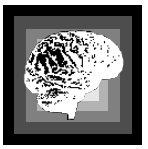

Letters to the Editor

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Dear Editor

Concerns regarding conclusions made about LSD-treatments
(received 25 October 2016)

In view of the renewed interest in psychedelics in neuroscience and psychiatry, J.K. Larsen's historical paper 'Neurotoxicity and LSD treatment: a follow-up study of 151 patients in Denmark' (*History of Psychiatry* 27(2): 172–189) about LSD therapy in the 1950–70s is very timely. However, we believe that the paper suffers from an inadequate discussion of the dataset, and that conclusions about 'a substantial risk of long-term side-effects' and LSD's 'obvious neurotoxic qualities' are unjustified. Our main concerns are listed here:

1. Context

The medical reports reviewed by Larsen were written *15–30 years after* the treatments had taken place, in order to serve as evidence for the Danish Government's 'LSD Tribunal'. This tribunal was contrived under a special law in April 1986 to offer compensations to patients who had been treated with LSD. The law employed a so-called 'reverse burden of evidence', which meant that LSD was identified as the cause of harm to the applicant – 'unless it was most likely that the harm was due to another cause'. This retrospective evaluation of (alleged) harm, in the context of a compensatory incentive, clearly represents a major confounder and a weak basis on which to draw medical conclusions. It is also telling that the conclusions of the original publications on LSD therapy in Denmark reached predominantly positive conclusions about its potential (Geert-Joergensen, Hertz, Knudsen and Kristensen, 1964).

2. Set and setting

When reading Larsen's paper, as well as the Danish-language original material from the book *De Sprængte Sind* (Larsen, 1985), quoting the original medical files, it is evident that the treatment regime used, in particular at Frederiksberg Hospital, conflicts with recommendations for good practice in clinical research with psychedelics (Grof, 1975; Johnson, Richards and Griffiths, 2008). None of the following factors, all known to ensure the safe use of psychedelics in therapy, were sufficiently addressed:

(a) Careful pre-treatment screening: A wide range of diagnoses was allowed at Frederiksberg Hospital, including psychotic illness and 'homosexuality'.
(b) Consent and preparation: Patients were persuaded to take high doses of LSD and there is no evidence that they were carefully briefed about its effects, including how psychologically challenging the experiences can be, and how best to navigate such experiences.

(c) Guiding/support during sessions: Patients at the Frederiksberg Hospital were often left alone during their LSD experiences, and integration work was not done, i.e. the therapists did not discuss with the patients what had occurred/arisen during their drug sessions. Importantly, none of the patients treated at Rigshospitalet, a treatment site where psychotherapy was an integrated part of the treatment regime, sought any compensation.

3. The drug

Some patients received up to 50 LSD sessions, were given doses up to 800 micrograms, and were given the drug in combination with other psychedelics. This approach is inconsistent with that of modern studies, where single session designs are common and doses of LSD typically do not exceed 200 micrograms.

4. Neurotoxicity

This term is used without definition or basis in the Larsen paper. The original material does not present any data on neurotoxicity and, to our knowledge, there is no evidence of psychedelic-induced neurotoxicity to humans, e.g. in terms of the integrity of serotonin neurotransmission (Erritzoe et al., 2011).

In our view, the conclusions of Dr Larsen's paper are unjustified. The history of litigious campaigning and poor practices, relative to modern standards, raises serious questions about its representativeness. These factors may explain why the conclusions of Dr Larsen's paper so starkly contrast with those of modern meta-analyses and clinical trials. Psychedelic drugs have a special tendency to polarize opinion. Just as we must be mindful of uncritical positive regard, so we should be suspicious of alarmist and/or moralist biases.

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Response by the author (received 29 November 2016)

I appreciate the interest in my recent paper (Larsen, 2016) and the critical comments on the discussion of the dataset and the conclusions.

Re (1) Context

The source material did not entirely consist of the medical reports written 15–30 years after the treatments had taken place. In almost all of the cases, medical case records and other case material have been preserved, as mentioned in my paper. Thus my retrospective evaluation has been based on a close reading of contemporary observations as well as later comments and statements. I fully agree, however, that the so-called 'reverse burden of evidence' in the context of a compensatory incentive represents a major confounder. On the other hand, as discussed in my paper, it is surprising that less than 40% of the total number of 400 patients treated with LSD applied for compensation.

Finally, a comparison of the conclusions of my paper with the rather positive conclusions of the 1964 Danish publication is hardly valid. That study dealt mainly with acute data and short-term follow-up data (Geert-Jørgensen et al., 1964 – see reference list above).

Re (2) Set and setting

First, I have to clarify that the book in Danish (The Broken Minds) was written by the Danish journalist Alex Frank Larsen (1985) and it is not a scientific analysis. It is premature to say that the treatment regime used, especially at Frederiksberg Hospital, conflicted with good clinical research with psychedelics. As published elsewhere, LSD treatment at Frederiksberg Hospital and other Danish psychiatric clinics was carried out in the same way as at leading international centres (Larsen, 2013).

However, at most Danish centres careful pre-treatment screening was not carried out, and patients with various diagnoses including psychotic illness and 'homosexuality' were included. On the other hand, as discussed in my paper, patients who had been carefully screened and diagnosed with obsessional neurosis also deteriorated with LSD treatment and suffered from long-term side effects. Careful pre-treatment screening should be a prerequisite for introducing LSD into clinical use today.

As to consent, my paper draws attention to three patients needing strong persuasion, while 83 patients (55%) consented according to the information given, whereas no information concerning consent is available for 65 patients (43%) (Larsen, 2016). Surely the standards of consenting to treatment, years before the Helsinki-II Declaration became established, did not come up to the standards of today.

Concerning psychotherapy with LSD treatment, quite a few misunderstandings exist. The Danish psychiatrist Thorkil Vanggaard regarded psychoanalytic psychotherapy and LSD treatment as alternative strategies. In his review of the LSD treatment at Powick Hospital, he was able to throw light on the setting of the LSD treatment. At this hospital, systematic psychotherapy was not carried out, although it was claimed in their publications (Sandison, Spencer and Whitelaw, 1954), and again the pre-treatment screening was unsatisfactory, allowing psychotic patients to be included (Vanggaard, 1964). Probably the reason why none of the patients at Rigshospitalet, Copenhagen, applied for compensation was due to a careful and skilled pre-treatment screening, rather than the psychotherapy.

The patients at Frederiksberg Hospital were left in peace in a closed room during the LSD sessions, with a nurse sitting outside the room all the time so that the patient could call him/her if necessary.

Re (3) Drug

Vanggaaard conducted a successful LSD treatment in a patient with obsessive-compulsive disorder, in which 57 sessions were carried through and LSD was given in doses between 60 microgram and 100 microgram (Brandrup and Vanggaard, 1977). Certainly, the dosages of LSD treatment in the 1950s and 1960s were far too high, and I fully agree that the approach of modern studies with a single-session design should be recommended. However, once again I stress the importance of pre-treatment screening, as some patients undergoing only a few LSD sessions with rather low dosages developed long-lasting side effects (one of the patients was being treated with LSD for stuttering) (Larsen, 2016).

Re (4) Neurotoxicity

I might have used the phrase: 'substantial risk of long-term side effects' and not 'neurotoxic potential', if my conclusions had relied only on clinical data. Also I did not define what I understand by neurotoxicity, which is a rather crucial point. On the other hand, I am convinced from the analysis of the LSD case material that many of the patients suffered from irreversible long-term mental side effects due to the LSD treatment. I cannot suggest any other hypothesis than the following: development of mental side-effects and psychopathological symptoms which are irreversible result from a change in brain function.

I am not trying to polarize opinions on LSD treatment, but merely want to bring the failures of the past into focus. Concerning modern clinical studies: they have yet to be carried out as controlled studies, and to a greater extent than we have yet seen, before we can reach a final conclusion on the use of LSD in clinical practice.

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