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REVIEW ARTICLE

Psychedelics and schizophrenia: A mystery in history

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ABSTRACT

This analysis of current and historical research and clinical reports observes that the relationship between psychedelics and schizophrenia is complex and there are reports of psychedelics benefiting this population. Specifically, lower doses of psychedelics (mostly LSD) appear to have a potential beneficial impact on the negative symptoms of schizophrenia.

KEYWORDS

psychedelics, schizophrenia, LSD

INTRODUCTION

Schizophrenia is a mental illness that typically manifests in late adolescence or early adulthood, affecting approximately 0.3% of the population globally (Charlson et al., 2018). Despite the low prevalence, the global burden of this disease is substantial (Charlson et al., 2018). Antipsychotic medications do not treat the negative symptoms, are only partially successful as treatments for positive symptoms and have frequent extrapyramidal actions, which are associated with a range of adverse side effects (Tandon, 2011; Tandon et al., 2008) including suicide which is the leading cause of premature death in this population (Meltzer, 2001). Moreover, functional outcomes of negative symptoms, defined as diminished expression (e.g., affective flattening) and amotivation (e.g., avolition/apathy), are more harmful and harder to treat in the long term than positive symptoms (e.g., auditory hallucinations) (Foussias, Siddiqui, Fervaha, Agid, & Remington, 2015; Tandon, Nasrallah, & Keshavan, 2009). Improving the treatment for this debilitating disease would benefit individuals who struggle with this chronic disease and their families.

Given that there is a renewed interest in using psychedelics to treat a wide variety of conditions, including PTSD (Mitchell et al., 2021; Mithoefer et al., 2013, 2018; Mithoefer, Wagner, Mithoefer, Jerome, & Doblin, 2010), palliative cancer anxiety (Griffiths et al., 2016; Grob et al., 2011), depression, anxiety, addictions (Dos Santos et al., 2016; Johnson, Garcia-Romeu, Cosimano, & Griffiths, 2014; Johnson, Garcia-Romeu, & Griffiths, 2017; Johnson & Griffiths, 2017; Krebs & Johansen, 2012), cluster headaches (Sewell, Halpern, & Pope, 2006), obsessive-compulsive disorder (Moreno, Wiegand, Taitano, & Delgado, 2006) and other mental health indications (Friedman, 2006), it is appropriate to widen the current range of indications for which psychedelics can be beneficial and review historical documents for both lessons learned and hidden gems.

The relationship between psychedelics and schizophrenia has a long history and is fraught with complexity. Prior to the ban on psychedelic research with the U.S. Controlled Substances Act in 1970, these substances were being used on a variety of patients including those with chronic schizophrenia. In contrast, present-day research holds this diagnosis as a

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contraindication to psychedelic use along with personal or family history of schizophrenia, schizoaffective disorder, Bipolar 1 disorder, suicidal ideation, and those who experience psychotic episodes in the setting of depression. Most of the early research with psychedelics focused on LSD. Initially, mescaline was primarily used, but when LSD was invented and made available it was rapidly preferred. Reasons for this switch included the observation that LSD was "*much stronger, with fewer physical side effects at high dosages, cheaper to produce and just as easily available*" and "*LSD had a freshly minted novelty perfectly suited to the rhetoric of the scientific revolution*" and was not associated with any indigenous historical group (Jay, 2019). While the focus of historical research was on LSD it is reasonable to assume that the implications drawn would also apply to the other classical psychedelics of psilocybin and mescaline as they all have similar 5-HT_{2A} receptor activity.

The strained relationship between psychedelics and schizophrenia began shortly after psychedelics were introduced to the psychiatric community in the 1950s. One of the earliest documents (Blewett, 1959) exploring LSD psychotherapy observed that LSD could be useful in the treatment of schizophrenia but curiously suggested the LSD be taken by the therapist to help increase empathy (Blewett & Chwelos, 1959). At this time, it was believed that psychedelics produce a schizophrenic-like experience, and they were therefore ingested by mental health staff and researchers to help them understand this mental illness. The first terms used for this class of medicines before the term "psychedelic" was coined were "psychotomimetic" (to mimic psychosis) and "model psychosis". Specifically, it was believed that the effects of LSD would mimic the hallucinations, delusions, and disordered thinking experienced by those with schizophrenia (Mills & Dyck, 2008). There was significant discussion regarding whether those with schizophrenia were more or less sensitive to the effects of psychedelics and this debate is succinctly summarized by Hintzen & Passie (2010). Following these trains of thought from the time, schizophrenic and other psychotic patients were given LSD in varying doses and protocols.

More recently, Gonzalez-Maeso (2009) noted an evolving relationship between psychedelic neurochemistry, neurochemical abnormalities, and antipsychotic medications and speculated that the continuation of this research could facilitate the development of improved treatments for schizophrenia via the unification of the serotonin and glutamate hypotheses for this illness (Gonzalez-Maeso & Sealfon, 2009). Psychedelics are generally treated as risk factors in the mainstream research literature with the potential to cause destabilization or exacerbations of schizophrenia. It is therefore interesting to note that in spite of this near unanimity, there appears to be examples in both historical literature and current (mostly survey) research where psychedelics have been reported to have a beneficial impact on those with this mental health diagnosis. While, currently, research is very limited, Turkia (Turkia & December, 2022) reported a case study where a teenager who was diagnosed with an acute schizophrenia-like psychotic disorder successfully self- treated with LSD and DMT.

This paper is an analysis using the lens of the present day on the historical clinical research on psychedelic use in schizophrenic populations, it includes an examination of dosage and reflects on the current surge in popularity of microdosing.

METHODS

The purpose of this paper is to examine the "mystery in history" of apparent contradiction between current beliefs and historical research and observations. As current psychedelic research excludes anyone with risk factors for schizophrenia, the authors looked to work from the early researchers in the 1950s and 1960s who gave psychedelics to this population and documented their observations prior to their being made illegal in the early 1970s. To review the literature, authors of this paper searched PubMed and other databases and reference sections of relevant papers. The search criteria used were the words "schizophrenia" or "psychosis" combined with all the classical psychedelics (i.e., LSD, psilocybin, DMT, and mescaline). Thirty-five relevant papers were identified and reviewed, eleven of which were direct clinical observations and summarized in Table 1. In addition to historical research, current survey research is also relevant, as individuals with schizophrenia report using microdoses of psychedelics (Rosenbaum et al., 2020) linking current day and historical reports in this population.

RESULTS

Of the articles returned in our search prior to prohibition, 11 involved investigational research of either case studies, experimental treatments, or observation (Table 1). The early research had significant methodological limitations as it is mostly qualitative/anecdotal, as controls were generally nonexistent and dependent variables were not clearly defined or objectively measured. Also, these early investigators had limited understanding of the importance of context to optimize psychedelic therapy (Robin L Carhart-Harris et al., 2018) as set (expectations), setting (therapy environment) (Hartogsohn, 2016; Johnson, Richards, & Griffiths, 2008) and matrix (home environment) (Eisner, 1997) were not fully understood and as a result, optimal circumstances were not constructed. Dosage was also not well understood. For example, LSD dosages given ranged from 25 to 1,500 μg (Cohen, 1960).

Katzenelbogen (1953) gave a low dose of LSD (10–50 μg) to schizophrenic patients to facilitate interviews and noted, "*Ventilation of emotions appears to be more marked with LSD than with either methedrine or sodium amytal*" and "*there is greater opportunity for the patients ventilation of emotions and for verbal production*" (Katzenelbogen & Fang, 1953).

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Table 1. Review of methodologies in studies covered in the present paper. Table contains the number of experimental subjects given the substance, the type of study, the type of patients assessed, whether or not a placebo was used, the number of dose sessions, the dose, and the substance(s) used

Author	Year	N given drug	Type of study	Type of subject	Placebo used?	# of dose sessions	Dose	Substance
Dewhurst, K. & Hatrick, J.A.	1972	19	Retrospective chart review	LSD-induced psychosis, British mental hospital patients	no	varied	varied	LSD
Roy, A	1981	37	Observational, retrospective chart review	Schizophrenic patients (3+ yrs), LSD use week preceding symptom onset	no	unknown	unknown	LSD
Sandison, R.A., et al.	1954	36	Experimental	Patients with 'extreme mental tension'	no	2–58	25–400 μg PO	LSD
Cholden, L.S., et al.	1955	20	Experimental	Chronic schizophrenic patients	yes	14 (1× day)	100 μg IM	LSD
Abramson, H.A., et al.	1958	2	Observational	Schizophrenic patients	yes	4	50 μg PO	LSD
Katzenelbogen S. & Fang, A.D.	1953	20	Experimental	Mental patients; schizophrenic (15), bipolar, psychoneurotic	no	LSD: ?, M: 2-3×, SA: 1×	LSD: 10–50 μg PO, M: 5–20 mg IV, SA: 0.3–0.5 g IV	LSD, Methedrine (M), Sodium Amytal (SA)
Busch, A.K. & Johnson, W.C.	1950	29	Experimental	Mental patients (27 F, 2 M); schizophrenia, mania	no	varied, unreported	varied, 30–40 μg avg. effective dose	LSD
Böszörmenyi, Z., Der, P. & Nagy, T.	1959	24	Observational	Female inpatients: schizophrenia (20), oligophrenia (2), psychopathy (1), conversion hysteria (1)	no	1	IM: 1 mg kg^{-1}, 3 pts repeat dose of 1.5 mg kg^{-1}	DET
Shirvaikar, R.V. & Kelkar Y.W.	1966	10	Experimental, double-blind, controlled	Adult male, schizophrenic (chronic, withdrawn, apathetic)	yes	16	Week 1: 50 μg LSD & 50 mg (3× daily) thioridazine; Week 2: 100 μg & 100 mg (3× daily); Week 3 (first 3 days): 0 μg/100 mg (3× daily), (day 4) 150 μg/100 mg (3×); Rest of Week 3 – only thioridazine	LSD, thioridazine
Fisher, G.	1970	1	Experimental	Female 12 y.o. child with schizophrenia	no	16	LSD: 50–300 μg, Psilocybin: 10–30 mg, Methedrine: 5 mg, Librium: 10–25 mg	LSD, psilocybin, methedrine, librium
Forrer, G.R. & Goldner, R.D.	1951	8	Experimental	Male schizophrenics (6); male blind (non-congenital; 2)	no	7; 1	0.5–6 μg kg^{-1} PO	LSD

Busch and Johnson (1950) gave 21 hospitalized patients with schizophrenia varying doses of LSD, including low doses (30–40 μg) and found: "*The mental effects were those of excitation. The patients moved about more, showed greater interest, responded more readily to stimulation, talked more, and exhibited more emotion. With this increase in activity, there was a greater verbal expression of psychopathology. There were occasional short periods of confusion and disorientation and occasional transitory visual hallucinations. Most of the patients showed some degree of euphoria.*"

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In the detailed descriptions, they observed mixed results, which included substantial improvements in some patients, and reported the following details in seven of the patients:

> *Age 24 female - schizophrenia - simple - Patient usually mute and withdrawn. After medication, writes letters, and occasionally sings to herself. More alert.*
>
> *Age 47 female - schizophrenia - paranoid - Speech is increased, but becomes incoherent frequently. With lower doses (30 μg), entered into ward activity and did drawing. Became quite disturbed when 3 cc. (60 μg) of LSD 25 were given.*
>
> *Aged 41 female - schizophrenia - catatonic and paranoid features - She became more talkative, more responsive and better able to express herself. Patient was more conscious of her difficulties and wanted to do something about it.*
>
> *Age 42 female - schizophrenia - paranoid - Patient became more expressive. Responded better to environment. She was more active and better able to discuss her problems.*
>
> *Age 32 female - schizophrenic - catatonic and paranoid features - Following medication, patient was able to express her feelings; better able to act out her hostility in an acceptable manner. She could discuss her problems.*
>
> *Age 23 female - schizophrenia - catatonic - Showed more feeling; talked more freely and easily; more insight into family situation; marked emotional tone. Dizzy immediately after administration.*
>
> *Age 25 female - schizophrenia - catatonic - Better able to talk about her early life. Showed some regressive behavior and seemed to re-live childhood experiences.*
>
> *Age 23 female - schizophrenia - catatonic - Response to LSD 25 was increased activity and interest in surroundings, as well as ability to discuss her problems...*

These authors concluded, "*On the basis of this preliminary investigation, LSD 25 may offer a means for more readily gaining access to the chronically withdrawn patients. It may also serve as a new tool for shortening psychotherapy*" (*Busch & Johnson, 1950*).

Boszormenyi, Der, and Nagy (1959) report in a paper on their experiences of giving a psychedelic to patients with schizophrenia. Specifically, they gave DET (N–N diethyltryptamine), a short-acting psychedelic and reported, "*The majority of the uncommunicative, chronic schizophrenics became more communicative in response to treatment with DET. Even the vegetative symptoms and disturbances of perception did not interfere with the improved contact and the patients were particularly communicative during the third hour of the DET effect*" (*Boszormenyi et al., 1959*).

In a double-blind study design Shirvaikar (1966) gave 20 chronic, withdrawn, apathetic, adult male, hospitalized schizophrenics either a daily placebo or LSD (initially 100 μg given incrementally over a few hours) and thioridazine (50 mg initially) and noted that patients in the active dose group were:

1. Euphoric laughing – first day
2. Restlessness – first week
3. Exaggerated mannerisms
4. Arousal in second week and interest in surroundings
5. Improved social behavior

The authors concluded "*further trials of this combination were warranted*" (Shirvaikar & Kelkar, 1966).

Sandison reported "*I successfully treated a patient with puerperal schizophrenia who showed little improvement with ECT and insulin*" and "*from the patient's point of view, LSD is something definite that constitutes a real treatment of his own mind. This is of great importance because it holds his interest and helps him to get down to his problems*" (Sandison, 1956).

Fisher (1970) reported on the successful treatment of a 12-year-old, traumatized girl, with childhood schizophrenia who had been institutionalized frequently since age five. The patient was given 14 LSD treatments (and two psilocybin treatments) with dosages of 100–200 μg and encouraged to lie down and listen to music and then engage in psychotherapy. The five year followup notes indicated that the benefits from these treatments were prolonged (Fisher, 1970).

Forrer (1951) gave LSD in varying dosages to people with schizophrenia and observed "*Euphoria occurring in outbursts, was prominent. Increased accessibility and amiability, with increased release of libido and greater accessibility of delusional material, was observed*" and "*Lysergic acid diethylamide appears to be a suitable substance for further therapeutic investigation in the psychoses*" (*Forrer & Goldner, 1951*).

DOSAGE

Patients in these studies were given a wide range of LSD dosages across these studies resulting in significant variability of both positive and negative results in those with significant mental health disorders.

High dosages were observed to be problematic by a number of authors. De Gregorio (2016) reported that "*LSD at relatively high doses produces a state of transient psychotic-like state…*" (De Gregorio, Comai, Posa, & Gobbi, 2016). Sandison reports in his review of "*the effects of LSD on psychotic subjects have been reported by Stoll (1947), Giacomo (1951), Condrau (1949), and Busch and Johnson (1950). Psychic changes in these patients are only found after large doses and take the form of an exaggeration of the psychotic state*" (Sandison, Spencer, & Whitelaw, 1954). Cohen surveyed 44 therapists serving 5,000 patients over 25,000 therapeutic sessions with dosages from 25 to 1,500 μg and observed: "*adverse responses tended to occur at the higher dosages (above 75 μg)*" (Cohen, 1960). Additionally, this report states that though not a representative sample, there was "*no instance of serious, prolonged physical side effects*" and of the adverse responses reported, "*they were almost always due to psychological factors*" (Cohen, 1960).

Low dosages were observed by a number of authors to be helpful. Abramson (1973) commented on the over 3,000 publications in 2 decades and reflected that "*I feel now, as I*

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did nearly two decades ago, that LSD administered in low doses (less than 150 μg) not only is harmless when employed in a suitable medical therapeutic procedure, but also is of value in the psychotherapeutic process" (Abramson, 1973). Katzenelbogen (1953) gave a low dose of LSD (10–50 μg) to schizophrenic patients to facilitate interviews (Katzenelbogen & Fang, 1953). Abramson et al., in 1958 report on the positive effects of low dose (40–50 μg) LSD on hospitalized patients with schizophrenia in a group context in comparison with a placebo group (Abramson et al., 1958). Busch and Johnson (1950) gave 21 hospitalized patients with schizophrenia varying doses of LSD, including low doses (30–40 μg) and specifically mentioned that a low dose was effective and a higher dose was problematic (Busch & Johnson, 1950).

TYPE OF SYMPTOM

In the DSM-5 the diagnosis of schizophrenia includes both positive symptoms (e.g., auditory hallucinations, disorganized thinking, delusions, abnormal motor behavior) and negative symptoms (e.g., diminished emotional expression, decreased motivation, decreased ability to experience pleasure, decreased ability to socialize). Most of the historical papers when describing the positive outcomes of giving psychedelics to individuals with schizophrenia report on the improvement of the negative symptoms of this illness.

HARMS AND BENEFITS FROM PSYCHEDELICS – MODERN SURVEY RESEARCH

Mason (2018) did a survey of self-selected psychedelic users from the general population regarding mental health issues and found "*Self-medication with psychedelics was not highly frequent; although when it occurred, it was rated as significantly more effective [than] treatment offered by a medical professional. Current findings support research exploring the potential of psychedelics in the treatment of psychopathologies*" (Mason & Kuypers, 2018).

In 2000, a risk assessment on mushrooms containing psilocybin was conducted by the Netherlands-based Coordination Centre for the Assessment and Monitoring of New Drugs and concluded that the health risk to the individuals, the public, and threats to public order was low. This has been confirmed by many researchers (Johnson, Griffiths, Hendricks, & Henningfield, 2018; Nutt, King, Saulsbury, & Blakemore, 2007; Nutt, King, & Phillips, 2010; van Amsterdam, Opperhuizen, & van den Brink, 2011) and the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA -European Monitoring Centre for Drugs and Drug Addiction, 2006). Psychedelics have been consistently assessed by researchers to have low dependency potential, low toxicity, and low risk of individual or social harms in the general population (Gable, 1993; Gable, 2006; Nutt, King, & Phillips, 2010; van Amsterdam, Opperhuizen, Koeter, & van den Brink, 2010).

Survey data of naturalistic use of classic psychedelics appears to show that these substances have a wide range of beneficial effects and do not increase mental health concerns in the general population. A large survey (n = 2,510) of psychedelic users specifically reported that psychedelic use was associated with a reduction of depression and anxiety and increased emotional well-being. Large scale population studies n = 130,000 (Johansen & Krebs, 2015) and n = 21,967 (Krebs & Johansen, 2013) which examined psychosis, suicidality, mental health treatment and many other mental health variables failed to find evidence for a link between psychedelic use and an increase in mental health concerns. A survey study of healthy young adults (n = 1,032) specifically looking for an association between psychedelic use and schizotypy found no association after controlling for concomitant drug use (Lebedev et al., 2021).

A web-based self-report questionnaire explored the recreational use of psychedelics, and over 600 respondents were explicitly asked about both benefits and harms. Prolonged psychotic reactions were observed by 1.3% of LSD users (6 of 463). This was observed to be a prevalence not significantly greater than might be expected in the general population (Rucker, Jelen, Flynn, Frowde, & Young, 2016). The above collection of survey results concerning harm are focused on the general population and, though relevant, the safety/harm data for those with psychotic disorders specifically is not well investigated or known.

MICRODOSING

Current research introduces the concept of microdosing to this discussion. The discussion about microdosing began with a book by Dr. James Fadiman (2011), and today there are numerous online communities discussing this practice including sharing methods and anecdotal outcome reports (e.g., www.microdosing.com; www.reddit.com/microdosing/wiki). Whereas a microdose is actually a mini-dose, it is popularly defined as approximately 1/10 of a "normal" dose, and individuals who are "microdosers" often ingest regularly (e.g., every three days). While there are discussions about microdosing a variety of psychedelic substances, LSD and psilocybin containing mushrooms are the most common.

Some researchers have published data observing positive effects of microdosing on reported mental health status (Anderson et al., 2019; Cameron, Nazarian, & Olson, 2020; Johnstad, 2018; Rootman et al., 2021; Rosenbaum et al., 2020), pain tolerance (Ramaekers et al., 2021), and creativity (Prochazkova et al., 2018). This information is promising but far from conclusive, as other researchers have not found a difference between a microdose and a placebo (Bershad, Van Hedger, Keedy, Bremmer, & De Wit, 2019; Marschall et al., 2021; Polito & Stevenson, 2019; Szigeti et al., 2021). It is relevant for this discussion that most microdose research does not recruit individuals with specific mental health disorders, and schizophrenia has only been briefly

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mentioned in the research to date. Specifically, Rosenbaum et al. reported that in their study of microdosers, 1.8% (n = 6) reported having schizophrenia and were microdosing regularly (Rosenbaum et al., 2020). Due to the recent surge in popularity of microdosing, there are likely other microdosers with schizophrenia. Information from these microdosers on their naturalistic use would be a welcome addition to this line of inquiry.

DISCUSSION

Four hypotheses

Investigating the papers returned by the beforementioned search method, we found hypotheses generally falling within four categories of possible relationships between schizophrenia and psychedelics: 1) psychedelics induce a temporary schizophrenia-like experience (model psychosis), 2) psychedelics cause chronic schizophrenia in those who do not have this diagnosis, 3) psychedelics are harmful and destabilizing to those with preexisting schizophrenia and, 4) psychedelics are helpful to those with schizophrenia.

The first hypothesis that psychedelics were a "model psychosis" (Cerletti, 1958) was put to rest by researchers who observed that there were two nails in this coffin. Specifically, differences between the experience of schizophrenia and psychedelics began to be observed (Hollister, 1962; Nelson & Sass, 2008), and the therapeutic potential of psychedelics for alcoholism became apparent (Abramson, 1966). The interest in treating alcoholism with LSD began with the belief that LSD was similar to delirium tremens (DT), which is the psychosis-like experience induced by withdrawal from alcohol. If the extremely unpleasant DT experience could be duplicated, perhaps alcoholics could be "scared straight". Strangely, LSD worked in treating alcoholics but not for the reasons believed, as these patients often had profound positive and mystical experiences which gave them insight and hope, and the results showed positive outcomes (Abramson, 1967; Krebs & Johansen, 2012). Current researchers have also failed to find a reliable link between psychedelics and model psychosis (R. L. Carhart-Harris, Brugger, Nutt, & Stone, 2013) and observe the paradox that LSD can produce acute psychosis-like symptoms yet improves psychological well-being in the mid to long term (R. L. Carhart-Harris et al., 2016).

The second hypothesis was that psychedelics could cause chronic schizophrenia (Dewhurst & Hatrick, 1972), but this idea was challenged by chart reviews (Roy, 1981) and clinical observations that observed LSD was safe when used responsibly (Cohen, 1985; Sidney Cohen & Ditman, 1963) and surveys of those doing psychedelic work with patients (Cohen, 1960). As a result, researchers offered cautious optimism about the therapeutic potential of psychedelics and suggested more research was indicated (Grinspoon, 1981).

The third possible relationship between psychedelics and schizophrenia was that psychedelics could be harmful to those with this disease and a number of authors reported that, while the effects were inconsistent, psychedelics were occasionally destabilizing to those with this disease (Blewett & Chwelos, 1959; Cholden, Kurland, & Savage, 1955; S. Cohen, 1960, 1985; Sandison et al., 1954). For example, Blewett states that LSD could have the effect of "*intensifying existing symptoms and increasing the patient's discomfort*" (Blewett & Chwelos, 1959). The Director of the Haight-Ashbury Free Clinic, which was in the center of the 1960s psychedelic movement, reported on exacerbation of preexisting psychiatric illness but observed the complexity of improper settings, impurities in street drugs and media scare tactics were also variables to be considered (Smith & Seymour, 1985).

Some authors observed inconsistency in outcomes. For example, Cholden reviewed the literature on giving LSD to people with schizophrenia, observing that sometimes LSD resulted in an intensification of symptoms and sometimes it resulted in reversal of symptoms and suggested that "*the reaction may be determined in part by the milieu*" (Cholden et al., 1955). This observation is consistent with other researchers who observe that the early researchers and clinicians were (understandably) unskilled at providing optimal therapeutic contexts (Krebs & Johansen, 2012).

The fourth hypothesis was that psychedelics could (in some circumstances) be beneficial for those with schizophrenia. Abramson et al. (1958) reported on the effects of low dose (40–50 μg) LSD on hospitalized patients with schizophrenia in a group context in comparison with a placebo group. They observed that the patients in the LSD group showed increased participation, spoke more often, made more other-oriented (as opposed to self-oriented) statements, and the quality of their interactions increased. They concluded, "*we tentatively suggest that LSD might prove useful in facilitating communication in psychotherapy*." They also observed that people with schizophrenia responded more than the "normal" response, and "*on average the patients exhibit a higher ratio of positive over negative socio-emotional acts during the LSD sessions than during the placebo sessions*" (Abramson et al., 1958).

Are dosage and type of symptoms crucial factors?

There are a number of variables that need to be considered when attempting to understand why some authors report negative and others report positive outcomes in the treatment of schizophrenia with psychedelics. The analysis of dosage and type of symptom does lead to some interesting observations. In a review paper on the treatment of negative symptoms of schizophrenia, Correll states that current treatments primarily target reducing the positive symptoms and the negative symptoms are more challenging to treat and concludes "*Negative symptoms clearly constitute an unmet medical need in schizophrenia, and new and effective treatments are urgently needed*" (Correll, 2020). The most oft reported beneficial effects were seen with low dose LSD in unlocking the negative symptoms in schizophrenic patients.

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One can observe from both the historical literature and current surveys that while psychedelics are not a panacea, there are circumstances where they have been shown to be helpful for individuals with schizophrenia. One possible explanation for the beneficial effect is the possibility of increased neural plasticity and cognition (Ornelas et al., 2022), particularly in light of the association between negative symptoms and cortical atrophy (Wolf et al., 2023). Current researchers now understand the importance of context as set, setting, and matrix are crucial factors in the creation of positive outcomes, but it appears that there are also other aspects to be considered when attempting to understand why historical researchers were so variable in their reports on the effects of psychedelic treatments on schizophrenia.

CONCLUSION

After reviewing the historical literature and current survey research, the authors of this paper tentatively observe that a low dose or a microdose of a psychedelic may be a possible treatment for the negative symptoms of schizophrenia. As schizophrenia is such a debilitating illness and current treatments are often ineffective and have problematic side-effects, exploring all potential alternatives is desirable. More research is needed to establish many details including, efficacy, dosage, specific psychedelic, the type and severity of schizophrenia and other circumstances, which are all variables that need to be considered to maximize the potential for psychedelics to be used as a medicine in this population.

SUGGESTIONS FOR FUTURE RESEARCH

The number of individuals with schizophrenia who respond to surveys is limited and therefore data is inconclusive. Therefore, encouraging a future meta-analysis of multiple surveys would be helpful. To facilitate this, researchers should ask consistent questions of both those with schizophrenia and their service providers. Questions regarding the specific diagnosis of schizophrenia with elucidation of both positive and negative symptoms and how these interact with different types of psychedelics and at different dosages could be collated in a meta-analysis to increase the ability to draw conclusions in the future. There is a survey currently active (Nov 2023) regarding psychedelics and mental health which can be accessed at https://quantifiedcitizen.com/digging.

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