

Pattern of use and subjective effects of *Salvia divinorum* among recreational users

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Abstract

Background: *Salvia divinorum* is a member of the Lamiaceae family and contains the psychotropic diterpene and kappa-opioid receptor agonist salvinorin-A. Originally a shamanic inebriant used by the Mexican Mazatec Indians, the plant and its preparations are becoming increasingly popular among non-traditional users.

Methods: Demographic data and information on pattern of use and subjective effects were obtained by means of self-report questionnaires from a sample of 32 recreational users of salvia and other psychedelics.

Results: Involvement with salvia appeared to be a recent phenomenon. Smoking the extract was the preferred form of administration. Subjective effects were described as intense but short-lived, appearing in less than 1 min and lasting 15 min or less. They included psychedelic-like changes in visual perception, mood and somatic sensations, and importantly, a highly modified perception of external reality and the self, leading to a decreased ability to interact with oneself or with one's surroundings.

Conclusions: Although some aspects of the subjective effects reported were similar to high doses of classical psychedelics with serotonin-2A receptor agonist activity, the intense derealization and impairment reported appear to be a characteristic of salvia. The observed simultaneous high scores on the LSD and PCAG subscales of the Addiction Research Center Inventory (ARCI) have been previously reported for other kappa-opioid agonists, and support kappa receptor activation as the probable pharmacologic mechanism underlying the modified state of awareness induced by salvia.

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1. Introduction

Salvia divinorum (Lamiaceae) is a psychotropic mint whose leaves are used for medicinal and religious purposes by Mazatec shamans in the Mexican state of Oaxaca (Wasson, 1962; Valdes et al., 1983). The Mazatecs, who call the plant “ska pastora” or “ska Maria pastora”, meaning “leaves of the shepherdess” or “leaves of Mary the shepherdess”, traditionally ingest the plant as a water infusion or by eating the fresh leaves (Wasson, 1962; Valdes et al., 1983). Early ethnological research found

that the Mazatecs regard the psychotropic effects elicited by the plant as weak and use it only in substitution of the psilocybin-containing mushrooms when these are scarce (Wasson, 1962). However, the plant's apparently weak potency could be due to limited absorption of the active principle when ingested orally (Ott, 1995).

Despite its initial reputation as a lesser drug, interest for salvia has greatly increased in recent years among recreational users for the modified state of awareness it can elicit. The use of salvia has spread to Europe and North America in a similar fashion to other natural drugs, as the DMT-containing ayahuasca did a decade ago (Riba and Barbanoj, 2005). However, unlike many ayahuasca users, current non-traditional users of salvia have accessed the plant and its preparations outside a religious context, mainly through “smart shops” and internet websites selling

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psychotropic plants and extracts, paraphernalia and dietary supplements (Dennehy et al., 2005). The term “smart shop” originated in The Netherlands and describes stores where natural psychoactive drugs such as ephedra, mescaline-containing cacti, psilocybian mushrooms and salvia extracts are sold. Such stores can also be found in Spain but their activities have been restricted since a decree was issued prohibiting the sale of a large number of plants, including salvia (see <http://www.boe.es>, number 32, 6 February 2004).

S. divinorum owes its psychoactive properties to salvininorin-A, its main active principle. This compound is a neoclerodane diterpene which was first isolated and identified by Ortega et al. (1982), and shortly after by Valdes et al. (1984). Recent pharmacological research has found it to be a highly selective full agonist of the kappa-opioid receptor (Roth et al., 2002; Butelman et al., 2004; Chavkin et al., 2004). Salvinorin-A is the only non-nitrogenous natural compound known to date to exert agonistic activity at these sites. Furthermore, in contrast with the classical psychedelics, salvinorin-A does not interact with the serotonin-2A receptor, but presumably induces its psychotropic effects through activation of the kappa-opioid receptor.

Contrary to what was initially assumed, salvinorin-A can be quite powerful. Inhalation of the vaporized active principle has been found to be active in doses as low as 200 µg (Siebert, 1994), in the same range as LSD. Recreational users have developed methods of administration that appear to lead to intense psychoactivity. These include chewing the leaves and retaining the juices in the mouth to allow absorption through the mucosa and obtaining concentrated extracts that can be administered either sublingually, applied to the buccal mucosa, or smoked (Siebert, 1994; Ott, 1995). The subjective effects described in self-experiments and case reports range widely, from increased relaxation, to laughter, colored visions, out-of-body experiences and loss of consciousness (Siebert, 1994; Bücheler et al., 2005; Dennehy et al., 2005).

In the present study we aimed to obtain systematic information on the pattern of use and the nature of the subjective effects elicited by salvia in recreational users. Self-report questionnaires were administered to the participants to obtain demographic and subjective effect data.

2. Methods

2.1. Sample

The sample was recruited by direct approach by the first author, who also conducted the interviews. Potential participants had to have used salvia at least once in their lifetime. Given the infrequent nature of the behavior under study, adaptive sampling was used with participants referring to acquaintances who had also had experience with the drug (Thompson and Collins, 2002). Several leads were followed, so participants did not belong to a single social network. After initial contact with the first author, participants were given the forms, which they took away, filled out and later returned to the investigator. Anonymity of the information was guaranteed and all the participants gave their written consent to participate. The study was approved by the ethics committee at the Hospital de Sant Pau in Barcelona. Participants had not taken part in any clinical study conducted by our group and did not receive any payment for their participation in the present survey.

Demographic information was collected from the participants, together with information on drug use history and salvia use history, route of administration,

pleasant and unpleasant after-effects, and any potential problems they might have experienced derived from salvia use. Information on salvia-induced subjective effects was obtained by means of the retrospective assessment of drug effects when they last took salvia.

2.2. Subjective effect measures

Retrospective assessment of the subjective effects induced by salvia was conducted by means of self-assessment questionnaires. The following questionnaires were administered:

The Hallucinogen Rating Scale or HRS (Strassman et al., 1994) measures psychedelic-induced subjective effects and includes 71 items distributed into six scales: *Somaesthesia*, reflecting somatic effects including interoceptive, visceral and tactile effects; *affect*, sensitive to emotional and affective responses; *volition*, indicating the volunteer's capacity to willfully interact with his/her “self” and/or the environment; *cognition*, describing modifications in thought processes or content; *perception*, measuring visual, auditory, gustatory and olfactory experiences; finally *intensity*, which reflects the strength of the overall experience. The range of scores for all scales is 0–4. In the present study, a Spanish version of the questionnaire was administered (Riba et al., 2001a). The HRS has proven sensitive to various psychedelics such as intravenous DMT (Strassman et al., 1994), oral psilocybin (Gouzoulis-Mayfrank et al., 1999) and ayahuasca (Riba et al., 2001b, 2003).

The ARCI (Martin et al., 1971) consists of five scales or groups: MBG, morphine-benzedrine group, measuring euphoria and positive mood; PCAG, pentobarbital-chlorpromazine-alcohol group, measuring sedation; LSD, lysergic acid diethylamide scale, measuring somatic-dysphoric effects; BG, the benzedrine group, measuring intellectual energy and efficiency, and the A scale, an empirically derived scale measuring amphetamine-like effects. The range of scores is 0–16 for MBG, –4 to 11 for PCAG, –4 to 10 for LSD, –4 to 9 for BG, and 0–11 for A. A validated Spanish version was administered (Lamas et al., 1994).

The State-Trait Anxiety Inventory-S (STAI-S) is a brief 20-item self-rating scale for the assessment of state anxiety (Spielberger et al., 1970). A validated Spanish version was administered (Seisdedos, 2002). The normative data for the Spanish adaptation differs from the original data for the American version. The reported mean (S.D.) values reported for State anxiety in the normal population are 20.54 (10.56) for male adults and 23.30 (11.93) for female adults (Seisdedos, 2002).

The Altered States of Consciousness Questionnaire (“Aussergewöhnliche Psychische Zustände”, APZ) developed by Dittrich (1998). It includes 72 items distributed in three subscales: *Oceanic Boundlessness* (“Ozeanische Selbstengrenzung”, OSE), measuring changes in the sense of time, derealization and depersonalization; *Dread of Ego-Dissolution* (“Angstvolle IchAuflösung”, AIA) measuring thought disorder and decreased body and thought control associated with arousal and anxiety and *Visionary Restructuration* (“Visionäre Umstrukturierung”, VUS) referring to visual phenomena, such as illusions, hallucinations and synesthesia and to changes in the significance of objects. The range of scores is 0–13 for OSE, 0–22 for AIA, and 0–14 for VUS. A Spanish version of the questionnaire previously used in clinical studies involving psychedelic drugs was administered (Riba et al., 2002).

2.3. Statistical analysis

The data presented in the present paper are descriptive in nature and accordingly, descriptive statistics are provided in Section 3. Percentages are reported for categorical variables and means and standard deviations for continuous variables obtained from subjective effect questionnaires.

Given the small sample size, no inferential statistics were used to find differences associated with gender or route of administration.

3. Results

3.1. Demographic characteristics of the sample

A total of 32 salvia users were recruited, 18 (56%) of whom were male and 14 (44%) were female. The mean age of the sam-

ple was 25 years (S.D.: 4.32; range: 18–40 years). Education level was high with 23 (72%) of the sample having completed high school and 7 (22%) having obtained a university degree. At the time of the survey, 22 (69%) were attending university. Seventeen participants (53%) were full-time students, 6 (19%) combined studies with part-time jobs, 7 (22%) worked exclusively, and 2 (6%) were unemployed.

3.2. History of drug use (other than salvia)

Except for two participants, all those in the study (93.7%) had a drink containing alcohol weekly. The average number of alcoholic drinks per week among the drinkers was 3.13 (S.D.: 2.69, range: 1–14). More than four-fifths of the participants (84.4%) were smokers, with a mean number of 14 cigarettes per day (S.D.: 6.74, range: 1–25). Except for one participant, all participants (96.9%) consumed cannabis at least once a week. The average number of cannabis joints was 21.32 per week (S.D.: 15.68, range: 2–70). They also had wide experience with other drugs; ecstasy had been used by 88%, cocaine by 84%, amphetamines 69%, opiates 56%, benzodiazepines 36%, and GHB 9%.

Ninety-four percent of the volunteers had at some time used a psychedelic/hallucinogen, the most frequent being psilocybian mushrooms (78% of all participants), followed by LSD (63%), ketamine (34%), ayahuasca (28%), *Amanita muscaria* (13%), peyote (6.3%) mescaline (3%) and *Datura stramonium* (3%). Ten volunteers (31%) reported having consumed “other psychedelics” not listed in the questionnaire. Specified were: 2C-B (four volunteers), San Pedro (one volunteer) and *Argyreia nervosa* (one volunteer).

3.3. History and pattern of use of salvia

Participants appeared to have first experienced salvia only recently, with 88% having used it for the first time in the last year. The average number of times the drug was consumed was 2 (range: 1–5). The source of the salvia was a “smart shop” in 88% of the cases and in the remaining 12% it had been obtained from a friend, without further specifying the source.

All participants had consumed salvia as an extract and three (9%) had also used the leaves. Commercially available extracts usually consist of ground salvia leaves impregnated with salvia tincture, so that the final product may contain 5, 10 or 20 times the original salvininorin-A concentration.

Regarding the preferred route of administration, 75% reported having smoked the extract, 22% reported combining sublingual and smoked administration and 3% (one subject) reporting smoking the leaves and the extract combined. As to the smoking technique, all volunteers reported using a bong or a pipe. No participant reported smoking it in the form of cigarettes or mixing salvia with tobacco or marijuana. When asked about the psychotropic potency of salvia, 75% of the participants described the experience elicited by salvia from “intense” to “very intense” or “extremely intense”, with only 19% as “moderate” and 6% describing it as “slight”.

Participants were asked to state the best and the worst aspects of their salvia experiences. These are listed in Table 1.

The most commonly cited positive effects were the “trip” the drug elicits (41%), followed by its euphoric (28%) and dissociative effects (19%). Among the worst aspects, its short duration (38%) was the most frequently cited. Sixteen percent of the volunteers mentioned the lack of control over the experience and 13% the unpleasant after-effects as the worst aspect of salvia. Thirteen percent of the volunteers could find no negative aspect related to the experience.

Fourteen volunteers (44%) reported having experienced some degree of malaise, hang-over or “comedown” immediately after the acute effects of salvia. These effects are also listed in Table 1 and essentially describe physical and mental tiredness. All volunteers unanimously agreed that these unpleasant effects were no longer present 1 day after salvia use, and that they had never experienced any mid-term unpleasant sensations they could attribute to salvia. Only one volunteer commented on having had problems with studies, work or relatives due to the use of salvia. He complained that friends who do not habitually use psychotropic substances were worried about his experimenting with drugs.

Twenty participants (63%) commented that the effects of salvia were similar to those of other drugs. Subjects in this subgroup cited the following drugs, from most to least frequent: psilocybian mushrooms (55%), ayahuasca (20%), ketamine (20%), LSD (20%), marijuana (20%), MDMA (15%), opium (15%), poppers (15%), 2C-B (15%), *Amanita muscaria* (10%) and DMT (5%).

Finally, when asked if they would like to take salvia regularly, only 44% of the subjects responded affirmatively.

3.4. Retrospective assessment of the most recent salvia consumption

Participants responded to the subjective effect questionnaires recalling the effects they had experienced when they last took salvia. Fifty-six percent of the participants had used salvia for the last time within the preceding month, and 38% had last used salvia between the preceding month and the preceding year. Only 6% of the participants had used salvia more than a year ago.

The preparation or part of the plant they had used on this last occasion was the extract in 91% of the cases and the leaves in 6% of the cases, while 3% declared having used a combination of smoked leaves plus smoked extract. Regarding the route of administration, 72% had smoked the extract, whereas 19% had combined smoking the extract and placing the extract sublingually. Two volunteers (6%) had smoked the leaves and one volunteer (3%) had combined smoking both the leaves and the extract.

As to the intensity of the experience, all participants declared having experienced psychotropic effects; these were “slight” for 6% of volunteers, “moderate” for 22% of the sample, “intense” for 12%, “very intense” for 41% and “extremely intense” for 19%.

The onset of effects was found to be “instantaneous” by 31% of the volunteers, “less than a minute” by 57% of the volunteers,

Table 1
Volunteers' written descriptions of the best and worst aspects of salvia and any unpleasant after-effect

Best things about using salvia	<i>n</i>	Worst things about using salvia	<i>n</i>	Unpleasant after-effects	<i>n</i>
The "trip", entering another reality	13	Short duration	12	Tiredness	4
Laughter, happiness, well-being	9	Lack of control over the experience	5	Heaviness of head, like after smoking many marihuana joints	4
Separation from body, dissociation	6	Unpleasant after-effects	4	Dizziness	3
Visual effects	5	None	4	Physically exhausted	3
Rapid onset of effects	3	Unpleasant physical effects	3	Grogginess	1
Its great potency	3	Excessively intense	2	Mental slowness	1
Relaxation	2	Effects are unreliable	1		
Perceptual modifications	2	Onset too rapid	1		
The "high"	2				
Loss of consciousness	2				
Novelty	2				
Pleasant after-effects	1				
Mental clarity	1				
Escape	1				
Auditory effects	1				
Dizziness	1				

n: number of subjects reporting a specific effect.

"from 1 to 5 min" by 6% of the volunteers. Only one volunteer (3%) declared that "from 5 to 15 min" had elapsed and another (3%) declared that "half an hour had elapsed". Separating by route of administration, the onset of effects after smoking the extract was found to be "instantaneous" or "less than a minute" according to 91% of participants who chose this route. Only 67% of those participants who combined sublingual extract plus smoked extract described the onset with one of these two categories.

Table 2
Mean (S.D.) scores obtained for the HRS, ARCI and APZ questionnaire subscales

HRS	Scores
Somaesthesia	1.42 (0.62)
Affect	1.66 (0.53)
Perception	1.53 (0.88)
Cognition	1.32 (0.70)
Volition	1.98 (0.55)
Intensity	2.50 (0.53)
ARCI	Scores
A	4.41 (1.81)
BG	-0.34 (1.64)
MBG	5.75 (3.06)
PCAG	2.75 (3.38)
LSD	4.25 (2.43)
APZ	Scores
OSE	6.09 (3.44)
AIA	6.28 (4.30)
VUS	4.78 (3.99)

A: amphetamine scale; BG: benzedrine group; MBG: morphine-benzedrine group; PCAG: pentobarbital-chlorpromazine-alcohol group; LSD: lysergic acid diethylamide scale. OSE: Oceanic Boundlessness; AIA: Dread of Ego-Dissolution VUS: Visionary Restructuralization.

The duration of effects was described as "less than a minute" by 6% of participants, "between 1 and 5 min" by 60% of participants, "between 5 and 15 min" by 19%, "between 15 and 30 min" by 9% of participants. Only one volunteer (3%) described the duration to be "between 30 min and 1 h" and another (3%) described duration "between 1 and 2 h". Separating by route of administration, 70% of those who had smoked the extract chose the options "less than a minute" or "between 1 and 5 min", compared to 50% who combined sublingual plus smoked administration. Effects lasting longer than 5 min were described by 13% of participants who smoked the extract, and by 33% of participants who combined sublingual plus smoked.

3.4.1. *HRS, ARCI and APZ questionnaires.* Table 2 shows mean scores and standard deviations for the different subscales of these three questionnaires.

3.4.2. *STAI-S.* A mean (S.D.) score of 27.3 (8.5) was obtained for the STAI-S questionnaire. Separated by gender, scores of 26.9 (1.6) were obtained for male participants and 27.8 (2.8) for female participants.

4. Discussion

Results from the present study show that awareness and involvement with salvia appears to be a recent phenomenon. Most participants had had their first contact with salvia during the last year, and had consumed it on average only on two occasions, mainly smoking the extract, which almost all participants had acquired in "smart shops". It is worth mentioning here that the survey was conducted during the second half of 2003 and the first-half of 2004. In February 2004 a decree from the Spanish government prohibited the sale of salvia in the country (www.boe.es, number 32, 6 February 2004), but the product was still available for some months after that date. It is likely that Spanish users will now turn to internet sites or to "smart shops"

in other countries, such as The Netherlands, in order to purchase the product.

Although the effects of salvia were compared by the participants to those of other psychedelics, they differed in various aspects, particularly their extremely short duration. The effects seem to be by far the shortest amongst perception-modifying drugs, surpassing intravenous DMT (Strassman et al., 1994). Other important qualitative differences found are discussed below.

Scores on the HRS subscales confirm the psychedelic-like effects of salvia. Mean scores on all but one subscale (cognition) were higher than the values our group had obtained in two clinical trials in which we evaluated the effects of fully psychotropic doses of ayahuasca equivalent to 0.50–1.0 mg DMT/kg body weight (Riba et al., 2001b, 2003) and fell between the scores obtained for intravenous doses of 0.2 and 0.4 mg DMT/kg body weight (Strassman et al., 1994). Interestingly, the score in the volition subscale, which reflects the subject's degree of incapacitation, is the highest ever observed by our group in clinical (Riba et al., 2001b, 2003) and in survey studies (Riba et al., 2001a) and is even larger than that recorded by Strassman and colleagues after the highest intravenous DMT dose they administered (Strassman et al., 1994).

The pattern of scores on the ARCI shows high values for the MBG and LSD subscales. We have also observed high scores on these subscales following ayahuasca (Riba et al., 2001b, 2003) and they highlight the coexistence of somatic and dysphoric effects with positive mood. A high score in the A scale and a low score in the BG are also typical of the psychedelics. Although these drugs display stimulant-like properties, they do not lead to high scores in the BG scale, which measures subjectively-perceived intellectual efficiency. However, what is remarkable about salvia is the score obtained in the PCAG subscale. The score is unusually high for a psychedelic. High scores on the PCAG subscale have usually been reported in individuals experiencing "fatigue, weakness and sluggishness" after sedatives, such as alcohol, benzodiazepines and the opiate pentazocine (Arasteh et al., 1999).

Scores on the APZ-OSE subscale provide insight into the high degree of derealization experienced by the participants, in line with the most frequently cited positive aspect of the drug, i.e. the sensation of entering another reality. The score obtained is higher than that observed by our group after the administration of an ayahuasca dose corresponding to 0.8 mg DMT/kg body weight (Riba et al., 2002). The APZ-AIA and APZ-VUS were also higher than in the mentioned study, pointing out the high intensity of the derealization and visionary phenomena induced by salvia.

Scores on the STAI indicated levels of state anxiety above the normative mean both for male and female subjects. The obtained values fall between percentiles 70 and 75 for the males and percentiles 65 and 70 for the females (Seisdedos, 2002). These results indicate that the experience induced by salvia causes a certain degree of anxiety. Taking into consideration these STAI scores, elevations in the PCAG can be interpreted as reflecting an incapacitating rather than an anxiolytic effect. This interpretation is in line with the decreased ability to interact with them-

selves or their surroundings reflected by the high HRS-Volition score and the marked degree of derealization and anxious depersonalization reflected by the APZ-OSE and APZ-AIA subscales, respectively. Thus, the pattern of responses obtained for salvia with the self-assessment instruments administered would reflect a psychedelic effect profile accompanied by a highly modified perception of external reality and a decreased ability of the individual to interact with themselves or their surroundings.

An interesting aspect of the subjective effect profile of salvia is the simultaneous high scores on the LSD and PCAG scales observed. This is not a characteristic feature of the classical psychedelics displaying serotonin-2A agonist activity. However, this unusual pattern combining modifications in somatic-dysphoric effects and sedation/impairment has been reported for agonists of the opioid kappa receptor. Thus, pentazocine (Arasteh et al., 1999; Zacny et al., 1998) and enadoline (Walsh et al., 2001) have been shown to elevate scores in the LSD and PCAG scales. At high doses, these drugs can cause modifications in visual perception and depersonalization (Walsh et al., 2001), which has led some authors to describe kappa receptor agonism as capable of inducing "psychotomimetic" effects (Pfeiffer et al., 1986; Walsh et al., 2001).

The present results constitute a preliminary approach to the subjective effects of salvia. The investigation has several limitations associated with its naturalistic and exploratory nature. Information was obtained from a small sample of experienced psychedelic/hallucinogen users. These volunteers were regular users of other psychoactive agents such as cannabis and had experimented with rarely used drugs like ayahuasca. The investigators had no control over the salvia doses consumed, and the possibility of an interaction with the participants' daily cannabis use cannot be ruled out. The pattern of subjective effects observed may therefore be difficult to extrapolate to the general population or to other drug users unfamiliar with psychedelics/hallucinogens. Also, the retrospective assessment performed does not substitute for the immediate assessment of the psychotropic effects of salvia, ideally in the context of clinical trials administering known doses of the drug and implementing optimal designs.

To sum up, smoking extracts of salvia appears to be the most common form of use of the drug among recreational users. In the sample studied, this form of administration led to a very fast onset of effects which were intense but short-lived. The psychotropic effects reported bear similarities to those induced by the classical psychedelics regarding changes in perception, mood and somatic sensations. However, the increased derealization observed and the consequent decrease in the ability to interact with themselves and their surroundings appears to be particularly high for salvia. Although the perception- and reality-modifying potency seems higher, the profile of subjective effects induced by salvia is compatible with that of other kappa agonists, thus supporting the activation of this receptor as the drug's mechanism of action in humans. However, considering the limitations associated with field investigations, the reported results should be considered as preliminary. Carefully planned clinical studies are warranted to further elucidate the pharmacology of salvia in humans.

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