



# Abuse and Effects of *Salvia divinorum* in a Sample of Patients Hospitalized for Substance Dependence

Antoine Karam<sup>1,2</sup> · Aida Said<sup>3</sup> · Chafika Assaad<sup>3</sup> · Souheil Hallit<sup>1,2,4,5,6,7</sup> · Georges Haddad<sup>1,2</sup> · Dory Hachem<sup>1</sup> · Francois Kazour<sup>1,7,8,9</sup>

Received: 31 August 2016 / Accepted: 19 October 2018 / Published online: 29 October 2018  
© Springer Science+Business Media, LLC, part of Springer Nature 2018

## Abstract

The study goal is to document the prevalence of salvia use among patients admitted for detoxification of other illicit drug use and to determine its effect. This cross-sectional study included 47 heavy drug users who were admitted for detoxification of other illicit drug abuse at a psychiatric hospital in Lebanon. The prevalence of salvia use was 66%. The salvia effect started and dissipated rapidly (15 min). No significant difference was found between salvia and non-salvia users in terms of affect, cognition and somaesthesia subscales of the Hallucinogen Rating Scale. Ratings of intensity and volition subscales were higher in non-salvia users than salvia users, while perception score was higher in users. Salvia use was correlated with perceptual alteration and hallucinogenic effects.

**Keywords** Salvia · Drug · Substance · Addiction · Hallucinogen

## Introduction

Despite its ancient discovery, the use of *Salvia divinorum* use in developed countries has emerged only recently and has gained increased attention (Appel and Kim-Appel 2007).

*S. divinorum* is a hallucinogen mint plant of the Lamiaceae family predominant in the Sierra Madre Mountains in Oaxaca Mexico (Appel and Kim-Appel 2007; Kelly 2011; Valdes 1994). Interest for this hallucinogen ethno botanical plant has greatly increased in recent years among young adults aged 18–21 than adults aged 22 and above (Nyi et al. 2010) and recreational users because it can elicit a modified state of awareness (González et al. 2006). The current increase in its use represents a broader trend of adolescents pursuing alternative psychoactive substances (Kelly 2011).

Usually, salvia products are commercially available as either dried leaves or materials impregnated with an extract of SA (Miller et al. 2009). The longer the leaves kept in the mouth, the more intense the effect of the drug will be (Siebert 1994). Inhaling the vaporized compound or smoking the dried leaves are the most rapid, effective and preferable ways to produce the psychoactive effect of this herb according to recreational users (González et al. 2006; Siebert 1994). Effects of smoking dried *S. divinorum* lasts for a short duration of about 15–20 min (Sumnall et al. 2011; Addy et al. 2015; Ranganathan et al. 2012), compared to 25 min for the chewed SD (Baggott et al. 2010).

A naturally-identified hallucinogen and a neoclerodane diterpene, ‘Salvinorin A’ (SA) is the most potent psychoactive component found in *S. divinorum*, a nonnitrogenous kappa opioid receptor agonist (Cunningham et al. 2011;

✉ Francois Kazour  
francoiskazour@hotmail.com

<sup>1</sup> Psychiatric Hospital of the Cross, 60096 Jal Eddib, Lebanon

<sup>2</sup> Faculty of Medicine and Medical Sciences, Holy Spirit University, Jounieh, Lebanon

<sup>3</sup> Faculty of Sciences, Lebanese University, Beirut, Lebanon

<sup>4</sup> Faculty of Pharmacy, Lebanese University, Beirut, Lebanon

<sup>5</sup> Faculty of Pharmacy, Saint Joseph University, Beirut, Lebanon

<sup>6</sup> Occupational Health Environment Research Team, U1219 BPH Bordeaux Population Health Research Center Inserm - University of Bordeaux, Bordeaux, France

<sup>7</sup> INSPECT-LB: Institut National de Sante Publique, Epidemiologie Clinique et Toxicologie, Faculty of Public Health, , Lebanese University, Beirut, Lebanon

<sup>8</sup> Faculty of Medicine, Saint Joseph University, Beirut, Lebanon

<sup>9</sup> INSERM U930, équipe 4 “Troubles affectifs”, Université François-Rabelais de Tours, Parc de Grandmont, 37200 Tours, France

Prisinzano 2005; Roth et al. 2002). This profile is different from the other classical hallucinogens (lysergic acid diethylamide LSD; dimethyltryptamine DMT; or psilocybin) that are serotonin (5HT<sub>2A</sub>) receptor agonist (Prisinzano 2005; Ansonoff et al. 2006; Chavkin et al. 2004). Currently, neither SA nor its metabolites can be detected by standard drug tests in biological fluids (Zawilska and Wojcieszak 2013).

A study conducted in the United States revealed that 10.9% of men and 3.8% of women reported lifetime use of any *S. divinorum*. Risk factors for its use included male gender, white race, a high level of family income, marijuana use, and a low level of self-control (Miller et al. 2009; Khey et al. 2008). Salvia users reported marked changes in perceptual integration and sensory processes as well as alteration in auditory and visual perception. Users also experienced both tactile and kinesthetic hallucinations, changes in emotional and thinking processes (Addy et al. 2015), and a decreased ability to interact with their surroundings and with themselves (Sumnall et al. 2011).

The systematic information on the pattern of use and the nature of the subjective effect evoked by SD are summarized by several themes: becoming object, experience of visual effects, including hallucinations, distorted images, merging of objects, and color changes, laughing uncontrollably, as well as dissociative effects including sensation of entering or perceiving other dimensions or realities and loss of body sensation or identity, loss of coordination or inability to control muscles or maintain balance, memories about past and childhood (Nyi et al. 2010; González et al. 2006; Siebert 1994; Addy 2012). The drug also increased the physical contact perception of the users and paranoid ideation (El-Khoury and Sahakian 2015).

Depression and anxiety symptoms were also associated with the use of salvia (El-Khoury and Sahakian 2015). The potential abuse for salvia according to Nyi et al. is relatively low since 50% of the participants reported they disliked the high they achieved from salvia inebriation because of the negative side effects it can elicit including fear, panic, paranoia, feeling sad, nausea, and irritability; and some simply lost interest in it (Nyi et al. 2010).

Clinicians in Lebanon may be less acquainted with the more current items that abusers are buying and utilizing. Patients may not deliberately declare the utilization of these substances, or the effects experienced, if not particularly questioned. It is more probable that salvia use is more frequent among illicit drug users who have used other hallucinogens and stimulants. Salvia is a new plant that entered to Lebanon as a new high drug. Smoking maybe the most frequent method used to ingest the drug in Lebanon (El-Khoury and Sahakian 2015).

In Lebanon, to date, there are no reliable statistics to add to the literature on the prevalence of salvia use and on the consumption of this substance among youth and adolescence

(El-Khoury and Sahakian 2015). For the latter reasons, this study was conducted to determine salvia's subjective effect and hallucinatory profile among Lebanese abusers.

## Methods

This cross sectional study was performed between January and May 2016, on patients admitted at the Psychiatric Hospital of the Cross (HPC)-Lebanon, the oldest and largest psychiatric institution in Lebanon, for illicit drug detoxification. All patients admitted to the hospital for the before mentioned reason during the study period were interviewed privately by a psychiatrist. Respondents were guaranteed that their names would not be recorded and that their responses would be kept entirely private. All study protocols and protections were clearly explained to participants that were asked to sign a consent form. The questionnaire was administered by trained personnel who received a thorough training by the research team prior to the beginning of the data collection; Patients were approached after the effect of the illegal substance wore off (7–10 days after admission), therefore, they were physically at ease, able to cooperate, aware of their environment and not agitated, as recommended by their treating physician.

Participants were excluded if: (1) questionnaire data was incomplete; (2) the participant reported having previously completed the survey; (3) patients demonstrated persistent psychosis; (4) patients not addicted to illicit drugs but to other prescription drugs (analgesics, anxiolytics and barbiturates). All other patients not fulfilling one of the exclusion criteria were enrolled in our study.

During the study period, 47 participants completed the survey and met inclusion criteria without having exclusion criteria. Four patients refused to participate in this study, two patients did not complete the questionnaires, and one patient has psychiatric co-morbidities other than personality disorders.

## Questionnaire and Variables

The questionnaire, adapted to local Arabic language (the native language in Lebanon), assessed the socio-demographic characteristics including age, gender, region, marital status, the level of education, employment status, etc. Questions about salvia addressed several aspects of its use such as age at first use, frequency (the highest frequency for salvia use in their lifetime), method of use, quantity used per time or per day and the concurrent use with other legal and/or illicit substances.

Lifetime *S. divinorum* use was determined based on the subsequent questions:

- Have you ever, even once, used *S. divinorum*?
- If yes, how many times have you ever tried it?
- How much time did salvia effects lasts?
- From where did you get/buy salvia?
- Did you enjoy the experience?

### Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV Alcohol- or Drug-Use Disorders (Abuse, Dependence)

We used the English translation edition 5 of the M.I.N.I. (Mini International Neuropsychiatric Interview) (Sheehan et al. 1998) to ensure that patients were of drug-use disorders. Respondents were asked a set of structured and substance-specific questions regarding abuse and dependence. The letter K module is assigned to non-alcohol use disorder, and was used in this study to determine the addictive state of the patients.

### Addiction Severity Index (ASI)

We used the ASI (McLellan et al. 1980) to collect information about alcohol and drug use and the frequency of use for each drug. In the drug use section, we asked the patient to state the highest frequency of alcohol use and the use of five specific drug categories during his/her lifetime, and other questions such as for needle sharing, etc.

### Positive and Negative Syndrome Scale (PANSS)

The Positive and Negative Syndrome Scale for schizophrenia PANSS is a validated medical scale and is customarily used to quantify the intensity of psychotic conditions. PANSS is used for measuring symptom severity in patients with schizophrenia and evaluating positive and negative symptoms of psychotic disorders. Of the 30 items included in the PANSS, 7 constitute a Positive Scale, 7 a Negative Scale, and the remaining 16 a General Psychopathology Scale.

We used PANSS to assess the positive, negative and the general psychopathology symptoms of drug-induced psychosis (Kay et al. 1987).

### Hallucinogen Rating Scale (HRS)

The subjective experience was assessed using the HRS questionnaire. Its rating significantly increased on all six clusters: affect, cognition, intensity, perception, somaesthesia, and volition. This self-reported questionnaire was initially outlined to measure the subjective effects experienced after the administration of *N,N*-dimethyltryptamine (DMT) (Strassman et al. 1994). The questionnaire has undergone several modifications and currently includes 71 items dispersed in six scales:

1. Somaesthesia, reflecting somatic effects or physical effects including interoceptive, visceral and tactile effects;
2. Affect, sensitive to emotional and affective responses;
3. Volition, indicating the subject's ability to intentionally interact with his/her 'self' and/or the environment;
4. Cognition, describing alterations in thought processes or content;
5. Perception, measuring visual, auditory, gustatory and olfactory experiences;
6. Intensity, which reflects the strength of the overall experience.

All items are scored based on a Lickert scale from zero to four (0\_not at all, 1\_slightly, 2\_moderately, 3\_quite a bit, 4\_extremely). The scores for the different scales are acquired by summing the scores obtained for the scale's individual items, over the number of questions included in a given scale. Patients were requested to answer this questionnaire recalling the effects they had experienced the first time they were under the influence of salvia.

### Data Analysis

Statistical Package for the Social Sciences (SPSS) version 22 was used for the data analysis. Descriptive statistics for continuous variables were shown as mean  $\pm$  standard deviation; categorical variables were expressed as number of cases (*N*) and percentage. Cross tabulations (chi square test) were used to examine the categorical variables. For categorical variables when at least, one cell in a contingency table has an expected frequency count less than five, Fisher's exact test was used. Normally distributed data were analyzed using T-test to compare the means of two samples (one categorical and one continuous variable). Levene's test for equality of variances is used to determine which *p* value of T test to use. All data were analyzed for normality using a one-sample Kolmogorov Smirnov test. Non-normally distributed data were analyzed using non-parametric Mann Whitney U tests. For all tests, a *p*-value < 0.05 was considered statistically significant.

### Results

Forty-seven patients were recruited for the study, 42 (89.4%) of whom were male and 5 (10.6%) of whom were female. The mean age of the sample was 28 (SD: 6.104; range 19–43 years). Education level was high with 20 (42.6%) participants having completed high school and 17 (36.2%) having obtained a university degree. The highest percentage was those employed full-time 28 (59.6%). 40 patients were

single (85.1%), 3 (6.4%) were married and the remaining 4 were divorced or separated.

Among participants, 91.5% used alcohol (36.2% at least once every week), 97.9% consumed cannabis (61.7% daily consumption), 76.6% used heroin, 91.5% used cocaine, 25.5% consumed amphetamines and 83% had opiates other than heroin. Heroin, opiates and cocaine users took these drugs daily at 63.8%, 59.6% and 40.4% respectively. 61.7% of patients used a psychedelic/hallucinogen like LSD, ecstasy and THC. However, 31.9% of participants reported using these drugs on occasion and rarely.

The mean age for the first use of drugs was approximately 19 years old. The prevalence of salvia use in our population was 66%. Student *t* test showed a significant association between age and salvia use ( $p=0.038$ ) where the frequency for salvia use is more popular in patients aged between 22 and 25. Twenty-seven males out of forty-two used it, while four females out of five took salvia at least once without significant correlation between salvia use and gender ( $p=0.466$ ). In addition, a significant association between the marital state and salvia use was found ( $p=0.009$ ), with 96.8% of salvia users being single. More than half of salvia users (54.8%) were working full-time within the past 3 years, with no significant correlation between employment state and salvia use. Salvia was used for the first time within the last 2 years of the patient's life. The mean age average for the first time use of Salvia was 24.94 (SD: 5.561, N: 31). Eleven (35.5%) patients used it daily, regarding the method of administration, all patients smoked the SD dried leaves, but only one inhaled it. Furthermore, only one patient smoked it with tobacco. According to participants, the mean duration for salvia's intense effect was 15.52 min (SD: 11.439). Salvia effects started after the first two puffs according to 11 participants (23.4%). Six participants (12.8%) smoked five puffs per time to get the effect. In total 16 (51.6%) participants liked the experience while 15 (48.4%) did not like the experience and indicated they will not repeat it.

The most noticeable finding in this study was that all salvia users took cannabis at least once in their lifetime. Twenty-nine cocaine users out of 43 took salvia (67.4%), 28 out of 43 alcohol users took salvia (65.1%), 25 heroin and other opiates users out of 36 took salvia (69.4%), 10 out of 12 of amphetamine users took salvia (83.3%), and 23 out of 29 hallucinogen users took salvia (79.3%). No significant relationship was found between salvia use and alcohol or other illicit drug use respectively. However, a significant relationship was found between hallucinogen substances (LSD, ecstasy and THC) use and salvia use ( $p=0.014$ ).

### Subjective Effects of Salvia on HRS Subscales

Three of the six clusters: intensity, perception and volition showed a significant difference between the scores of salvia

users and non-salvia users ( $p=0.01$ ,  $p<0.001$ ,  $p<0.001$  respectively). Ratings of somaesthesia was higher in salvia users (mean = 2.04) than non-salvia users (mean = 1.74) but this difference was not statistically significant ( $p=0.152$ ). Affect and cognition ratings did not differ significantly between salvia users and non-salvia users. Non-salvia users (3.31 and 2.51 respectively) scored significantly higher than salvia users (2.72 and 1.70 respectively) for the intensity and volition subscales ( $p=0.01$  and  $p<0.001$  respectively). Salvia users (1.53) scored significantly higher than the non-salvia users (0.70) for the perception subscale ( $p<0.001$ ).

### PANSS Scores

Scoring in all PANSS scales did not show any significant difference between salvia users and non-salvia users.

### Discussion

To the best of our knowledge, this is the first study in Lebanon that investigates the prevalence and hallucinogenic profile of *S. divinorum*. Most participants had their first contact with salvia during the last 2 years. However, the prevalence of this plant within the community/society is 66%, which is relatively high as compared to other similar drugs (Kazour et al. 2016). A significant association was found between salvia use and age, marital status and the use of hallucinogen substances.

The overall age of salvia users in this study sample appears to be consistent with other studies (Nyi et al. 2010; Perron et al. 2012; Substance Abuse and Mental Health Services Administration, Office of Applied Studies (SAMHSA) 2008), with more common among young adults aged 18–25 than among adults ages 26 and above. Our results showed that salvia use is independent of gender, in contrast with other studies that demonstrated that salvia use was up to four times more common in males than in females (Khey et al. 2008; Lange et al. 2008; Wu et al. 2011). Approximately half of the patients used this plant more than five times in their lifetime, in opposite to the findings of Nyi et al. (2010) where most of the participants reported using it less than five times in their lifetime.

As with other studies, we have found similar results regarding the short-lasting psychoactive effect: 15 min on average, and a rapid onset of the effect within seconds to minutes as detected on HRS 'intensity' subscale (Ranganathan et al. 2012; Addy 2012). This rapid effect is due to the rapid brain uptake of salvia as shown by the positron emission tomography (PET), accounting for 3.3% of the total administered dose in 40 s and clearing with a half-life of 8 min (Hooker et al. 2008).

According to epidemiological data, salvia use is associated with polydrug use especially other hallucinogens (Perron et al. 2012). As showed in our results when comparing the frequency of drug use between salvia users and non-salvia users, it is noted that most salvia users were also engaged in other illicit drug use. One can note that the majority of users of each drug category were also using salvia. Participants with history of hallucinogen use (LSD, ecstasy, THC) were significantly more engaged in using salvia as well; this can be expected since regular hallucinogen users seek more to explore other emerged hallucinogens.

Furthermore, our results revealed that salvia users did not like the substance, findings consistent with previous studies (Addy et al. 2015; Khey et al. 2008; Addy 2012). This suggests that salvia has a low continuance rate thus a low potential of abuse.

In our study, there was no significant difference between salvia users and non-salvia users in all PANSS scoring since PANSS is administered long after salvia use and according to the patient's present state. Our results contradict those of a previous study where the total PANSS scoring increased significantly, especially the Positive and General Psychopathology scores which indicate the psychotomimetic effects of salvia, an hour following the administration of 8 mg of salvinorin A to ten participants (Ranganathan et al. 2012). Thus, the results emphasize the fact that salvia does not have any adverse long-term effects (Addy et al. 2015; Ranganathan et al. 2012; Addy 2012).

The effects of salvia were examined on the HRS scale in comparison with the effects of other psychedelics (heroin or cocaine). Participants that took salvia in their lifetime showed an elevation in HRS scoring on each cluster, confirming the hallucinogenic effect of salvia (González et al. 2006; Albertson and Grubbs 2009). Previous studies have used the HRS questionnaire to compare the subjective effect of salvia in comparison to placebo control (Cunningham et al. 2011; Addy 2012; Johnson et al. 2011). The active condition (1017 µg salvinorin A) versus the placebo condition (100 µg salvinorin A) increased HRS ratings, including somatosensory, intensity, affective, perceptual and cognitive effects, according to Addy (2012). In addition, at high doses (> 15 µg/kg), all the HRS scoring increased significantly in comparison to the placebo except the volition subscale; which indicates the overlap of the somatosensory, intensity, perceptual and cognitive effect of salvia with classical serotonergic hallucinogens (MacLean et al. 2013). The current HRS scoring is similar to the scoring of Gonzalez et al. (2006), Maclean et al. (2013), Addy (2012) and Albertson and Grubbs (2009). Surprisingly, all scores are similar but only somaesthesia and cognitive are more elevated in this case. This could be attributed to the impurity of the salvia taken as most

participants reported that salvia is injected with ketamine, which is known to induce changes in cognition and sensory processing (Featherstone et al. 2012).

The salvia effect on HRS scoring of affect, cognition and somaesthesia is the same between salvia and other illicit drugs (heroin or cocaine) and appears to overlap with the psychotic alterations these illicit drugs can induce. However, intensity and volition scores are elevated in non-salvia users indicating that heroin and cocaine result in a more intense experience and users are less able to interact with themselves and their environment than when using salvia. The only subscale that shows an increase in scoring for salvia use than the score for heroin and cocaine use is the perception subscale. This confirms the perceptual alteration effects that salvia has and shows that it can induce visual hallucinations (Zawilska and Wojcieszak 2013). Knowing that *S. divinorum*'s subjective effects are apparently comparable to those of marijuana, LSD, and ketamine (Albertson and Grubbs 2009), exploration is necessary to investigate the setting of Salvia use and to evaluate health risk connected with its consumption in conjunction with different substances (e.g., risk for inebriation, accidents, injuries, psychiatric disorders, and overdose). The provided information serves to inform therapeutic intervention and to assess the psychoactive effect of salvia that cause potential health problems to young people, especially those with existing substance use disorder.

## Limitations

This survey has several limitations to be acknowledged. Patients were regular users of other psychoactive agents such as heroin, cannabis and other psychedelics, making it difficult to assess the specific effects of this drug. The dose of salvia used was not evaluated, and this constitutes a limitation to our study. The dose of SA delivered by smoking may have varied between participants. The pattern of subjective effects observed may be difficult to extrapolate to the general population. Additionally, the retrospective evaluation performed does not substitute for the immediate assessment of the psychotropic effects of salvia, leading to a possible information bias. Furthermore, the sample size is too small in order to generalize our results. Although the patients were sober at the time of interview, and despite admitting that the episode of illegal drug use was not a multiple one, and that he used salvia only prior to being admitted to the hospital, an information bias might still be present. Cross sectional study does not allow the establishment of causality. Moreover, analysis was only done at the bivariate level and not the multivariate, so associations found are not binding. In addition, the scales were not validated for use in Lebanon.

## Conclusion

The information gathered from this study will help better understand the pattern of use and serves as an initial step toward filling the gap in literature concerning this drug: heavy illicit drug and alcohol users tend to abuse a variety of substances, including salvia. Salvia is a new psychedelic drug that entered the illicit drug scene within the last 2 years in Lebanon. It is highly prevalent among illicit drug particularly those who are hallucinogen users, and more common among young adults aged between 18 and 25. Salvia facilitates hallucinogenic states of consciousness as shown on the HRS scales with a short and rapid onset of its effect. It may be a significant public health problem in Lebanon due to its potential complications as manifested on HRS scoring. Salvia users did not show any adverse long-term effects. Future studies should consider looking for the effects of *S. divinorum* in the general population, and its impact on the development of psychiatric symptoms, independently of the use of other psychoactive substances.

## Compliance with Ethical Standards

**Conflict of interest** The authors declare that they have no conflict of interest.

## References

- Addy, P. H. (2012). Acute and post-acute behavioral and psychological effects of salvinorin A in humans. *Psychopharmacology (Berlin)*, 220(1), 195–204.
- Addy, P. H., Garcia-Romeu, A., Metzger, M., & Wade, J. (2015). The subjective experience of acute, experimentally-induced *Salvia divinorum* inebriation. *Journal of Psychopharmacology*, 29(4), 426–435.
- Albertson, D. N., & Grubbs, L. E. (2009). Subjective effects of *Salvia divinorum*: LSD- or marijuana-like? *Journal of Psychoactive Drugs*, 41(3), 213–217.
- Ansonoff, M. A., Zhang, J., Czyzyk, T., Rothman, R. B., Stewart, J., Xu, H., et al. (2006). Antinociceptive and hypothermic effects of salvinorin A are abolished in a novel strain of kappa-opioid receptor-1 knockout mice. *Journal of Pharmacology and Experimental Therapeutics*, 318(2), 641–648.
- Appel, J., & Kim-Appel, D. (2007). The rise of a new psychoactive agent: *Salvia divinorum*. *International Journal of Mental Health and Addiction*, 5(3), 248–253.
- Baggott, M. J., Erowid, E., Erowid, F., Galloway, G. P., & Mendelson, J. (2010). Use patterns and self-reported effects of *Salvia divinorum*: An internet-based survey. *Drug and Alcohol Dependence*, 111(3), 250–256.
- Chavkin, C., Sud, S., Jin, W., Stewart, J., Zjawiony, J. K., Siebert, D. J., et al. (2004). Salvinorin A, an active component of the hallucinogenic sage *Salvia divinorum* is a highly efficacious kappa-opioid receptor agonist: Structural and functional considerations. *Journal of Pharmacology and Experimental Therapeutics*, 308(3), 1197–1203.
- Cunningham, C. W., Rothman, R. B., & Prisinzano, T. E. (2011). Neuropharmacology of the naturally occurring kappa-opioid hallucinogen salvinorin A. *Pharmacological Reviews*, 63(2), 316–347.
- El-Khoury, J., & Sahakian, N. (2015). The association of *Salvia divinorum* and psychotic disorders: A review of the literature and case series. *Journal Psychoactive Drugs*, 47(4), 286–292.
- Featherstone, R. E., Liang, Y., Saunders, J. A., Tatar-Leitman, V. M., Ehrlichman, R. S., & Siegel, S. J. (2012). Subchronic ketamine treatment leads to permanent changes in EEG, cognition and the astrocytic glutamate transporter EAAT2 in mice. *Neurobiology of Disease*, 47(3), 338–346.
- González, D., Riba, J., Bouso, J. C., Gómez-Jarabo, G., & Barbanoj, M. J. (2006). Pattern of use and subjective effects of *Salvia divinorum* among recreational users. *Drug and Alcohol Dependence*, 85(2), 157–162.
- Hooker, J. M., Xu, Y., Schiffer, W., Shea, C., Carter, P., & Fowler, J. S. (2008). Pharmacokinetics of the potent hallucinogen, salvinorin A in primates parallels the rapid onset and short duration of effects in humans. *Neuroimage*, 41(3), 1044–1050.
- Johnson, M. W., MacLean, K. A., Reissig, C. J., Prisinzano, T. E., & Griffiths, R. R. (2011). Human psychopharmacology and dose-effects of salvinorin A, a kappa opioid agonist hallucinogen present in the plant *Salvia divinorum*. *Drug and Alcohol Dependence*, 115(1–2), 150–155.
- Kay, S. R., Fiszbein, A., & Opler, L. A. (1987). The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophrenia Bulletin*, 13(2), 261–276.
- Kazour, F., Soufia, M., Rohayem, J., & Richa, S. (2016). Suicide risk of heroin dependent subjects in Lebanon. *Community Mental Health Journal*, 52(5), 589–596.
- Kelly, B. C. (2011). Legally tripping: A qualitative profile of *Salvia divinorum* use among young adults. *Journal of Psychoactive Drugs*, 43(1), 46–54.
- Khey, D. N., Miller, B. L., & Griffin, O. H. (2008). *Salvia divinorum* use among a college student sample. *Journal of Drug Education*, 38(3), 297–306.
- Lange, J. E., Reed, M. B., Croff, J. M., & Clapp, J. D. (2008). College student use of *Salvia divinorum*. *Drug and Alcohol Dependence*, 94(1–3), 263–266.
- MacLean, K. A., Johnson, M. W., Reissig, C. J., Prisinzano, T. E., & Griffiths, R. R. (2013). Dose-related effects of salvinorin A in humans: dissociative, hallucinogenic, and memory effects. *Psychopharmacology (Berline)*, 226(2), 381–392.
- McLellan, A. T., Luborsky, L., Woody, G. E., & O'Brien, C. P. (1980). An improved diagnostic evaluation instrument for substance abuse patients. The Addiction Severity Index. *The Journal of Nervous and Mental Disease*, 168(1), 26–33.
- Miller, B. L., Griffin, O. H., Gibson, C. L., & Khey, D. N. (2009). Trippin' on Sally D: Exploring predictors of *Salvia divinorum* experimentation. *Journal of Criminal Justice*, 37(4), 396–403.
- Nyi, P. P., Lai, E. P., Lee, D. Y., Biglete, S. A., Torrecer, G. I., & Anderson, I. B. (2010). Influence of age on *Salvia divinorum* use: Results of an Internet survey. *Journal of Psychoactive Drugs*, 42(3), 385–392.
- Perron, B. E., Ahmedani, B. K., Vaughn, M. G., Glass, J. E., Abdon, A., & Wu, L. T. (2012). Use of *Salvia divinorum* in a nationally representative sample. *The American Journal of Drug and Alcohol Abuse*, 38(1), 108–113.
- Prisinzano, T. E. (2005). Psychopharmacology of the hallucinogenic sage *Salvia divinorum*. *Life Sciences*, 78(5), 527–531.
- Ranganathan, M., Schnakenberg, A., Skosnik, P. D., Cohen, B. M., Pittman, B., Sewell, R. A., et al. (2012). Dose-related behavioral, subjective, endocrine, and psychophysiological effects of the kappa opioid agonist salvinorin A in humans. *Biological Psychiatry*, 72(10), 871–879.

- Roth, B. L., Baner, K., Westkaemper, R., Siebert, D., Rice, K. C., Steinberg, S., et al. (2002). Salvinorin A: A potent naturally occurring nonnitrogenous  $\kappa$  opioid selective agonist. *Proceedings of the National Academy of Sciences*, 99(18), 11934–11939.
- Sheehan, D. V., Lecrubier, Y., Sheehan, K. H., Amorim, P., Janavs, J., Weiller, E., et al. (1998). The Mini-International Neuropsychiatric Interview (M.I.N.I.): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *The Journal of Clinical Psychiatry*, 59(Suppl 20), 22–33 (quiz 4–57).
- Siebert, D. J. (1994). *Salvia divinorum* and salvinorin A: New pharmacologic findings. *Journal of Ethnopharmacology*, 43(1), 53–56.
- Strassman, R. J., Qualls, C. R., Uhlenhuth, E. H., & Kellner, R. (1994). Dose-response study of N,N-dimethyltryptamine in humans. II. Subjective effects and preliminary results of a new rating scale. *Arch Gen Psychiatry*, 51(2), 98–108.
- Substance Abuse and Mental Health Services Administration, Office of Applied Studies (SAMHSA). (2008). The NSDUH report: Use of specific hallucinogens: 2006. Retrieved from <http://www.oas.samhsa.gov/2k8/hallucinogens/hallucinogens.htm>
- Sumnall, H. R., Measham, F., Brandt, S. D., & Cole, J. C. (2011). *Salvia divinorum* use and phenomenology: Results from an online survey. *Journal of Psychopharmacology*, 25(11), 1496–1507.
- Valdes, L. J. 3rd (1994). *Salvia divinorum* and the unique diterpene hallucinogen, salvinorin (divinorin) A. *Journal of Psychoactive Drugs*, 26(3), 277–283.
- Wu, L. T., Woody, G. E., Yang, C., Li, J. H., & Blazer, D. G. (2011). Recent national trends in *Salvia divinorum* use and substance-use disorders among recent and former *Salvia divinorum* users compared with nonusers. *Substance Abuse and Rehabilitation*, 2011(2), 53–68.
- Zawilska, J. B., & Wojcieszak, J. (2013). *Salvia divinorum*: From Mazatec medicinal and hallucinogenic plant to emerging recreational drug. *Human Psychopharmacology*, 28(5), 403–412.