]. Furthermore, research with end-of-life patients has shown that psilocybin-induced mystical experience, characterised by enhanced spirituality and existential well-being [21,22] and in conjunction with psychotherapy, resulted in significant long-lasting anti-depressant, anxiolytic effects and enhanced quality of life [1,21].

LITERATURE REVIEW

Current framework

The type of psychological support in psilocybin trials is informed by a range of generalised theoretical and clinical frameworks. There is a lack of studies to outline a consistent therapeutic approach in psychedelic therapy [6,22-26,]. In an attempt to marry PT's sociocultural context with modern clinical research, a miscellany of spiritual and clinical language has emerged, aiming to be accessible to the mainstream, while arguably isolating itself from it. Furthermore, terms are used interchangeably to define the therapist's role, from guide [27] to sitter [28,29] and to therapist [30-32] furthering the inconsistency and fragmentation between the various PT clinical studies.

Meanwhile, research literature also offers several hypotheses concerning the clinical perspectives shaping therapeutic methodologies in PT. Starting from its 1950s origins, psychedelic methodologies were developed in the US alongside psychoanalytic psychology [6,33]. These methodologies and their applications in empirical psychotherapy shaped the role of the therapist through a relational and person-centred lens, emphasising principles such as non-directiveness, unconditional positive regard, empathy and congruence [6,34]. This approach can be seen as conducive to a strong therapeutic alliance [35,36]: The collaborative bond between therapist and patient [37] shown to be a consistent predictor of positive clinical outcome independent of the psychotherapy model [38-41]. This factor may be of even greater significance in PT, due to the depth of the material that may emerge in the psychedelic experience [6,42]. While more robust clinical investigation is needed, recent study on psilocybin therapy for major depressive disorder found evidence that therapeutic alliance positively affects treatment outcome [8].

Another central psychotherapeutic framework adopted since the origins of PT is transpersonal psychotherapy. Grof, et al. [43] made noteworthy contributions to this model, defining the patient's transpersonal experience under psychedelics as "the feeling that his or her consciousness has expanded beyond the usual ego boundaries and has transcended the limitations of time and space" [43]. Grof, et al. [43] concluded: "All that psychedelic drugs can do in and of themselves is to activate the psyche and mediate emergence of the unconscious and super conscious contents into consciousness. Whether this process will be therapeutic or destructive and disorganizing is then determined by an entire spectrum of other influences that have nothing to do with the pharmacological effects of these compounds. Since the factors of the set and setting are of such paramount importance, no magic results should be expected from a simple administration of psychedelics; they should always be used in the framework of a complex psychotherapeutic program" [43].

More recently, the incorporation of transpersonal models by the Multidisciplinary Association for Psychedelic Studies' (MAPS) 3,4-Methylenedioxymethamphetamine (MDMA)-assisted-psychotherapy for Post-Traumatic Stress Disorder (PTSD) highlighted how PT may facilitate meaningful transpersonal experiences that may be non-verbal in nature and may include experiences of closeness and empathy [44], deep spiritual significance and cathartic physical sensations [45]. Therapists training in this modality are invited to work with the awareness of the multiplicity of 'parts' described in the Internal Family System (IFS) model and, in a non-directive manner, facilitating the patient's capacity to access their own internal resources, or their "innate capacity to heal the wounds of trauma" [45]. This is defined as inner healing intelligence [46,47] an 'inner-directed' approach adopted in all modern PT trials [48]. This method encourages the patient to direct their attention inwardly, exploring insights generated by their direct experience [49]. Furthermore, MDMA's promotion of empathic rapport may enable a deepening of the therapeutic process by allowing for a more profound therapeutic alliance and corrective experience of secure attachment with the therapists [50,51].

Therapeutic modalities nestled within transpersonal, integrative, mindfulness and somatic therapy have been considered suitable backgrounds for therapists working on MDMA studies [45]. Conversely, Cognitive Behavioural Therapy (CBT) is considered limiting due to its prescriptiveness, if not used in combination with relational approaches [45]. However, CBT, as a more contemporary

and evidence-based model, has shown promising results in studies investigating psilocybin therapy in substance abuse [52] and has been considered by some researchers as PT 'gold standard' [53], based on the findings that it can facilitate cognitive reframing of negative self-talk and self-identity constructs [52]. This is aligned with the National Institute for Health and Care Excellence (NICE) guidelines for treating depression, which shows some evidence that CBT is effective in the treatment of chronic depressive symptoms, alongside Behavioural Activation (BA), counselling and short-term psychodynamic psychotherapy (NICE,2022). Another closely related methodology to CBT and often incorporated in PT is Acceptance and Commitment Therapy (ACT); [23], used in studies with psilocybin for TRD. This has been shown to support the decreasing of experiential avoidance in patients by developing their capacity to accept uncomfortable internal processes and external inputs and enhancing their openness and acceptance toward all experiences presented during drug administration [23]. Based on ACT, researchers have proposed the Accept, Connect and Embody (ACE) model theorised as a method to increase psychological flexibility [54]. More recently, researchers have proposed the EMBARK model (existential-spiritual, mindfulness, body-aware, affective-cognitive, relational, and keeping momentum), a transdiagnostic and trans-drug framework aimed to synthesizes current PT models [55].

This examination of contemporary frameworks is not exhaustive, and researchers continue to enquire into the various psychological support models adopted in modern trials. In the table below, we have reproduced a collection of the support models provided during preparation (pre-treatment), dosing, and integration (post-treatment) in contemporary psychedelic research [55,56], with various studies investigating the therapeutic effectiveness of different types of psychedelics, namely psilocybin [1,20,24,26,32,57-60], LSD [18] and ayahuasca [5]. This collection demonstrates the heterogeneous nature of PT models of support, although a 'nondirective' approach is common to every study (Table 1).

Table 1: Accompanying models of support.

Study	Pre-treatment	Therapy content treatment	Post-treatment
Anderson BT, et al. [51]	Therapeutic relationship and brief Supportive Expressive Group Therapy (SEGT) (3 group and 1 individual therapy sessions)	Nondirective support	4-6 group and 1 individual therapy sessions
Liebes GA, et al. [57]		(Follow-up to Ross et al.)	
Harris CRL, et al. [3]	Therapeutic relationship (1 preparation visit)	Nondirective support	Integrative (2 sessions in person (one day and one week post dosing; second session optional))
Harris CRL, et al. [16]		(Follow-up to Carhart-Harris et al.)	
Harris CRL, et al. [58]	Therapeutic relationship (1 preparation visit) Accept Connect Embody (ACE)	Nondirective support	Integrative (3 in-person sessions (one day after each dosing and three weeks after second dosing); and 6 optional integration telephone/video calls)
Davis AK, et al. [15]	8 hours of preparation meetings	Nondirective support	8 × 1-2 hr in-person integration/follow up sessions, 4 of which before primary outcome (1 day and 1 week after each dosing), and rest at subsequent follow ups (1, 3, 6, 12 month)

Gasser P, et al. [18]	2 preparatory psychotherapy sessions	Nondirective support (Brief support, focus on inward exploration, 2 investigators, private practice setting)	Integrative (3 × 60-90 min sessions)
Griffiths RR, et al. [26]	Therapeutic relationship (2 or more pre-dosing meetings (mean=3))	Nondirective support (2 therapists)	2 or more meetings between dosing (mean=2.7); 2 or more meetings after second dosing (mean=2.5)
Grob CS, et al. [32]	Therapeutic relationship Existential approaches	Nondirective support (Brief support, focus on inward exploration, therapy team present, in a hospital clinical research unit)	(Follow-up meetings mentioned, amount not specified)
Goodwin GM, et al. [1]	Minimum of 3 preparation visits	Nondirective support	Safety assessment on dosing day and two integration sessions, Day 2 and Week 1
Gukasyan N, et al. [24]		(Follow-up to Davis et al.)	
Fontes P, et al. [5]	No formal preparation meetings besides clinical evaluation at screening including 'anamneses'	Nondirective support	No formal integration meetings besides 'debriefing' once psychedelic effects ceased on dosing day
Ross S, et al. [20]	Existential approaches, psychodynamic/ psychoanalytic, and narrative therapy	Nondirective support (Psychotherapy, emphasis on meaning making, 2 therapists, comfortable room with a couch and music available)	Eclectic
Bordin ES, et al. [37]	No formal preparation except for 'detailed information regarding the effects of ayahuasca' provided prior dosing	Nondirective support	No formal integration

This may suggest that there is no ubiquitous methodology that would be suitable for all psychedelics and all indications. Furthermore, this brief review of traditional and contemporary PT models still tells us very little about the therapeutic relationship, while clearly indicating its importance. We have seen that the therapeutic alliance, the central component of the therapeutic relationship, is considered fundamental for positive therapeutic outcomes. We have also seen that the significance of the therapeutic alliance in PT is in its early days of clinical research, as are many other important extra-pharmacological factors which, while anecdotally noteworthy, are still speculative. Meanwhile, research on the therapeutic effects of 'mystical' or 'peak' experience in PT has been undertaken [21,61], with results showing that these experiences are likely only feasible if within an environment of psychological safety. Thus, establishing an environment of psychological safety with complex patient populations requires nuanced and specific clinical competencies, some of which we will cover in this article when discussing object relation and attachment theory in PT.

Mystical/peak experiences are defined as the maximal positive experiences of the psychedelic state, which include feelings of ineffability and paradoxically, transcendence of time and space, a sense of interconnectedness, and deeply felt positive mood such as joy, peace, and love [21,26,61]. The concept of peak experience was first coined by the humanistic and transpersonal psychologist Abraham Maslow, defining it as 'ego-transcending' and as a temporary experience of self-actualisation. Here self-actualisation is defined as the realisation of a person's full potential through introspection, contemplation and self-discovery. Despite their transient nature, peak experiences were described by Maslow as the ultimate integration of the split within the person, and as a "momentary experience of health" [62].

Object relation theory and the oceanic state

Object Relation Theory (ORT) is a broad and diverse area of thinking in psychoanalysis and offers numerous correlations to the clinical study of mystical experience and ego dissolution in PT. The term ORT, in a wider sense, refers to the meaning of what a person calls real, and its connection to their internal and external world. These inner and outer realities exist simultaneously and are made of relationships with important others and their image within our mind, or the internal 'objects' representing them. From this concept, several theories explore the significance of these relationships for psychological functioning [36]. The exploration of reality, and its meaning and nature, is a central subject within the psychedelic experience [6,24] where the mystical experience has been described as 'ultimate reality'[63,64]. As such, we may find that ORT's psychoanalytic formulation offers valuable frameworks in the understanding and treatment of psychological conditions effecting one's sense of reality.

For the purposes of this paper, ORT is discussed in relation to the experience of union and separation with the primary object, or the object of satisfaction of needs, such as the primary carer or the therapist, and considered as crucial for psychological wellbeing [6]. It is proposed that to enable psychological development in early years, defences are developed as unconscious processes aimed at regulating anxieties associated with the potential loss of the primary object [65]. The threat of this loss exists both on an interpersonal level, concerning the loss of the other, and on an intrapsychic level, where the fear of losing the primary object is experienced as a threat to one's own being [66]. This threat is internalised as ego identity, forming our self-concept, social relations and points of intersecting sociocultural identities.

When looking to understand the therapeutic validity of mystical experiences in PT, we find this concept associated to the one of Oceanic Boundlessness (OBN). Akin to mystical type of experience, OBN is assessed in conjunction with the experience of Dread of Ego Dissolution (DED), related to acute anxiety, and with the experience of Visionary Restructuralization (VRS), the non-ordinary experience of meaning, visual hallucinations and synaesthesia. These are the three primary factors of the Altered States of Consciousness (ASC) questionnaire, used to measure the acute subjective experience in the psychedelic state, where high OBN and low DED have been associated with long-term positive clinical outcomes produced by mystical/peak experiences in studies with psilocybin for TRD [10,58,61].

The concept of oceanic boundlessness has a long history within psychoanalysis and its inquiry into the nature of mystical experience. Also defined as 'oceanic state', or 'oceanic feeling' [12] it was originally coined by Nobel-prize novelist Roman Rolland, who presented it to Freud for psychoanalytic evaluation during some correspondence in 1930, and who subsequently developed it as a paradigmatic psychoanalytic concept. While Rolland's metaphysical understanding of oceanic boundlessness as the feeling of the 'eternal' was closely related to its corresponding PT concept, it was met with a very different interpretation in Freud's scrutiny, which considered it solely as a regressive need to withdraw from a harsh reality, by experiencing a sense of oneness with the universe.

Rolland's words to Freud seem deeply aligned to what all PT clinicians should keep in mind: "You, doctors of the Unconscious, instead of making yourselves citizens of this boundless empire and possessing yourselves of it, do you ever enter it except as foreigners, imbued with the preconceived idea of the superiority of your own country and incapable of ridding yourselves of the need, which itself deforms your vision, of reducing whatever you catch a glimpse of in this unknown world to the measure of the one already familiar to you?"

This evocative statement speaks loudly to the concerns of this article, challenging a paradigm that may compartmentalise patients' experience by breaking it down into its component parts to fit a familiar and finite scientific model [67]. While this may seem to permit empirical investigation, when it comes to studying the psychedelic experience, this approach has little to say about its nature, and even less of the meaning the patient conveys to it. Along with a growing invitation for a more holistic view of psychedelic medicine and the value of meaning-making in the psychedelic experience [8] Rolland's words vividly recall Cameron' s famous words "Not everything that can be counted counts, and not everything that counts can be counted [68]".

While both metaphysical and psychoanalytic understanding of OBN remain open to interpretation, psychedelic research seems to offer a valuable opportunity to deepen its theoretical considerations, especially in the light of its part played in significant therapeutic outcomes for suffering patient populations. OBN is also a fundamental concept of psychodynamic and Winnicottian ORT, which sees this state as one of undifferentiating between self and other, and defined as "the original psychological universe" [69]. Attempting to convey this state, Balint uses the word 'arglos', the German term describing the state where "the individual feels that nothing harmful in the environment is directed towards him and,

at the same time, nothing harmful in him is directed towards the environment" [70]. While this concept of oceanic boundlessness theoretically relates to early years of infancy in the relationship with the primary carer [70], it also bears striking similarity with reports of mystical experience for PT patients.

To date, psychoanalytic perspectives are being considered PT's most adopted theories [70], possibly due to the influence of psycholytic therapy rising in Europe while psychedelic therapy was being developed in the US back in the 1950s. With the psycholytic model we see a much more explicit adoption of traditional psychoanalytic approaches, with the use of talk therapy over several sessions, with multiple administrations of low-to-moderate doses of psychedelics, theorised to facilitate the therapeutic process due to an increased accessibility to the patient's unconscious material [71]. Despite their historical influence on PT, psychoanalytic perspectives remain unexplored in modern clinical research and PT trainings. This contradiction shows that despite a lack of formalised psychoanalytic theory, PT sees a silent agreement in the adoption of central psychoanalytic models, such as the existence of an unconscious, and that psychedelics are "mind-manifesting" [72] substances which enable us to observe the patient's unconscious mental processes [18,24,28,29,43,73]. Thus, it seems important to explore what we intend when we speak of the 'unconscious'. In other words, what is essential to the foundations of psychedelic therapy to work effectively with the 'mind' (psyche) that we see 'manifested' (delein)?

PT may serve as an important contribution to the development of a theory of the unconscious. Equally, as existing psychoanalytic models continue to influence psychedelic research, there is a need to study unconscious processes in PT, conceptualised as transference and countertransference and their reported intensification in the therapeutic relationship when within the effects of psychedelics [19,29,32]. These core psychoanalytic concepts are defined respectively as the process in which the patient's unconscious material is associated with the therapist, and vice versa, when therapists unconsciously project their material onto the patient [10]. In being highly intensified during psychedelics experiences, the emergence of these unconscious intersubjective dynamics in PT has been reported to permit deep regressive states [43] and possibly evoking early attachment wounds [44] calling for the therapist to develop skilful therapeutic competencies when observing and working with one's countertransference. On this note, current research maintains that the development of a positive transference to the therapists, enhanced by psychedelics, leads to good therapeutic outcomes [74].

An example of this can be found in the following case study, where the therapist supported a TRD patient while they relived and worked through traumatic experiences associated with suicidality, during a psilocybin-assisted session. From an initial experience of hyperarousal, and relying on a safe and secure therapeutic alliance, the patient contacted what they described as "the core of my suicidality", realising that their tendency to see life as worthless was in fact concealing the worthlessness they attributed to themselves, based on the early trauma of abandonment and the belief that they "deserved it". In this context, psychoanalytic theory demonstrates how the patient's unconscious material may reveal identification with both victim and perpetrator of the trauma. In the psychedelic 'mind-manifesting' phenomenon, effective working with transference means facilitating the patient's awareness of this "doubles identification" and work towards its integration during the post-dosing therapy session [21]. Furthermore, the therapist must become aware and make use of one's countertransference while supporting a patient during psychedelic treatment sessions. In relation to this case study, this would be the therapist's maternal countertransference eliciting the desire to 'save the patient'. Informed by the awareness of this countertransference, the therapist saw positive therapeutic outcomes by placing particular attention to not interfere with the natural unfolding process of the patient, allowing for its more destructive material to emerge while maintaining a genuine alliance, a calming presence and offering verbal reassurance in reminding them they are safe and not alone. Furthermore, the therapist offered validation of the patient's insights and welcomed their vocal and physical expression, making use of breathing exercises to facilitate self-regulation and connection with their somatic experience. Conversely, in the absence of these therapeutic considerations, researchers have reported circumstances in which therapists enacted the patient's transferential material, causing them distress and interfering with their capacity to gain insight from their experience. The reason for this is explained by psychoanalytic theory as the activation of the therapist's own unconscious material, especially if aligned with maladaptive behaviour in the patients, such as avoidance, withdrawal and aggression. When this occurs, a positive processing of the patient's transferential experience is obstructed, impeding the development of an effective therapeutic alliance, which we have seen being necessary to facilitate mystical experiences and the associated therapeutic outcomes.

An important consideration about countertransference in PT is referred to as the possibility of the therapist's vicarious traumatization from experiencing the participant's traumatic state [45]. On this subject, therapists are invited to practice dedicated self-care and to exercise awareness of their body's responses and make use of breath awareness to enable self-regulation. This concept is also highly relevant in patient's therapeutic support. With evidence suggesting that psilocybin induces an experience of heightened arousal [9], we may postulate that in this occurrence, the reassuring voice of the therapist, as a co-regulating agent, may at times be sufficient to support the patient to mobilise their own self-regulating capacities. For example, the therapist reminding the patient that they are safe, and to 'trust, let go and be open' [75]. However, with complex trauma and during an acute psychedelic experience, we suggest that facilitating a patient's connection with their body would enable deeper calming and therapeutic effects. With the use of somatic and body-awareness techniques, such as breathing exercises that extend exhalations longer than inhalation, we see the activation of the parasympathetic nervous systems, facilitating a state of calm and enabling the patient to evaluate their perceived and actual safety more accurately [76]. The somatic aspects of trauma are considered pervasive in re-experiencing traumatic states and central to modern development of trauma-informed approaches in modern psychoanalytic thinking [77]. In relation to PT, the importance of embodied experience is found in recent studies [45,49,56] and is predominant in numerous accounts of participants' psilocybin experience [57]. With 'embodied', we refer to the hypothesis that trauma has a detrimental effect not only on a person's psyche, but also on their body and sensorial experience [78]. This postulates that the emotional and sensory states experienced during trauma can be triggered by their reminders, precluding a person's capacity for self-regulation and for processing the information on a symbolic level, but rather in a literal way, as if the traumatic event was reoccurring in the present

[79]. From a psychoanalytic perspective, symbolization means the capacity to create an internal representation of the lived experience as something that can be related to and reflected upon [80] rather than something to be solely identified with [6].

This theory suggests that through the somatic expression of the traumatic material (i.e., by shaking and crying) the person may access a profound experience of their body's innate capacity to heal itself [17], used as reference in PT when discussing the psyche's inner healing intelligence [45]. On this basis, we may consider how in the above case study, the patient's new-found capacity for self-regulation, embodiment and emotional expression within the psychedelic state enabled them to mentalise their suicidality as symbolic, rather than literal, by experiencing and thus understanding their emotions and sensory experience associated to it, as opposed to avoiding or fighting them. In other words, they were able to symbolically view their suicidal ideation as a desire for transformation, as a question rather than an injunction: "What wants to die within me, which is no longer serving my life?"

In keeping with psychoanalytic language, we use the model of ORT to elaborate on the psychological mechanisms that enable a traumatised person to experience themselves as safe enough to access the experience of symbolisation. Under the effects of psychedelics and within the oceanic state, the patient's established unconscious defences may dissolve [25]. Free from them, the patient may reconnect to primary processing, or a state described by Freud as a timeless, prelinguistic and visually rich: A symbolic representation of the perceived reality [11]. The unconscious defence, such as distraction, intellectualising emotionally charged experiences or repressing unconscious material as an attempt to control and resist it, are known as secondary processes [21]. Such secondary processes can be thought of as identifications necessary to establish a separate sense of self and were hypothesized by Freud to characterise what we call 'ego', the rational and conscious mind, or the 'neural mass' that contains and directs the more primitive and unconscious primary processes [12]. Within ordinary states of consciousness, examples of secondary process are the state of being identified with a developmental narrative or ideology, sociocultural group or even one's physical body. When these identifications dissolve into oceanic boundlessness, new internal states may become catalysts to the creation of new self-concepts, or a new capacity to conceive the idea of oneself beyond existing beliefs about who and what the self is [2].

Within this new reality, contradictions can contentedly coexist, and symbolization allows for multiplicity to signify oneness, and oneness to signify multiplicity. A realm of non-duality, or a state of non-dual awareness in which the subject (the sense of who we are) and the object (all internal and external sense of reality) are experienced as one. An example of psychotherapeutic application of this idea can be seen in the following case study: A patient haunted by shame due to history of emotional abuse and neglect, during a psilocybin-assisted session became able to experience self in other, victim in abuser, and experience themselves in different ways, stating that they are innocent. The split between the two conflicting sense of selfhood found integration when the patient experienced themself as if at the top of a high mountain peak. From there, they could see all their life, including their traumatic history, and heard a voice saying, "you have already arrived, you don't need to work so hard". This was profoundly meaningful for this patient, who then felt themselves transforming into an 'innocent child', whereupon the voice continued by saying "and since you have arrived, you might as well enjoy yourself". The patient experienced themselves sliding down the mountain on rays of colours and light. In this scenario, during therapeutic support in post-administration integration session, and with a solid therapeutic alliance, the patient continued developing this newfound capacity for flexibility around one's self-concepts. Learning to tolerate both internal realities, they could work towards self-acceptance as opposed to attempting to avoid thoughts, memories and feelings associated to the traumatic events. As a TRD patient with a long history of depression, they completed their participation in the study on psilocybin-assisted therapy stating that they no longer identify themselves as a depressed patient.

While this case study shows one example of good therapeutic outcome, this also comes with necessary caveats: Anecdotal in nature, the experience of this patient may likely not represent the average response to psilocybin from the TRD population, and we do not wish to offer an overoptimistic portrayal of the potential therapeutic application of psychedelics. They do come with risks. Yet, it gives us the opportunity to consider what the therapist did, or did not do, to co-create with this patient a solid enough therapeutic relationship that successfully enabled this patient's therapeutic process and its outcomes.

DISCUSSION

The therapeutic relationship

According to ORT, to make use of the therapeutic relationship patients first need to perceive and experience the therapist as 'good' by evoking feelings and promises of safety, empathy, validation and authentic relatedness [81]. Here, good refers to the concept of 'good object', or Klein's idea that in our early development we perceive others as 'one-dimensional objects' that are either 'good' or 'bad' towards us at any given time [82]. To the extent possible, the internalization of the therapist as a "good object" can be thought about as one of the objectives of psychoanalytic-based treatments [82], and highly relevant to PT. In the context of the case-study, 'internalization' means all those mental processes by which the patient transformed their interactions with, and perceptions of, the therapist (whether real or imagined) into "inner regulations" [83]. Specifically to PT, the capacity of the therapist to build robust therapeutic alliance and be internalised as good object enables in the patient the cultivation of an internal good state of mind, or the good set in PT's set and setting [84] , a condition essential for positive clinical outcomes [21]. Conversely, internalization of what would have been considered by the patient as 'bad object', such as the therapist being inflexible, tense, or distracted would contribute to negative alliance [85] and may instigate a state of internal confusion, disorganization and ultimately fragmentation in the patient [70]. On this concern, Romero and Richards write that "considering the potentially substantial influence that the therapeutic alliance may have in psychedelic therapy, it is evident this element should be assessed more carefully in future research using appropriate existing measures" [21].

In order to facilitate this process, the therapist uses the preparation sessions to build rapport with the patient, exploring their intentionality towards the psychedelic experience, offer psychoeducation around the psychedelic's mechanisms of action, normalise and alleviate potential anticipatory anxiety and assure to discuss patient's needs around managing challenging experiences [21]. The preparation session is also where therapists begin facilitating the patient's capacity to access their inner healing

intelligence which we can see here as the effectively internalised good object. One might say that the core purpose of preparation is developing a capacity to explore this internalised good object able to offer guidance and healing. In facilitating and embodying the good object for the patient, the therapist offers a way for this to represent not so much the good object hoped for, but rather the foundation for hope. It is from this hope that trust may emerge, and with trust the courage to engage with the unthinkable, or the traumatic event, the thought associated to the threat to one's very sense of being and reality [86].

Understanding how to work with the unthinkable, and its meaning in patient's experience, is key to exploring the psychedelic state from an ORT lens. Winnicott's definition of the unthinkable proposes that being with someone is a reality that exists before any capacity to think about the experience, nor of its presence or absence [87]. In other words, our primary relationship becomes the reality in which we learn to exist, and only subsequently do we develop the capacity to think about our existence. From this understanding, if during the psychedelic experience the therapist becomes representative of the primary object, they must hold this role with awareness of its meaning and power, and only until the patient can do so themselves. By doing so, the therapist works to support the development of secure attachment, or the sense of trust and security within a safe environment from which the patient may explore the psychedelic experience. Hypothesized as contributing to the formation of a stable therapeutic alliance, the concept of secure attachment features in recent clinical studies on psilocybin therapy, where it is seen as positively influencing the psychedelic experience, which in turn may facilitate an increase in attachment security, a decrease of attachment anxiety and a corrective emotional experience for the patient [51].

PT and attachment theory

Attachment theory may give us a clinically meaningful perspective on the development of an effective PT framework, and on how to better understand the therapeutic relationship and patient's needs. Developed by Bowlby, et al. [88], Attachment Theory (AT) offers a working model of the self, based on the idea that we all have what he calls an attachment behavioural system, or innate and specific behaviours based upon the fulfilment of a sense of protection in the relationship with significant others, or attachment figures [89]. In AT, it is theorised that early childhood experiences concerned with the relationship with attachment figures become the foundation of a person's interpersonal interactions later in adulthood [90]. This is considered a powerful developmental process, operating mostly unconsciously, that influences a person's cognitions, behaviours, and wellbeing [89].

In childhood and throughout adulthood, when relationships with attachment figures provide a sense of empathy, availability and responsiveness in times of need, the facilitation of secure attachment is promoted, eliciting a capacity for curiosity and exploration [89]; which we have seen plays an essential role in the patient's ability to meaningfully engage with the psychedelic experience [21]. Conversely, in the absence of a reliable and supportive attachment figure during threatening circumstances, this sense of security is not achieved. In its absence, new strategies of affect regulation are formed, defined as hyperactivation and deactivation of the attachment system [90]. Hyperactivation indicates the compulsive strive to attain closeness with attachment figures, as an attempt to receive their attention and care, and it is referred to as anxious attachment style. Deactivation, on the other hand, shows the complete inhibition of these traits, to the extent that any inclinations for closeness is suppressed, and so are any feeling that may instigate the need for the attachment figures. This attachment style is referred to as attachment avoidance [77].

These concepts may be of particular importance to PT, in the way that these different styles of attachment have specific expressions and predicaments, and thus can be worked with in specific ways throughout preparation, dosing and integration sessions. For example, during the preparation session, the therapist discusses with the patient the subject of needs, with the acknowledgment that they will always maintain an available and supportive stance towards the patient. In this way, therapist and patient begin to co-create a mutual language that may elucidate the patient's attachment style and specific needs. In the case of a patient with attachment avoidance, the idea of asking for help may be particularly challenging and may point to the hypothesis that a ameliorative and transformative experience will not be solely based on the psychedelic experience, but also and perhaps especially on the formation of secure attachment with the therapist and study team.

It is also important to note that extreme displays of challenging attachment styles can be considered useful assessment tools in PT. For instance, a patient with attachment avoidance may show a strong need to rely on their coping strategies by rejecting the therapist, emphasising a sense of self-reliance and an intense discomfort with any form of closeness with others, or contact with distressing thoughts and emotions [89]. This may be a sign that the possibility of therapeutic alliance is compromised. Also, it shows that the patient may not be able to make good use of the therapist or of the psychedelic experience, in the attempt to resist and reject the intense emotional material that may emerge [21]. This type of coping mechanism implying the omission of distressing material from one's awareness [91], in psychedelic research has been referred to as experiential avoidance [60]. Specifically, in studies with psilocybin for TRD it was found that psychedelics facilitate a movement from avoidance to acceptance, associated with positive therapeutic outcomes [4]. While this seems to point to successful promises for the avoidantly attached patient, it is important to note that when their experiential avoidance shows extreme displays throughout preparation, and coupled with not sufficient rapport, it may be elucidating a lack of a fundamental sense of psychological safety for the patient, suggesting a contraindication to proceed with the dosing session. On the other hand, a patient with severe anxious attachment style is particularly sensitive to any signs of possible rejection or abandonment and may establish an extreme form of dependence and idealisation towards the therapist. If not managed with sensitivity, clarity and appropriate boundaries, this may cause the patient an unhelpful state of distress and impede on their ability to regain a sense of agency and empowerment once their participation in the study comes to an end. On this topic, researchers speculate how this patient may feel as if the psychedelic experience 'saved' them, pointing to a possible fragile and precarious recovery [59].

With both attachment styles, it will be important for the therapist to establish whether the patient is aware of denying or exacerbating their need of security and support, as such needs may only manifest suddenly, abruptly and even violently during the dosing session. With painful memories of attachment figures and overwhelming feelings of anger and hostility toward their unavailability, and

possibly towards the present availability of the therapist, the patient may experience a simultaneous need to reject and to be close to the therapist and what they may represent [92]. By exploring and facilitating awareness of these possible unconscious dynamics during preparation, therapist and patient co-create a safe environment in which the patient can confidently engage with the psychedelic experience and its promises of healing, despite the potentially intense emotional challenges it may bring. During the dosing session, the therapist remains present [21] reminding the patient, both verbally and non-verbally, of their presence as facilitators of an internalised good object. Where the patient's inner healing intelligence may act as a reparatory and re-parenting internalised self-object or attachment figure [45], it may facilitate a sense of deep connectedness towards oneself and 'the other', which is considered as a fundamental component of the therapeutic efficacy of PT [21,93,94]. Subsequentially, during the integration session, an exploration of the patient's attachment experience during the psychedelic state may shed a new light on their healing and recovery, and on their desire to cultivate a new relationship with themselves based on acceptance, as well as healthier relationship dynamics with their attachment figures [95].

Object relation and ego dissolution

We have seen that the psychedelic experience produces a state of suggestibility [21] in which the boundaries of the ego dissolve and, with them, the mechanisms of defence towards the unthinkable used in everyday consciousness [73]. This may serve as catalyst of transformation particularly in depressive presentations, associate with issues of rigidity of thinking and resistance to change [15,96].

Despite the potential effectiveness of psychedelic substances in dissolving such defences, it is of great importance that therapist's honour and acknowledges the protective significance of such defences and learns to work with them, rather than against them [97]. By meeting a patient in their defences, expressing curiosity and acceptance towards them, the therapeutic alliance is strengthened by genuine empathy, revealing the nature of what in ORT is known as false self, or the "defence against the unthinkable" [66] and its role in having enabled the patient to survive, literally and psychologically, severe developmental trauma [98]. Understanding the protective factors of this psychological construct, the therapist can learn about its limitations and use them as guidance to recognise that which the false self is not: The patient's authentic being, or the true self which existed prior to the traumatic events that signified the experience of non-being [66,98]. This idea of non-being, the traumatic 'self-annihilation' that generated the existence of the false self, may offer valuable insight when thinking of the phenomenon of ego dissolution in the psychedelic experience [42]. This concept requires further clinical consideration to understand what is dissolving, what is left in its absence, and how this complex and elusive process may facilitate good therapeutic outcomes [100-102].

For the purpose of explaining the concept of ego dissolution in relation to ORT, we will be using the terms ego, self and subject interchangeably [103]. In the mystical experience induced by psychedelics, our subjective reality is no longer experienced in relation to the subject (self) and its familiar references, but rather as being one with the object (the other, the world, our perceived reality) [104]. When this occurs, we have what has been defined as ego dissolution [105]. In the absence of separation from reality, there is no 'self' to relate reality and its meaning to. Here, from a psychotherapeutic perspective, psychedelics may be revealing that in the experience of ego dissolution, the ego that gets dissolved is not 'who we truly are'. No longer able to define reality by conventional parameters, the patients may experience a loss of ego boundaries and a deep sense of connection, even communion, with reality, with both the 'good' and 'bad' objects now becoming one, and the patient becoming one with them [106]. In the experience of this unitive state, the meaning discovered in the 'one object' may represent a realer version of the object itself, and thus of oneself [107]. Reality may be experienced as 'truer', and self-concept as representative of this truth, of the original state of being which existed prior to the emergence of the false self and its trauma-defined reality [108]. We might then postulate that by dissolving, the ego associated to a false sense of self may reveal a self whose truth is defined by its indissolubility, a self which exists independent from trauma and its correlated constructions of past and future, but rather as something inherently present and eternally new: The self as a reflection of a timeless, possibly incomprehensible, arguably uncontainable, expression of who we truly are [109].

CONCLUSION

This paper has explored the conceptualised 'mind-manifesting' nature of psychedelics from a psychoanalytic perspective and invites the reader to relate to its complexities and inherit unknowns as 'perpetual students'. In the attempt to bring some clarity to the psychoanalytic language we view as intrinsic to PT, the authors hope this may help therapists to consider various aspects of the patient's reality, as it transforms through the psychedelic experience, as well as in the experience of sincere human encounter in the therapeutic alliance. To that end, we consider the 'treatment' and the therapeutic relationship as synonyms. We conclude with stating that there is no such a thing as an expert of psychedelic therapy, just as in psychoanalysis there cannot exist an expert of the unconscious. Ultimately, this invites us to question what of PT has anything to do with the patient, replicating one of the fundamental questions of development, such as 'what a parent's wish for the child, has to do with the child?'. As social beings, however, we do know about the devastating significance of relationships, and how they have meant, at times, an experience of cure or illness. As we study the medical application of psychedelics, nature's compounds at least as old as mankind, we may learn to think of the concept of cure not so much as a substance to be consumed, a state to be achieved, or even as something to be. Rather, as a relationship: To cure (from curare, take care of), an encounter between us, ourselves and the other, where psychedelics continue 'manifesting' the mystery of what we like to call reality.

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DATA AVAILABILITY

The data that support the findings of this study are available from

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