Nordic Journal of Psychiatry

ISSN: 0803-9488 (Print) 1502-4725 (Online) Journal homepage: http://www.tandfonline.com/loi/ipsc20

LSD treatment in Scandinavia: emphasizing indications and short-term treatment outcomes of 151 patients in Denmark

Jens Knud Larsen

To cite this article: Jens Knud Larsen (2017): LSD treatment in Scandinavia: emphasizing indications and short-term treatment outcomes of 151 patients in Denmark, Nordic Journal of Psychiatry, DOI: 10.1080/08039488.2017.1336251

To link to this article: http://dx.doi.org/10.1080/08039488.2017.1336251

Published online: 05 Jul 2017.

NORDIC JOURNAL OF PSYCHIATRY, 2017
https://doi.org/10.1080/08039488.2017.1336251

Taylor & Francis
Taylor & Francis Group

RESEARCH ARTICLE

LSD treatment in Scandinavia: emphasizing indications and short-term treatment outcomes of 151 patients in Denmark

Jens Knud Larsen

Department Q, University Hospital of Aarhus, Risskov, Denmark

ABSTRACT

Background: New research has suggested the clinical use of lysergic acid diethylamide (LSD) and psilocybin in selected patient populations. However, concerns about the clinical use of LSD were advanced in a large Danish follow-up study that assessed 151 LSD-treated psychiatric patients approximately 25 years after their treatment in the 1960s.

Aims: The purpose of the present study was to give a retrospective account of the short-term outcome of LSD treatment in these 151 Danish psychiatric patients.

Methods: The LSD case material in the Danish State Archives consists of medical case records of 151 LSD-treated patients, who complained and received economic compensation with the LSD Damages Law. The author carefully read and reviewed the LSD case material.

Results: LSD was used to treat a wide spectrum of mental disorders. Independent of diagnoses, 52 patients improved, and 48 patients worsened acutely with the LSD treatment. In a subgroup of 82 neurotic patients, the LSD dose-index (number of treatments multiplied by the maximal LSD dose) indicated the risk of acute worsening. In another subgroup of 19 patients with obsessive-compulsive neurosis, five patients later underwent psychosurgery. A small subgroup of 12 patients was treated with psilocybin. The long-term outcome was poor in most of the patients.

Conclusions: Despite the significant limitations to a retrospective design, this database warrants caution in mental health patients. The use of LSD and psilocybin in mental health patients may be associated with serious short- and long-term side effects. Until further trials with rigorous designs have cleared these drugs of their potential harms, their clinical utility in these groups of patients has not been fully clarified.

ARTICLE HISTORY
Received 3 August 2016
Revised 28 February 2017
Accepted 21 May 2017

KEYWORDS
LSD; LSD damages law; LSD therapy; flashbacks; psilocybin

Background

Recently, new research suggested that psychedelic drugs, such as lysergic acid diethylamide (LSD) and psilocybin, may benefit patients with difficult-to-treat anxiety, including end-of-life anxiety, addiction or post-traumatic stress disorder (PTSD) (1). A small open-label study found support for the use of psilocybin in treatment-resistant depression (2). Furthermore, a review from 2008 found that hallucinogens, including LSD, could safely be studied in humans provided there are strict safeguards, including careful pre-treatment screening and preparation, as well as the establishment of trust and rapports between sessions (3). Finally, Hendriks et al., in their analysis of 190,000 adult US respondents pooled from the last five available years of the National Survey on Drug and Health (2008–2012), found that classic psychedelics may hold promise in preventing suicide (4). For a long time, psychedelics were abandoned in clinical use in accordance with previous international warnings from a decade after the introduction of these drugs in psychiatry (5,6). In my Danish, long-term follow-up study of 151 patients approximately 25 years after they were treated with LSD in the 1960s, the prospects of their clinical use were likewise found to be worrying (7). In the latter study, most patients suffered from severe side effects from LSD many years later. In particular, flashbacks independent of diagnoses were observed in two-thirds of the patients (7).

LSD was extracted from *Claviceps purpurea* (ergot) in the laboratories of the pharmaceutical company Sandoz in Basel in 1938 by Albert Hofmann; however, the psychoactive potentials were not observed until 1943, when Hofmann took 25 μg of the substance in a self-experiment (8). In 1947, Sandoz marketed LSD under the trade-name Delysid with the following indications: (1) analytical psychotherapy, to elicit the release of repressed material and provide mental relaxation, particularly in anxiety states and obsessional neuroses and (2) experimental studies on the nature of psychoses; by taking LSD, the psychiatrist can gain insight into the world of ideas and sensations of mental patients. LSD can also be used to induce psychosis with a short duration in normal subjects, facilitating studies on the pathogenesis of mental disorders (7,9).

In 1950, one of the first reports of LSD as an aid for psychotherapy in eight cases of psychoneurosis was published (10).

Almost a decade passed until the treatment was introduced in Scandinavia. The Scandinavian treatment was

CONTACT Jens Knud Larsen jens.knud.larsen@ps.rm.dk Department Q, University Hospital of Aarhus, Skovagervej 2, DK-8240 Risskov, Denmark

initiated after study visits to leading European centres for LSD treatment: Powick Mental Hospital, Worcestershire in England (11) and the University Clinic for Psychiatric and Nervous Disorders, Göttingen in West Germany (12). In Sweden, at the University Clinic in Lund, the treatment started in 1957; however, little was published, and there were no comments on the short-term treatment effect (13). In Denmark, the treatment was officially started in 1960 at Frederiksberg Hospital (14); however, one of the first papers on LSD treatment in Denmark referred to 1959 as the first year of treatment (15). In Norway, the treatment started in 1961 at Modum Bads Nervesanatorium (16). As in Denmark, follow-up studies on LSD-treatment were performed; however, they were completed 18 years after the collection of data in 1968. Little and only casuistic information about the short-term treatment outcome was presented. Additionally, positive and negative experiences were reported by the patients (17).

Aims

The aims of the present study were to give a retrospective account of the short-term or acute treatment outcome of LSD treatment in a population of Danish psychiatric patients. The long-term outcome of the same population of 151 patients has been published elsewhere (7). The purpose of this study was to estimate the possible beneficial and damaging effects of LSD treatment.

Materials and methods

In Denmark, from 1959 to 1973, nearly 400 patients were treated with LSD. The majority were at the Department of Psychiatry, Frederiksberg Hospital; however, LSD treatment was administered at psychiatric departments and clinics all over the country (8). Medical case records and other case material of the 151 LSD-treated patients are kept in the Danish State Archives (LSD case material). These materials consist of the data of those patients, who complained that they were damaged by the LSD treatment and referred to the LSD Damages Law, 1986 (18). Referring to the law, reparatory compensation could be given for LSD-inflicted physical and psychological damage. Section 1, subsection 2 of this law defines the so-called reversed burden of proof, stating: 'For harm, which is caused by or may be caused by treatment with LSD, this treatment is considered to be the cause (of the harm), unless it is most likely that the harm is due to another cause' (18).

Referring to the law, applications for compensation must have been received no later than 1 June 1988. In May 1986, The Danish National Health Service prepared a circular that was sent to all Danish doctors with the following title: Circular on compensation for damages due to LSD-treatment. On page 2 of the circular, the doctors were informed that they can ask for an application form from the Ministry of Social Affairs. Furthermore, the circular reported that in June 1986, the Ministry of Interior Affairs was going to insert an advertisement in all Danish daily newspapers and that municipality and county authorities were going to be briefed on the law (19).

Each application was handled in a tribunal under the Ministry of Social Affairs (the LSD tribunal).

All LSD-treated applicants received compensation.

A detailed description of the basis for the LSD tribunal to make a verdict has been published elsewhere (7,8). However, among eight questions, the LSD tribunal also asked the following questions:

1. What was the patient's psychiatric diagnosis, and what was the patient's mental state before LSD treatment?
2. What was the patient's mental state immediately after LSD treatment?

The questions were critically examined in specialist certificates in 111/154 patients (74%) from more than 20 psychiatrists. In the remaining cases, the matter was elucidated by obtaining written responses from the various psychiatric departments. In all cases, the reports were written approximately 25 years after LSD treatment occurred, which were based on contemporary case records and other case material, such as the patients' applications and statements. The original questionnaires for scientific use in the 1960s had only been preserved in fewer than five cases; furthermore, these were all either blank or insufficiently completed. No subgroups were established.

The present author was granted access to the LSD case material in the Danish State Archives and respected confidentiality per the Archives Law. All LSD case material was carefully reviewed twice: the first time in winter to spring 2013 and the second time in autumn 2013. The long-term complications of the LSD treatment, based on this reading, has been published elsewhere (7); however, an analysis of the short-term effect of LSD treatment in these materials has not previously been performed. Only the number of patients: improved (52), unchanged (34) or worsened (48) were presented (7). No attempt has been made to more specifically differentiate the response.

To obtain an idea of a possible correlation between the harmful effect and dose of LSD, the LSD dose-index was constructed by multiplying the maximal LSD dose with the number of sessions divided by 100 for each patient.

Results

LSD was used on a wide spectrum of mental disorders, as shown in Table 1. Clinical illustrations of the acute effect have been published elsewhere (7). The LSD tribunal established the diagnosis in accordance with the International Classification of Diseases of that time, elaborated by the World Health Organization. The 6th edition (ICD-6) was used at the start of the LSD treatment; however, from 1965, the 8th edition (ICD-8) gradually took over (7,20,21). Improvement was rated according to any objectively described or subjectively reported longer lasting or transient recovery of the symptoms.

Table 1. The acute effect of LSD treatment in 151 patients, diagnosed per the 6th and 8th editions of the International Classification of Diseases, which were used in the 1960s.

The main ICD psychiatric diagnosis	Improved $N = 52$ (34%)	Unchanged $N = 34$ (23%)	Deteriorated $N = 48$ (32%)	Unknown $N = 17$ (11%)
Abuse of alcohol and medicine $n = 2$ (1%)	1	1	0	0
Schizophrenia and paranoid psychosis $n = 8$ (5%)	3	2	3	0
Borderline psychosis $n = 1$ (1%)	0	1	0	0
Depression and manic-depressive psychosis $n = 17$ (11%)	4	3	9	1
Depressive neurosis $n = 5$ (3%)	2	2	1	0
Character neurosis $n = 53$ (35%)	16	10	17	10
Anancastic neurosis $n = 19$ (13%)	5	4	7	3
Anxiety neurosis $n = 30$ (20%)	11	8	9	2
Unspecified neurosis $n = 6$ (4%)	6	0	0	0
Anorexia nervosa $n = 2$ (1%)	2	0	0	0
Personality disorder $n = 2$ (1%)	0	0	1	1
Sexual dysfunction and gender identity deviation $n = 4$ (3%)	2	2	0	0
Stuttering $n = 2$ (1%)	0	1	1	0

Table 2. The outcome of LSD treatment, number of sessions and dose of LSD in a subgroup of patients suffering from depressive neurosis, character neurosis, anxiety neurosis and unspecified neurosis ($N = 82/134$ (66%)).

	Improved $N = 35$ (43%)	Unchanged $N = 20$ (24%)	Deteriorated $N = 27$[a] (33%)
Number of sessions Median (range)	18 (2–54)[b]	11.5 (1–47)	11 (3–70)
Max LSD dose (μg) Median (range)	250 (80–700)[c]	230 (30–800)[d]	275 (100–800)[e]
LSD dose-effect index Median (range)	38 (8–252)[f]	65 (3–376)	70 (10–252)

[a]One patient treated with psilocybin alone.
[b]Missing data for three patients.
[c]Missing data for 16 patients.
[d]Missing data for seven patients.
[e]Missing data for 17 patients.
[f]Improvement vs deterioration: $p < .01$ (Fisher's exact test).

Independent of the diagnoses, a few patients developed a transient state of overexcitement with LSD treatment. There was one patient in each of the depressive neurosis and anancastic neurosis groups and two patients in the anxiety neurosis and character neurosis groups (Table 1).

An unchanged or doubtful effect was rated when it definitely was described or reported that the mental state after LSD treatment was unchanged. Deterioration of the mental state was rated when this outcome was obvious per the clinical description or report (Table 1).

Subgroup analyses

A subgroup of the patients had the diagnoses of depressive neurosis, character neurosis, anxiety neurosis and unspecified neurosis (82/134 (61%)) (Table 2). The outcome of the LSD treatment in this subgroup of patients was compared with the number of LSD sessions and LSD dose. A significantly higher LSD dose-index was found in the group of patients who acutely deteriorated compared to the improved patients ($p < .01$).

The number of LSD sessions in 123/151 (81%) patients was six or more sessions, including five patients who completed more than 50 sessions. The initial dose was often between 25 and 50 μg; however, the dose was rapidly increased to a maximum of 200–250 μg, and the dose was increased to more than 400 μg in 14 patients. In the aforementioned subgroup of neurotic disorders, nine patients received a dose above 400 μg, including three each in the improved, unchanged or deteriorated patient groups (Table 2).

Considering the observation that LSD might benefit otherwise difficult to treat patients with obsessive-compulsive neurosis (13,22), the 19 patients in the LSD case material with anancastic neurosis were more closely examined (Table 3). Five of the eight patients who later underwent psychosurgery were from this group of patients, and another two patients were recommended to undergo psychosurgery; however, they declined. The remaining three patients in the LSD case material who underwent psychosurgery were classified with depression (two patients) and anxiety neurosis (one patient).

LSD treatment continued for months or even years in many patients, thus in 35/144 (24%) patients, more than 20 sessions were completed (Table 4). The number of sessions was not recorded in seven patients. In nine patients who completed more than 20 sessions, the mental state deteriorated with the first treatment or later (Table 4). One female patient who completed 27 sessions with a maximum dose of 550 μg did not understand why, after no improvement, LSD treatment and group therapy was discontinued by the therapist. She believed that LSD treatment should continue until she recovered, although LSD treatment was very 'scary' and she often felt depressed, agitated and alarmed between sessions. Another patient in the same group that lacked improvement after 56 LSD sessions with a maximum dose of 450 μg had a psychotic breakthrough and was compulsorily detained to a psychiatric ward. Many years later, the LSD tribunal awarded her maximal compensation; she was one of the 12 patients awarded free treatment for the damages.

Psilocybin treatment

The LSD tribunal also handled applications for compensation due to psilocybin treatment according to the LSD Damages Law because the tribunal did not differentiate between the two psychedelics in terms of their potential risk of causing harm (7,8). A closer reading of the LSD case material has shown that 12 patients were treated with psilocybin, either alone or in combination with LSD. Referring to the renewed

Table 3. The acute effect of LSD treatment in 19 patients with anancastic neurosis correlated with the treatment data and outcome.

Improved $N=5$	Age (years)	Sex	Number of treatments	Maximal dose (μg)	Flashbacks	Psychosurgical intervention
	27	Male	12	500	Yes	Yes
	36	Female	15	–[a]	Yes	Yes
	23	Female	15	550	Yes	No
	24	Female	13	150	Yes	Suggested
	43	Female	–[a]	psilocybin	–[a]	Suggested
Unchanged $N=4$						
	37	Female	15	–[a]	Yes	Suggested
	51	Male	20	–[a]	Yes	No
	20	Female	10	140	Yes	No
	48	Male	12	430	–[a]	No
Deteriorated $N=7$						
	30	Male	10	–[a]	Yes	No
	20	Male	2	400	Yes	No
	30	Female	12	–[a]	Yes	Yes
	23	Male	6	180	Yes	No
	36	Female	24	–[a]	–[a]	Yes
	30	Female	7	125	–[a]	Yes
	36	Female	11	175	Yes	No
Unknown $N=3$						
	24	Female	17	–[a]	Yes	No
	25	Female	26	–[a]	–[a]	No
	30	Female	8	–[a]	Yes	No

[a]No data.

Table 4. The ICD psychiatric diagnoses per the 6th and 8th editions of the International Classification of Diseases in patients who improved or deteriorated after more than 20 LSD sessions.

	Improved $N=14$	Comments, sequelae	Deteriorated $N=9$	Comments, sequelae
Depression	1		1	Cingulectomy
Depressive neurosis	1	Hypomanic		
Character neurosis	8	Reduced anxiety and depression in most of the patients	5	More anxiety, one patient with a psychotic breakthrough
Anancastic neurosis			1	Lobotomy
Anxiety neurosis			1	Constant depression
Unspecified neurosis	3	Scary LSD experiences		
Personality disorder			1	More depressive
Sexual dysfunction	1	Improved sexual dysfunction		

Table 5. The acute effect of psilocybin treatment and long-term inflicted harm at follow-up (1986–1988) in 12 patients diagnosed in the 1960s per the 6th and 8th editions of the International Classification of Diseases and in 1986–1988 according to the 8th edition.

ICD-6/ICD-8 diagnosis	Number of treatments: *N*	Max dose	Acute effect	Long-term effect 1986–1988
Depressive neurosis	LSD: 30 Psilocybin: few	LSD –[a] Psilocybin –[a]	Improved (1963–1964)	Flashbacks
Anancastic neurosis	Psilocybin: 15	Psilocybin 32 mg	Improved (1965)	Psychotic development
Anxiety neurosis	LSD 26 Psilocybin –[b]	LSD 250 μg Psilocybin –[a]	Unchanged (1965–1967)	Flashbacks
Depression	LSD 15 Psilocybin 33	LSD 22 μg Psilocybin 18 mg	Unchanged (1963–1965)	Flashbacks
Depression	Psilocybin 8	Psilocybin –[a]	Unchanged (1961)	Psychotic development
Anxiety neurosis	Psilocybin 2	Psilocybin –[a]	Deterioration (1967)	Depression flashbacks
Anxiety neurosis	LSD 16 Psilocybin –[b]	LSD –[a] Psilocybin –[a]	Deterioration (1966–1967)	Possibly flashbacks
Anxiety neurosis	LSD 15 Psilocybin 7	LSD –[a] Psilocybin –[a]	Deterioration (1965–1966)	Depression flashbacks
Depression	Psilocybin 24	Psilocybin 24 mg	Deterioration (1967–1968)	Psychotic development
Anxiety neurosis	Psilocybin –[b]	Psilocybin 8 mg	Deterioration (1967–1968)	Depression
Depression	Psilocybin 8	Psilocybin 8 mg	Unknown (1965)	Unknown
Character neurosis	LSD 6 Psilocybin 11	LSD 150 μg Psilocybin 10 mg	Unknown (1966–1968)	Depression

[a]No information on the dose.
[b]No information on the number of treatments.

interest in the clinical use of psilocybin (2), the consequences of psilocybin treatment at follow-up were also included (Table 5).

Discussion

It is important to make it clear that the LSD case material includes more detailed clinical data at follow-up (1986–1988) than at the time of LSD treatment in the 1960s. The medical records from the 1960s were often not preserved, or they were meagre and incomplete. Although the LSD tribunal also asked for the diagnosis and mental state immediately after LSD treatment, the answers to these questions were far from being exhaustive. It can reasonably be stated, as it appears in Table 1, that one third of the patients experienced a transient improvement in their mental state independent of the diagnosis, while the mental state of another third of the patients deteriorated with treatment. This contrasts with the contemporary finding of the follow-up study from 1964 according to which no deterioration in the mental state was seen in any patient (12). At the same time, however, this study recorded two suicides, four tentative suicides and one homicide as side effects (12). One explanation for the possible underreporting of the side effects can be that the doctors focused more on the content of the psychedelic experiences than on the underlying mental disorder and that many patients, although scared by the psychedelic experiences, willingly accepted or begged for continuation of the treatment.

Although 109/151 (72%) patients who applied for compensation were treated at Frederiksberg Hospital (7), I made no attempt to differentiate between the outcome of treatment at Frederiksberg with similar outcomes at other Danish hospitals. Acute deterioration was seen in applicants from all hospitals, even if only a few patients were compensated (7). Furthermore, we have no information about the number of patients treated at other hospitals; however, a handwritten addition (without names or registration numbers; instead, a stroke was recorded for each patient) was preserved from Frederiksberg according to which either 318 or 331 patients had been treated between 1960 and 1972. In the conclusion of the Danish National Health Service in the 'Account of the course of the LSD-case' in 1985, it was concluded that LSD treatment at Frederiksberg Hospital was performed as it had been performed abroad in terms of the diagnoses treated, dose of LSD and extent of psychotherapy (23). The patients at Frederiksberg Hospital were left alone in a closed room during the LSD sessions, while a nurse sat outside the door at all times so that the patient could call her, if necessary.

In the early days of LSD treatment in Denmark, very little was written about diagnostic selection criteria. Additionally, apart from a single case study from Rigshospitalet (22), very little was written about the treatment procedure. It is clear that early international precautions were not known or were disregarded. In 1960, Cohen wrote that patients ought to be carefully selected and that pre-psychotic individuals might react in an abnormal way (24). A number of the patients from Frederiksberg Hospital and other clinics were psychotic or pre-psychotic patients.

However, it is interesting that of the approximately twenty patients who were treated with LSD from two psychotherapeutic clinics in Copenhagen (Montebello Hospital, Gentofte and the Psychotherapy Clinic of Rigshospitalet), none applied for compensation (8). Of the nine patients from Rigshospitalet, five patients were reported to be cured or much improved, and four patients were unchanged (25). Only in one of these patients did detailed treatment data exist. A 30-year-old male with compulsive neurosis underwent 57 sessions during 15 months; at the first three sessions, 60 μg of LSD was given, and 100 μg of LSD was given at the remaining sessions (22). The diagnoses of the other eight patients were not reported; however, the independent experience of LSD-provoked anxiety was considered to be of the greatest therapeutic value (25).

The Danish psychiatrist Thorkil Vanggaard suggested that the indications for LSD treatment 'depend upon fairly high ego strength in the patients, like that found in true neurotics with comparatively well-functioning habitual personalities'. Additionally, that treatment is contraindicated for patients 'in whom the habitual personality and the psychopathological state reveal signs of ego weakness indicating, for instance, the possibilities of psychopathic, schizophreniform (borderline), schizophrenic or manic-depressive development' (26). This conclusion was obtained in a follow-up study of 22 randomly selected patients from Powick Hospital from 1961 to 1964. Of these patients, five were classified as completely recovered at follow-up. However, 13 patients were unchanged or deteriorated (25). The Norwegian psychiatrist Ole Herman Robak also did not find LSD therapy 'encouraging' for borderline cases (27).

According to the material in the Danish State Archives, the patients were neither carefully selected nor did the therapists adhere to the aforementioned contraindications. This may explain the high percentage of acute deterioration for patients suffering from depression and manic-depressive psychosis seen in Table 1. Even if the indications for LSD treatment became more restricted over time and LSD foremost was applied to otherwise difficult to treat neurotic patients, including patients with anancastic neurosis, the great expectations for the therapeutic potential of LSD remained unabated at the leading treatment centres in Denmark and Norway (28,29).

Even if the Swedish psychiatrist Lennart Kaij mainly discussed the mechanisms of action, he stated that the therapeutic value of LSD was indisputable; thus, he saw major improvement or recovery in four out of five treatment-resistant patients with anancastic neurosis. The fifth patient underwent psychosurgery (13,30). This may be a better outcome than in the Danish subsample of 19 patients with anancastic neurosis (Table 4); however, per selection criteria, Kaij only stated that the selection of patients should be performed with great care (30). Anancastic neurosis is also currently considered to be rather treatment resistant; however, deep brain stimulation for OCD recently received United States Food and Drug Administration approval (31).

The Norwegian follow-up studies from Modum Bads Nervesanatorium also included a wide spectrum of diagnostic categories, including therapy-resistant patients (16,32). The contemporary evaluation ended with: 'We have undoubtedly opened up new possibilities for these patients before whom we formerly stood helpless. Furthermore, the treatment has given both patient and doctor wider insight on the connection between symptoms and their causal mechanisms' (16). The follow-up study of the Modum Bad sample 1961–1967 found 24/239 (10%) patients worsened independent of the diagnosis (17). Careful selection criteria, closer follow-up and assessment before LSD treatment and no outpatient treatment could explain the lower number of deteriorated patients in the Norwegian study than in the present Danish sample (6,16,17,32). Additionally, the LSD doses were usually 25–100 μg, and they were seldom more than 300 μg, which is much lower than in the Danish sample (7). However, at Lier Mental Hospital in Norway, up to 500 μg was used to obtain a psychedelic ('mind-opening') effect as a time-saving form of psychotherapy (33).

For many years, experts, psychiatric societies and health authorities have warned against the illicit use of psychedelics. The most common serious side effects in LSD-treated patients include psychotic development, suicidal ideation and depression, flashbacks and anxiety (5,6,34,35).

However, in 2013, Krebs and Johansen concluded that the use of psychedelics was not an independent risk factor for mental health problems (36). In a large population study of 130,152 US respondents, 21,967 reported lifetime psychedelic use. The data processing did not find any correlation between the use of psychedelics (LSD, psilocybin, mescaline and peyote) and panic disorder, major depression, mania, social phobia, general anxiety disorder, agoraphobia, PTSD, and non-affective psychosis (36). For flashbacks, no correlation was found between the lifetime use of psychedelics and past year use of LSD. The authors suggested that one explanation might be the low validity of the diagnosis of HPPD, meaning that 'flashbacks' may be mistaken for panic attacks, hallucinations or recurrent psychotic episodes (36). In a further analysis of the data, the authors were unable to find any association between psychedelic use and mental health or suicidal behaviour (37). However, the methodology of both studies has been criticized, and the critics questioned 'the public health relevance of the findings' (38). In another recent, large population study on 190,000 US adults, Hendriks et al. found support for the assumption that psychedelic use is associated with reduced psychological distress and suicidality (4).

A major clinical concern is the selection of patients for LSD treatment. No guidelines were available in the 1960s, and screening before treatment was often poor, especially in Denmark. Guidelines for safety, which were prepared by Johnson et al. in 2008, are necessary and welcome (3). The guidelines include the selection and preparation of volunteers as well as the standards of the study personnel and physical environment (3). Individuals with a history of meeting DSM-IV criteria for schizophrenia or other psychotic disorders or bipolar I or II disorder were excluded, as were those with a first or second-degree relative with these disorders. It was also found appropriate to exclude those with other psychiatric disorders and to select a psychiatrically healthy population. For example, individuals whose symptoms of depression or anxiety are sufficiently severe to warrant immediate treatment with medication should be excluded (3). The findings of the present study are not necessarily contradicted by the aforementioned studies by Krebs and Johansen (36,37) and Hendriks et al. (4). The LSD case material represents a highly-selected sample of severely mentally ill patients who had ever used LSD before LSD treatment was established. Only one person with illicit use of LSD applied for compensation with the LSD Damages Law. However, the application was turned down because he had never been treated with LSD. In the Norwegian follow-up study, the patients were asked whether LSD treatment had tempted them to use LSD on their own. Only eight patients (3%) answered yes, and 169 patients (71%) answered no. The study does not tell if any of the eight patients used LSD illicitly (19).

The LSD case material does not throw light on the motives for applying for compensation. Only in one case was the author aware of an economic motive for the application:

> A 75-year-old man applied for compensation, which was highly prompted by his family. Twenty-five years prior, he received 12 LSD treatments as an outpatient, with a maximal dose of 430 micrograms. The indication was anancastic neurosis, which completely disabled him at the time. He was content with the treatment; however, his mental state was unchanged. Also, he did not complain of short- or long-term side effects, but he willingly accepted the application forms and underwent a psychiatric examination. He was awarded 75,000 DKK (30% of the maximal amount), as he was considered to be very ill before the LSD treatment and was rather unaffected by the treatment.

One might wonder why the remaining 200–250 patients who received LSD treatment did not apply for compensation. Unfortunately, the question cannot be answered. Neither the names nor the case records have been preserved in any archive. Certainly, the economic incentive is a major confounder to the conclusions of the study.

The study also leaves many other questions unanswered, including whether the number of treatments or dose is important. Acute deterioration was also seen with both few and many treatments and with low or high doses; however, as in Table 2, a higher LSD dose-index seems to increase the risk of deterioration, which has not been documented in other studies.

Finally, in evaluating the discrepancies between the US population studies (4,37,38) and present studies, it is obvious that, as Cohen already noted in 1960, LSD may be better tolerated by individuals without severe pre-existing psychopathology (24).

Whether this was the case in recent studies on the use of psychedelics in patients with life-threatening cancer has not been reported. However, in double-blind, randomized, placebo-controlled studies, a single dose treatment of LSD or psilocybin in combination with psychotherapy was found to produce sustained decreases in depression and anxiety scores (39–41).

Conclusions

In conclusion, the use of psychedelics, such as LSD and psilocybin, in severely ill mental health patients may be associated with a high risk of serious short- and long-term side effects. Careful selection of the patients, including excluding those with severe psychopathology, keeping the dose low and not providing outpatient treatment may diminish the risk. However, there is no guarantee of an unproblematic course, as even individuals with an apparently low grade of psychopathology deteriorated with LSD treatment. I fully agree that further trials with psychedelics in mental health patients should respect rigorous study designs (2,4) as in the above-mentioned studies in which a positive outcome was found in selected patient populations. At this point, the clinical use of psychedelics in general psychiatry has not been clarified.

Disclosure statement

No potential conflict of interest was reported by the authors.

References

1. Tupper KW, Wood E, Yensen R, Johnson MW. Psychedelic medicine: a re-emerging therapeutic paradigm. CMAJ Open 2015;187:1054–9.
2. Carhart-Harris RL, Bolstridge M, Rucker J, Day CMJ, Erritzoe D, Kaelen M, et al. Psilocybin with psychological support for treatment-resistant depression: an open-label feasibility study. Lancet Psychiatry 2016;3:619–27.
3. Johnson MW, Richards WA, Griffiths RR. Human hallucinogen research: guidelines for safety. J Psychopharmacol 2008;22:603–20.
4. Hendriks PS, Thorne CB, Clark B, Coombs DW, Johnson MW. Classic psychedelic use is associated with reduced psychological distress and suicidality in the United States adult population. J Psychopharmacol 2015;29:280–8.
5. Grinker RR. Lysergic acid diethylamide. Arch Gen Psychiatry 1963;8:425.
6. Rinkel M. Psychedelic drugs. Am J Psychiatry 1966;122:1415–6.
7. Larsen JK. Neurotoxicity and LSD treatment: a follow-up study of 151 patients in Denmark. Hist Psychiatry 2016;27:172–89.
8. Larsen JK. LSD-behandling i dansk psykiatri. Bibl Læger 2013; 205:224–65.
9. Hofmann A. LSD, my problem child. New York: McGraw-Hill Book Company; 1980.
10. Busch A, Johnson W. LSD 25 as an aid in psychotherapy. Dis Nerv System 1950;11:241–3.
11. Sandison RA, Spencer AM, Whitelaw JD. The therapeutic value of lysergic acid diethylamide in mental illness. J Nerv Ment Dis 1954;100:491–507.
12. Leuner H, Holfeld H. Ergebnisse und Probleme der Psychotherapie mit Hilfe von LSD-25 und verwandten Substanzen. Psychiat Neurol 1962;143:379–9.
13. Kaij L. LSD-behandling av neuroser. Sven Lakartidn 1963;60: 926–32.
14. Geert-Jørgensen E, Hertz M, Knudsen K, Kristensen KK. LSD-treatment. Experience gained within a three,-year period. Acta Psychiatr Scand 1964;40suppl180:373–82.
15. Knudsen KP. Et års erfaringer med indlagte og ambulante patienter under LSD-behandling. Nord Psyk Tidsskr 1962; 16:108–16.
16. Johnsen G. Three years' experience with the use of LSD as an aid in psychotherapy. Acta Psychiatr Scand 1964;40suppl180:383–8.
17. Madsen JD, Øyslebø T, Hoffart A. A follow-up study of psycholytic therapy with the aid of LSD. Nord J Psychiatry 1996;50:487–94.
18. LSD Damages Law. Law on compensation for damages by LSD-treatment. Christiansborg Slot: Law no. 219; April 23th, 1986.
19. Cirkulære om erstatning for skader ved LSD-behandling. Danish National Health Authority (Sundhedsstyrelsen): May 28, 1986.
20. World Health Organisation (WHO). Manual of the International Statistical Classification of Diseases. Injuries and Causes of Death, 6th edn (ICD-6). Geneva: WHO; 1949.
21. World Health Organisation (WHO). Manual of the international Classification of Diseases (ICD-8). Geneva: WHO; 1965.
22. Brandrup E, Vanggaard T. LSD-treatment in a severe case of compulsive neurosis. Acta Psychiatr Scand 1977;55:27–41.
23. Sundhedsstyrelsen: Redegørelse for LSD-sagens Forløb. Rigsarkivet. [NHS: Account of the course of the LSD case]. Danish State Archives, IM. I. s. kt., j.nr.5740/0-1985.
24. Cohen S. Lysergic acid diethylamide: side effects and complications. J Nerv Ment Dis 1960;130:30–40.
25. Vanggaard T. Redegørelse vedr. T. Vanggaards fire besøg på Powick Hospital I årene 1961–1964. Bilag 2 i: Redegørelse for LSD-sagens forløb. København; Rigsarkivet (IM.1.s.kt.,j.nr. 5740/0-17/ 1985):1985.
26. Vanggaard T. Indications and counter-indications for LSD treatment. Acta Psychiatr Scand 1964;40:427–37.
27. Robak OH. LSD-25 som psykoterapeutisk hjelpemiddel. Tidsskr Nor Legeforen 1962;82:1360–3.
28. Geert-Jørgensen E. Hallucinogenbehandling I. Hallucinogenbehandling II. Månedsskr Prakt Lægegern 1973;51:352–76.
29. Johnsen G. Indications for psycholytic treatment with different types of patients. In: Abramson HA, ed. The use of LSD in psychotherapy and alcoholism. New York: The Bobbs-Merrill Company, Inc.; 1967:333–40.
30. Kaij L. Om psykolyticas terapeutiska verkningssätt. Nord J Psychiatry 1965;19:480–9.
31. Naesström M, Blomstedt P, Bodlund O. A systematic review of psychiatric indications for deep brain stimulation, with focus on major depressive and obsessive-compulsive disorder. Nord J Psychiatry 2016;70:483–91.
32. Madsen JD, Hoffart A. Psychotherapy with the aid of LSD. Nord J Psychiatry 1996;50:477–86.
33. Alnæs R. Therapeutic application of the change in consciousness produced by psycholytica. Acta Psychiatr Scand 1964; 40(suppl. 180):397–409.
34. Strassman RJ. Adverse reactions to psychedelic drugs. A review of the literature. J Nerv Ment Dis 1984;172:577–95.
35. Abraham HD, Aldridge AM. Adverse consequences of lysergic acid diethylamide. Addiction 1993;88:1327–34.
36. Krebs TS, Johansen P-Ø. Psychedelics and mental health: A population study. PLoS One 2013;8:e63972.
37. Johansen P-Ø, Krebs TS. Psychedelics not linked to mental health problems or suicidal behaviour: A population study. J Psychopharmacol 2015;29:270–9.
38. Nesvåg R, Bramness JG, Ystrom E. The link between use of psychedelic drugs and mental health problems. J Psychopharmacol 2015;29:1035–40.
39. Gasser P, Holstein D, Michel Y, Doblin R, Yazar-Klosinski B, Passie T, et al. Safety and efficacy of lysergic acid diethylamide-assisted psychotherapy for anxiety associated with life-threatening diseases. J Nerv Ment Dis 2014;202:513–20.
40. Ross S, Bossis A, Guss J, Agin-Liebes G, Malone T, Cohen B, et al. Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: a randomized controlled trial. J Psychopharmacol 2016;30:1165–80.
41. Griffiths RR, Johnson MW, Carducci MA, Umbricht A, Richards WA, Richards BD, et al. Psilocybin produces substantial decreases in depression and anxiety in patients with life-threatening cancer: a randomized double-blind trial. J Psychopharmacol 2016;30: 1181–97.