



# The link between use of psychedelic drugs and mental health problems

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The March issue of *Journal of Psychopharmacology* included a study of the relationship between use of psychedelics (defined as lysergic acid diethylamide (LSD), psilocybin, and mescaline) and mental health problems (Johansen and Krebs, 2015). The data on 135,095 adult US citizens participating in the National Survey on Drug Use and Health (NSDUH) between 2008 and 2011 were obtained from a freely available database (<http://oas.samhsa.gov/nsduh.htm>, accessed 8 April 2015). The paper is a follow-up of a similar paper by the same authors on NSDUH data between 2001 and 2004 (Krebs and Johansen, 2013). For their analyses in the most recent paper, the authors distinguished between 19,299 individuals (13.4% of the study population) who reported lifetime use of psychedelic drugs, and the remaining group of individuals who did not report use of psychedelic drugs. Individuals were also asked about a range of mental health problems, and if they had been in contact with mental health service during the previous year.

The authors ran a series of logistic regression models to estimate the risk of having each of the mental health outcomes given lifetime use of psychedelic drugs. From these analyses, the authors concluded that use of psychedelics was not linked to mental health problems or suicidal behavior. In a recent issue of *Nature News*, the results from the Johansen and Krebs (2015) study were presented under the heading “No link between psychedelics and psychosis” (Cormier, 2015). In the following we will argue that the authors’ conclusions in their latest paper are not substantiated by their results and will propose supplemental analyses to validate or potentially revise their conclusions.

According to Table 2 in the paper, 97.8% of the individuals reporting use of psychedelic drugs did also report lifetime use of cannabis, 71.3% reported use of cocaine, and 49.7% reported use of opiates. In the comparison group of individuals who did not report lifetime use of psychedelic drugs, the lifetime prevalence of use of other drugs was 36.0% for cannabis, 7.5% for cocaine, and 9.5% for opiates. From these figures, it is clear that the vast majority of users of psychedelic drugs have also used one or more substances other than psychedelic drugs. According to Table 2 in the paper, only 400 of the users of psychedelic drugs had never used cannabis, but a number of these had presumably used other drugs than cannabis. Notwithstanding this high degree of concomitant use of different types of drugs, the authors chose to include lifetime use of all other drugs than LSD, psilocybin, and mescaline as covariates in the logistic regression models of the relationship between psychedelic drugs and mental health outcomes.

From the numbers in Table 3 in the paper it is clear that the group of individuals who reported lifetime use of psychedelic drugs had two to three times higher prevalence of all mental health outcomes when not adjusting for lifetime use of other drugs. However, in the logistic regression analyses, correcting for all other types of drugs, the risk for having a mental health problem was not higher among psychedelic drugs users and the rest of the study population. In our view this is a typical example of over adjustment, a common, but relatively basic fallacy in epidemiological research (Rothman and Greenland, 1998). Since the authors did not report unadjusted risk estimates in their results section, not even as supplemental material, we have calculated odds ratios based on the prevalence figures presented in the paper. As shown in our new Table 1, use of psychedelic drugs was indeed associated with increased risk of mental health problems, e.g. a three times higher odds of being admitted to mental health hospital the previous year.

Given the high prevalence of concomitant drug use among the users of psychedelic drugs, it is difficult to use the NSDUH data to estimate the specific risk of psychedelic drugs for mental health problems in general. This argument is not related to the variance inflation factors, as mentioned by the authors in the statistical methods section of their paper, but to the effect sizes of their estimates. The results of the Johansen and Krebs (2015) paper cannot be generalized to the entire group of psychedelic drug users, and one might question the public health relevance of their findings. This comes in addition to other problematic factors in the paper, like selection bias. To validate their conclusion, we encourage the authors to report the exact number of individuals who had only used psychedelic drugs, and to present results of logistic regression models without adjustment or with different models for adjustment for lifetime use of other drugs.

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**Table 1.** Association of psychedelic use with mental health.

	Ever used psychedelics <i>N</i> = 19,299	Never used psychedelics <i>N</i> = 115,796	OR (95% CI)	<i>p</i>
<b>Serious psychological distress in worst month of past year</b>				
K6 scale	4165	15,525	1.8 (1.7–1.8)	<0.001
<b>Mental health treatment in past year</b>				
Inpatient	694	1349	3.2 (2.9–3.5)	<0.001
Outpatient	3108	8343	2.5 (2.4–2.6)	<0.001
Medication	3472	11,282	2.0 (1.9–2.1)	<0.001
Needed but did not receive	2534	6990	2.4 (2.2–2.5)	<0.001
<b>Suicidal thought and behavior in past year</b>				
Thought about killing self	1748	5533	2.0 (1.9–2.1)	<0.001
Planned to kill self	527	1654	1.9 (1.8–2.1)	<0.001
Attempted to kill self	266	904	1.8 (1.5–2.0)	<0.001
<b>Depression and anxiety in past year</b>				
Symptoms of major depressive episode	2446	8178	1.9 (1.8–2.0)	<0.001
Diagnosis of depression	2,352	7,648	2.0 (1.9–2.1)	<0.001
Diagnosis of an anxiety disorder	2,095	5,747	2.3 (2.2–2.5)	<0.001

Note. OR: unadjusted odds ratio; CI: confidence interval.

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# Reply letter: Mental health of people who have used classical psychedelics and no other illicit drugs

Teri Suzanne Krebs and Pål-Ørjan Johansen

We have reported that in two large population surveys of randomly selected US adults psychedelic use was not associated increased risk of range of past year mental health outcomes, after adjusting for sociodemographic, psychological, and illicit drug use confounders (Johansen and Krebs, 2015; Krebs and Johansen, 2013). Nesvåg et al. (2015) present a table with crude odds ratios unadjusted for any confounders. These crude odds ratios do not take into account that people who have used psychedelics also have higher than typical rates of childhood depression, extremely traumatic experiences, illicit drug use, and other predictors for

mental health problems (Johansen and Krebs, 2015; Krebs and Johansen, 2013). There are shared factors that predispose people to both illicit drug use and to mental health problems (e.g. Proal et al., 2014). By considering use of other illicit drugs we are able, to some extent, to adjust for these other factors. In our original analyses, we also examined a stratified sub-sample of people without any past-year illicit drug use, to exclude mental health problems caused by direct drug effects (Johansen and Krebs, 2015; Krebs and Johansen, 2013).

Nesvåg et al. (2015) suggest that we look at mental health of people who had used psychedelics but no other illicit drugs. People who have used psychedelics and no other illicit drugs are not representative of the total population of people who have used psychedelics.

However, we have now repeated our analyses in both the 2008–2011 sample and the earlier 2001–2004 sample, excluding people who had ever used other illicit drugs, following the methods described previously (Johansen and Krebs, 2015; Krebs and Johansen, 2013). Results are shown in Table 2.

## Survey years 2001–2004

In the 2001–2004 sample, there were 192 adult respondents who reported using classical psychedelics (psilocybin, LSD, mescaline, or peyote) and no other illicit drugs (cannabis (marijuana), heroin, opiate pain relievers, cocaine, tranquilizers (benzodiazepines), sedatives (barbiturates), stimulants (amphetamine, methamphetamine, methylphenidate), MDMA (ecstasy), inhaled anesthetics (nitrous oxide, ether), alkyl nitrites (poppers), other

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**Table 2.** Association between psychedelic (LSD, psilocybin, mescaline, peyote) use and mental health, excluding people with use of other illicit substances.

	Survey years 2001–2004	p	Survey years 2008–2011	p
	aOR <sup>a</sup> (95% CI)		aOR <sup>b</sup> (95% CI)	
Serious psychological distress in worst month of past year				
K-6 scale	1.4 (0.8 – 2.5)	0.25	1.6 (0.7 – 3.5)	
Mental health treatment in past year				
Inpatient	0.4 (0.1 – 1.8)	0.23	4.1 (0.9 – 18.7)	0.07
Outpatient	1.5 (0.7 – 3.2)	0.29	3.2 (1.2 – 6.7)	0.02
Medication	1.3 (0.6 – 2.7)	0.44	2.8 (1.3 – 6.2)	0.01
Needed but did not receive	1.9 (1.1 – 3.2)	0.29	0.4 (0.1 – 1.9)	0.25
Suicidal thought and behavior in past year				
Thought about killing self	<i>Not available</i>		2.8 (0.8 – 9.8)	0.10
Planned to kill self	<i>Not available</i>		3.0 (0.4 – 22.9)	0.29
Attempted to kill self	<i>Not available</i>		0.8 (0.1 – 6.1)	0.80
Diagnosis by a physician in the past year				
Diagnosis of depression	<i>Not available</i>		3.4 (1.3 – 8.8)	0.01
Diagnosis of an anxiety disorder	<i>Not available</i>		1.3 (0.3 – 4.8)	0.71
Symptoms of mental disorders in past year				
Major depressive episode	2.4 (0.8 – 7.0)	0.12	1.2 (0.3 – 4.4)	0.76
Panic disorder	1.7 (0.9 – 3.2)	0.09	<i>Not available</i>	
Social phobia	1.2 (0.3 – 4.1)	0.79	<i>Not available</i>	
Generalized anxiety disorder	3.9 (1.2 – 12.9)	0.03	<i>Not available</i>	
Agoraphobia	4.8 (0.6 – 42.1)	0.15	<i>Not available</i>	
Posttraumatic stress disorder	1.9 (0.5 – 6.6)	0.33	<i>Not available</i>	
Mania	2.0 (0.5 – 8.2)	0.34	<i>Not available</i>	
Non-affective psychosis	0.3 (0.1 – 1.7)	0.17	<i>Not available</i>	
Specific psychotic symptoms in past year				
Heard voices others could not	0.6 (0.1 – 3.4)	0.58	<i>Not available</i>	
Felt force taking over mind	0.5 (0.1 – 3.3)	0.45	<i>Not available</i>	
Felt force inserting thoughts	0.7 (0.1 – 7.8)	0.77	<i>Not available</i>	
Felt force steal thoughts	0.4 (0.0 – 4.0)	0.42	<i>Not available</i>	
Force used special signals	0.4 (0.1 – 2.5)	0.35	<i>Not available</i>	
Believed plot to harm you	1.3 (0.4 – 4.1)	0.69	<i>Not available</i>	
Saw vision others could not	1.6 (0.4 – 7.0)	0.51	<i>Not available</i>	

<sup>a</sup>Adjusted for age (11 categories, treated as a continuous variable), gender (male, female), race/ethnicity (white, Hispanic, black, Asian, Native American, Native Hawaiian or Pacific Islander, more than one), household income (less than \$20,000, \$20,000–\$49,999, \$50,000–\$74,999, \$75,000 or more), education (not high school graduate, high school graduate, some college, college graduate), married (unmarried, married), likes to test self by doing risky things (never, seldom, sometimes, always), and extremely stressful event (no, yes).

<sup>b</sup>Adjusted for depressive episode before age 18 years (no, yes) and above covariates, except for extremely stressful event.

inhalants (solvents, volatile chemicals), and PCP (phencyclidine)). In a logistic regression analysis adjusting for sociodemographic and psychological confounders, rate of symptoms of generalized anxiety disorder was increased with weak statistical significance in psychedelic users (adjusted odds ratio (aOR) = 3.9;  $p = 0.03$ ). We failed to demonstrate an association between psychedelic use and increased rate of mental health treatment or symptoms of other psychiatric disorders, including major depressive disorder, panic disorder, posttraumatic stress disorder, mania, non-affective psychosis, and individual symptoms of non-affective psychosis including visual hallucinations. Notably, symptoms of non-affective psychosis were reduced in psychedelic users, but this was not statistically significant (aOR = 0.3;  $p = 0.17$ ).

## Survey years 2008–2011

In the 2008–2011 sample, there were 156 adult respondents who reported using classical psychedelics and no other illicit drugs. In logistic regression analysis adjusting for sociodemographic and psychological confounders, we found that people who had used psychedelics had increased rate of self-reported past-year outpatient mental health treatment (aOR = 3.2;  $p = 0.02$ ), prescribed psychiatric medication (aOR = 2.8;  $p = 0.01$ ), and physician diagnosis of depression (aOR = 3.4;  $p = 0.01$ ), with weak statistical significance. Note, these are not independent outcomes, as people who seek psychiatric treatment would be expected to also have increased rates of psychiatric medication prescription and

psychiatric diagnosis. In contrast, rate of self-reported needed but not receive psychiatric treatment was decreased but this was not statistically significant (aOR = 0.4;  $p = 0.25$ ). We failed to detect statistically significant increases in rates of self-reported inpatient mental health treatment, physician diagnosis of anxiety disorder, or any symptoms of psychiatric problems: serious psychiatric distress, major depressive episode, suicidal thoughts, suicidal plans, or suicidal attempts.

## Age onset of major depressive episode

Because the adjusted odds ratio of physician diagnosis of depression (but not symptoms of major depressive episode or suicide attempt) was increased amongst people who had used psychedelics but no other illicit drugs in the 2008–2011 sample, we examined reported symptoms of depression in more detail in this group by comparing age at first major depressive episode against age of first use and last use of “hallucinogens” (a broad, vaguely defined category which includes psychedelics). This data was not available in the 2001–2004 sample. Out of 22 respondents with available data on age at first major depressive episode, only two people experienced their first major depressive episode during the years they were using hallucinogens (plus one person reported first major depressive episode 8 years after first using hallucinogens but was missing data on age at last use of hallucinogens), of the remainder, nine people reported that their first major depressive episode occurred years before first using hallucinogens, and 10 people reported that their first major depressive episode occurred 3 years or more after last use of hallucinogens. Thus, data from this sample of people who have used psychedelic hallucinogens and no other illicit drugs does not suggest a temporal connection between psychedelic use and onset of major depressive episode.

## Limitations

The confidence intervals on the adjusted odds ratios were large, so in most cases it is not possible to say with confidence if the associations are positive, negative, or neutral. It is possible that rates of both psychiatric symptoms and psychiatric treatment were increased in the psychedelic using group. It is also plausible, based on the 2008–2011 sample, that the select group of people who choose to try psychedelics but decline to try other illicit drugs might have an increased interest in psychology and mental health and be more predisposed than the general population to seek mental health treatment, even if they do not have increased rate of mental health problems. People who have used psychedelics and no other illicit drugs are unlikely to be representative of the total population of people who have used psychedelics.

The major difference between the 2001–2004 and 2008–2011 datasets is that exposure to an extremely traumatic event was available as a confounder only in the 2001–2004 dataset and childhood depression (major depressive episode before age 18) was available as a confounder only in the 2008–2010 dataset. Traumatic events and childhood depression were both correlated with psychedelic use and were both strong predictors of all indicators of mental health problems. It would be preferable to have a data set with data on both exposure to traumatic events and

childhood depression, as well as other risk factors, such as history of childhood abuse, and family history of mental illness (McCann et al., 2014; Proal et al., 2014). Note, a study of 52 people hospitalized for first psychotic episode shortly after LSD use found that they had elevated rates of parental psychiatric hospitalization, similar to people with schizophrenia (Vardy and Kay 1983).

The statistical significance of all the “statistically significant” results presented here were weak ( $p > 0.01$ ), and so should be considered with caution. When conducting multiple statistical tests, it is likely to have false-discovery findings simply by chance. None of these “findings” would be considered statistically significant if we adjusted for multiple tests (13 tests for the 2001–2004 sample, not counting the specific symptoms of non-affective psychosis, and 11 tests for the 2008–2011 sample) using either the Bonferroni method (with alpha of 0.05) or the less stringent Benjamini–Hochberg method (with a false-discovery rate of 0.05) (Benjamini and Hochberg, 1995).

A cross-sectional population study cannot demonstrate causation. We looked only at the population level; it is possible that psychedelics could hurt some individuals and help others. For example, there are some reports of first-episode psychosis after taking psychedelics (Catts and Catts, 2010), but on the other hand there are also reports of sustained recovery from chronic paranoid psychosis in hospitalized patients following a single dose of psychedelics (Denber and Merlis, 1954; Denber, 1956). See the original articles for more limitations and discussion (Johansen and Krebs, 2015; Krebs and Johansen, 2013).

## Comments

Overall, there is a lack of evidence that psychedelics increase the rate of mental health problems on a population level (Bonson, 2012; Catts and Catts, 2010). As Jorgen Bramness said in response to our population study of psychedelics and mental health: “The study shows, in agreement with previous studies, that we probably have exaggerated the danger of the use of psychedelics in general, and LSD in particular, at least if we are to judge on the basis of drug laws” (Tveito, 2013).

Data on mental health of psychedelic users is also available from communities where psychedelic use is legal and less stigmatized. A longitudinal case-control study found that people who had used ayahuasca (a South American psychedelic beverage containing dimethyltryptamine which is chemically similar to psilocybin) over 360 times each in legally-protected religious ceremonies scored significantly lower on all psychopathology measures compared to people who regularly participated in non-psychedelic religious groups, both at baseline and at one year follow-up (Bouso et al., 2012). A case-control study of Native Americans failed to find any evidence of cognitive or mental health deficits among people who regularly used peyote in legally-protected religious services compared to those who did not use peyote, and reported that total lifetime peyote use (mean 300 occasions, range 150–500) was associated with overall better mental health (Halpern et al., 2005). A four-year observational study by a psychiatrist on a Native American reservation estimated the rate of serious adverse psychiatric reactions to peyote as 1 per 70,000 occasions of peyote use in legally-protected religious ceremonies, participants included people with schizophrenia and other mental illness (Bergman, 1971). In the Netherlands,

where psychedelic psilocybin mushrooms are legally sold in shops, the rate of ambulance calls leading to hospitalization for acute psilocybin-related psychiatric problems or injury has been estimated at one hospitalization per 50,000 servings of psilocybin mushrooms sold (most cases involved alcohol and other drugs) (CAM, 2007). And out of 4 million attendees at large electronic dance music festivals in the Netherlands, there were only 35 visits to first-aid stations that involved psilocybin mushrooms (none required further medical attention) (Krul, 2011), demonstrating that legal sale of psilocybin mushrooms creates very few problems at “rave” festivals.

The most definitive way to determine adverse effects of psychedelics would be randomized controlled trials. Recent randomized controlled trials of psilocybin of approximately 1000 doses in approximately 400 volunteers (screened for pre-existing mental health problems) have not reported any adverse emotional reactions lasting beyond a few weeks or any prolonged psychotic reactions (e.g. Studerus et al., 2011). Likewise, clinical trials of LSD and mescaline from the 1950s–1970s are typically interpreted as showing low rates of prolonged problems (McWilliams and Tuttle, 1973). Studies from the 1950s–1960s of LSD and mescaline in people with schizophrenia and other serious mental illness generally reported that psychedelics can temporarily exacerbate pre-existing psychiatric symptoms during the drug effects, but with few or no prolonged adverse effects, and as noted above occasionally lasting remission from psychosis or other psychiatric problems. In the most commonly cited study of prolonged effects of LSD in people with schizophrenic, after 158 total administrations of LSD (dose up to 840 mcg) to 65 patients with chronic psychosis (hospitalized on average for 5 years) there were three instances of prolonged exaggeration of prior symptoms (no details) with onset soon after LSD (Fink et al., 1966), but there was no control group and some of these patients would have been expected to worsen regardless of LSD.

The idea that psychedelics often cause lasting mental health problems or are otherwise “extremely dangerous” appears to have been based on case reports, rumors, “worst-case scenarios,” politics, cultural biases, and outdated theories about the inherent dangers of “self-exploration,” rather than epidemiological data (Johansen and Krebs, 2015; Krebs, 2015; Rucker 2015). In many ways the mid-20th century “moral panic” against psychedelics paralleled claims from previous generations that mental illness and suicide were caused by activities involving introspection, creativity, and fantasy, such as Christian mystical contemplation (from the influential psychiatrist Philippe Pinel, 1790: “the mind remains in a kind of imbecility during which they speak only of marvels and miracles”) (Murat, 2014), reading fictional novels (from 1869: “Common novel-reading is a fearful evil... the safest rule is total abstinence”; from 1820: “his soul kindled into ardor at scenes of imagined bliss, which probably he will never realize, but which will only prepare his mind for bitter disappointment”) (Crane, 1869; Dodge, 1820), masturbation (from 1834: “self-abuse” leads to over-stimulation, brain inflammation, insanity, and “mental decay”) (Whorton, 2001), and jazz music (from 1921: “the effect of jazz on the normal brain produces an atrophied condition on the brain cells.... it is harmful and dangerous, and its influence is wholly bad”) (Knowles, 2009). Restrictions on all these activities were enacted or proposed on pseudo-medical grounds. It was possible

to point to case examples of, for instance, a young woman who read many books and then killed herself, and there is evidence that poets, jazz musicians, mathematicians, and other creative professionals do have higher rates of mental illness, but of course this does not demonstrate that these activities directly cause mental health problems (Kaufman and Paul, 2014).

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