

ORIGINAL ARTICLE

Prolonged hallucinations and dissociative self mutilation following use of *Salvia divinorum* in a bipolar adolescent girl

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Abstract

The case of a bipolar 17-year-old girl who developed prolonged vivid hallucinations and a dissociative state involving self-destructive behaviour following the use of *Salvia divinorum* is presented. The herb has mostly short-term (10–15 min) hallucinogenic properties. Salvatorin A, the main active compound, is a highly selective agonist of the kappa-opioid receptor. The plant is available at tobacco or other specialized stores in many countries such as France, UK, Canada, and USA, where it is legal. The clinical case reported in this article suggests that the recreational use of *Salvia divinorum* may result in serious psychiatric consequences in vulnerable individuals.

Keywords: *Adolescents, Salvia divinorum, prolonged hallucinations, dissociative state, bipolarity.*

Past history

Marylin was first evaluated in a Child Psychiatry Outpatient department (OPD) at the age of 9 years for phobias, and disruptive and anxious behaviour triggered by separation from her mother. Her father was diagnosed as bipolar and her mother was chronically depressed. Further investigations revealed that her mother was also bipolar with cycles of depression and mania. Marylin had two brothers older than herself. She was born at 30 weeks gestation and hospitalized several times for asthma. She had one episode of febrile convulsions. A diagnosis of generalized anxiety disorder was made, and individual psychotherapy and parental guidance were recommended. The child missed several appointments, as her mother was not very supportive of the therapeutic intervention. Both mother and child discontinued the treatment after 18 months.

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At 14 years of age Marylin was admitted to an adolescent in-patient unit as a result of her emotional outbursts, increased energy, reduced sleep, irritability, and sadness. A diagnosis of bipolar disorder type 1, with mixed episodes, was made. Lithium was initiated and her mood status improved. However, partly as a consequence of the parents' psychiatric problems, family relationships remained chaotic and conflictual. At that time, the adolescent started using cannabis and became over weight. She was emotionally unstable, impulsive, performed poorly at school, and presented with chronic sleep problems (mostly initial insomnia). She had difficulty accepting her diagnosis of bipolar disorder and, consequently, took her medication irregularly. She had to be hospitalized three times in the same year for mixed episodes with visual hallucinations, self-mutilation, and oppositional behaviour. She was diagnosed with borderline personality disorder, later confirmed with the Diagnostic Interview for Borderlines—Revised (Zanarini, Gunderson, Frankenburg, & Chauncey, 1989), in addition to the diagnosis of Bipolar disorder. Clonidine and quetiapine were added to decrease aggressive behaviours and improve sleep. She was finally referred to a residential centre for 18 months, but had to be hospitalized twice for suicidal crises and self-mutilation.

Current episode

At the time of the *Salvia divinorum* consumption, the patient was 17 years old and living in a block of flats supervised by an educator, who was resident at the site. Marylin was undergoing a period of symptomatic remission and expected to make good progress. She did not take cannabis and had not self-mutilated for the past 9 months. She was enrolled in a university teaching hospital Mood Disorders OPD. Her daily pharmacological treatment was lithium 900 mg, loxapine 15 mg, clonidine 0.1 mg, fluoxetine 10 mg, and lipitor 10 mg (for elevated cholesterol). On a Sunday night in July, she smoked dried leaves of *Salvia divinorum* with two other male adolescents. The dried leaves were bought legally in a store. The legality and ease of access led the adolescents to believe that the plant was not harmful. The three adolescents smoked the 'joint' of *Salvia* seated on a bench in a park. The two boys encountered immediate changes in perception with feelings of derealization (being in a spatial vessel for one and moving very rapidly for the other), which lasted for 10–15 min.

Marylin was bewildered because she felt no effect of smoking *Salvia divinorum*. However, 3 h later, while going to bed, she started to experience feelings of derealization with frightening visual, auditory, olfactory, and somatic hallucinations. Everything was unreal, with the floor moving like the surface of water and voices coming out of furniture. She saw dead people, heard screams and moaning, felt burning smells and the sensation of a puff on her neck. In the past, the visual hallucinations she experienced occurred only during her mixed episodes. She became very frightened and called both her mother at home and her educator at the site. The educator went up to her flat and was able to progressively calm her down. The hallucinations continued the next day, and worsened over the afternoon and the evening. She went to bed with her eyes still open (unable to sleep) and had what she later described as a 45-min 'blackout'. Upon arousal she saw blood on the sheets, discovered several cuts on her left forearm and abdomen, and realized with anguish that she had been self-mutilating during this episode. She had absolutely no recollection of her behaviour. She panicked and called her educator and the emergency services of two hospitals to get help. Her educator came up and was again able to calm her down. The emergency calls were cancelled. The frightening hallucinations decreased slowly and she was able to sleep. The next morning, she got in touch with our Mood Disorders Clinic and had an

appointment with the child psychiatrist (JJB) and the nurse (SR) the following day. At the mental examination, she was very anxious, but not psychotic. She reported suicidal urges when near a metro station. Loxapine was increased, and a follow-up meeting with Marylin and her educator was planned the following day. The hallucinations and the suicidal urges decreased progressively over the following 4 days. She recovered completely after 1 week from her episode and returned to her previous adequate level of functioning.

Salvia divinorum

Description. *Salvia divinorum* is a plant in the sage genus belonging to the mint family. The Sage genus encompasses 700 species. The herb was originally cultivated in the state of Oaxaca, Mexico by Mazatec Indians, and used for spiritual and religious purposes as a substitute for psilocybes, when these mushrooms were not available. The herb has mostly hallucinogenic properties. In traditional societies, the plant is often a reincarnation of Mary, who appears and speaks to the user. Other names include ‘Mary herb’, ‘Magic Mint’ and ‘Diviner’s Sage’. The plant can be chewed, drunk (as a juice) or smoked (Hostettmann, 2002). Smoking is the preferred method of use (Dalgarno, 2007). It is known as a very short-acting drug with psychedelic effects starting immediately after inhalation and lasting for 5–15 min and not exceeding 2 h. In addition to hallucinations, the drug generates euphoria, identity disturbance, derealization and dissociative phenomena (Dalgarno, 2007; Gonzales, Riba, Bouso, Gomez-Jarabo, & Barbanoj, 2006; Nortier, 2007).

The plant is available on many web sites and is also available through tobacco or other specialized stores in countries where it is legal. The drug is presented as a safe, legal, and undetectable product by usual routine tests, characteristics that make it very appealing for use by both adults and adolescents. Indeed, web sites devoted to drugs are proliferating with a large number of commercial sites ignoring the risks and harms related to the use of psychedelic drugs (Montagne, 2008). A 2005 survey in France revealed that hallucinogens were used over lifetime by 5.2% of boys and 2.1% of girls 17 years [Observatoire français des drogues et toxicomanies (OFDT), 2007] and in Quebec, 9% of 12–17-year-old adolescents in secondary schools reported having used hallucinogenic drugs in 2006 (Dubé & Fournier, 2006). The drug is legal in many countries like France, UK, Canada, and USA, although not in all states, but prohibited in Spain, Australia, Italy, Sweden, and Denmark. A recent survey among 1526 college students in the United States revealed that 4.4% of the sample reported using *Salvia* over the previous year. Being male, white, member of a fraternity/sorority group, a heavy alcohol- and drug-user were associated with increased probability of *Salvia* use. Alcohol and drug use represented the highest risk factor for taking *Salvia* (OR of 11) (Lange, Reed, Ketchie Croff, & Clapp, 2008).

Mechanisms of action. *Salvia divinorum* is a hallucinogen with specific properties different from indolealkylamines and phenylalkylamines, the two major classes of hallucinogens (Nortier, 2007; Stahl, 2008). Indolealkylamines encompass psilocybin and psilocin, the active compounds of psilocybe mushrooms, dimethyltryptamine (DMT) coming from virola’s bark, ibogaine from *Tabernanthe iboga*, as well as the classic synthetic hallucinogen LSD. They act mainly as agonists at 5-HT_{2A} receptor sites with additional effects on other neurotransmitter systems. The second class is represented by phenylalkylamines encompassing mescaline, the active compound of cactus peyote and synthetic drugs, such as the well known MDMA or ecstasy. They have complex interactions at norepinephrine and dopamine receptor sites (OFDT data base; Stahl, 2008).

Table I. Main characteristics of hallucinogenic compounds used for recreational purposes

	Active compounds	Mechanism
Mushroom <i>Psilocybe</i> (<i>Psilocybe cubensis</i> , <i>hoogshagenii</i> , <i>mexicana</i> , <i>muliercula</i> , <i>zapotecorum</i>)	Psilocybin, Psilocin Agonist R 5HT-2	Interaction with 5HT network
Mushroom <i>Panaeolus</i>		
Mushroom <i>Gynopilus Boletus manicus</i>		
Morning glory (<i>Ipomea</i>)	Amide of d-lysergic acid	Interaction with 5HT network
Ololuiqui (<i>Rivea corymbosa</i>)		Agonist R 5HT-2
Virola (<i>Virola calophylla</i>)	Indolealkylamins	Inhibition of mono-amine oxydase
		Agonist R 5HT1 and R-5HT2
Iboga (<i>Tabernanthe iboga</i>)	Indolealkylamins	Agonist of γ and κ -opioid R
	Ibogaine	Antagonist R NMDA
Cactus peyote (<i>Iophophora Williamsi</i>)	Mescaline	Agonist dopamine R,
Cactus San Pedro	Agonist noradrenaline	
Scarlet sage (<i>Salvia divinorum</i>)	Salvinorin A	Agonist of κ -opioid R

Based on OFDT data (Observatoire français des drogues et toxicomanies).

Salvatorin A is the main active compound of *Salvia divinorum*. Salvatorin A does not have binding affinity for 5-HT_{2A} receptor compared with many hallucinogens. This compound is a highly selective agonist of the kappa-opioid receptor (Babu, McCurdy & Boyer, 2008; see Table I). A gender effect difference in elimination was observed in the only study using intravenous administration on two male and two female rhesus monkeys with males having a shorter elimination half-life than females. The sedative effect lasted about 15 min (Grundmann, Phipps, Zadezensky, & Butterweck, 2007).

Discussion

The case of Marylin is very unusual because of the delay in the psychedelic effects and the week-long duration of the vivid hallucinatory phenomena. Moreover, this adolescent presented a dissociative state with self-injury behaviour the day after taking the substance. The suicidal urges reported during her first visit at our Mood Disorders Clinic appear to be secondary to the psychological distress. The two other male adolescents had a very short hallucinatory experience, but the gender effect observed in a non-human primate study cannot obviously account for such a substantial difference in reactions.

We did not find in the literature any other case describing effects lasting for several days following the use of *Salvia divinorum*. The bipolarity of this patient with previous episodes of visual hallucinations, self-mutilation, and suicidal crises made her more vulnerable. In addition, the psychotropic medication taken by Marylin, with molecules having affinity for alpha adrenergic, dopamine, and 5-HT receptors, might have contributed to the intense and prolonged reaction in this bipolar girl, although the molecular mechanisms involved in neurotransmitter systems are quite difficult to elucidate. Hallucinogens act at serotonin and dopamine systems on reward circuits consisting of the ventral tegmental area, the nucleus accumbens, and the amygdala (Stahl, 2008). A neurochemical adaptation of the dopamine system and its receptors related to the chronic use of the psychotropic medication, especially loxapine, might have contributed to the delayed and prolonged hallucinatory phenomena. Use of psychotropic medication as such by adolescents with mental disorders could then be a major risk factor for serious complications following use of hallucinogens.

Overall, it appears clear that the recreational use of *Salvia divinorum* can result in serious psychiatric problems in vulnerable individuals. In addition to prolonged hallucinatory phenomena, a dissociative state involving self-destructive behaviour (self-mutilation in this case) following use of the drug can have harmful consequences. Discussion about the legal status of the drug in many countries should take into consideration descriptions and comments, such as the one presented in this clinical case-study.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

- Babu, K. T., McCurdy, C.R., & Boyer, E.W. (2008). Opioid receptors and legal highs: *Salvia divinorum* and Kratom. *Clinical Toxicology*, 46, 146–152.
- Dalgarno, P. (2007). Subjective effects of *Salvia divinorum*. *Journal of Psychoactive Drugs*, 39, 143–149.
- Dubé, G., & Fournier, C. (2006). *Enquête québécoise sur le tabac, l'alcool, la drogue et le jeu chez les élèves du secondaire, 2006*. Institut de la statistique du Québec, Publications du Québec.
- Gonzales, D., Riba, J., Bouso, J.-C., Gomez-Jarabo, & Barbanoj, M. J. (2006). Pattern of use of *Salvia divinorum* among recreational users. *Drug and Alcohol Dependence*, 85, 157–162.
- Grundmann, O., Phipps, S. M., Zadezensky, I., & Butterweck, V. (2007). *Salvia divinorum* and salvitorin A: An update on pharmacology and analytical methodology. *Planta Med*, 73, 1039–1046.
- Hostettmann, K. (2002). *Les plantes qui deviennent des drogues*, Éditions Favre.
- Lange, J. E., Reed, M. B., Ketchie Croff, J. M., & Clapp, J. D. (2008). College students' use of *Salvia divinorum*. *Drug and Alcohol Dependence*, 94, 263–266.
- Montagne, M. (2008). Drugs on the Internet. 1: Introduction and web sites on psychedelic drugs. *Substance Use and Misuse*, 43: 17–25.
- Nortier, E. (2007). Drogues anciennes, drogues nouvelles, pratiques actuelles (2ième partie), *Psychiatric Science and Human Neuroscience*, 5, 71–88.
- Observatoire français des drogues et toxicomanies (2007). *Hallucinogènes: une consommation limitée mais plus présente chez les adolescents et les jeunes adultes*. Synthèse OFDT, March 2007. Available at: <http://www.ofdt.fr/ofdtdev/live/produits/hallucin/conso.html>
- Stahl, S. (2008). *Stahl's essential psychopharmacology. Neuroscientific basis and practical applications*, 3rd edn. Cambridge: Cambridge University Press.
- Zanarini, M. C., Gunderson, J. G., Frankenburg, F. R., & Chauncey, D. L. (1989). The Revised Diagnostic Interview for Borderlines. *Journal of Personal Disease*, 3, 10–18.