

# Salvia divinorum induces body awareness changes comparable to metamorphic symptoms in the Alice in Wonderland syndrome

Jan M Keppel Hesselink<sup>1,2\*</sup>

<sup>1</sup>Department of Health, University of Witten, Herdecke, Germany

<sup>2</sup>Institute for Neuropathic Pain, Bosch en Duin, Netherlands

## Abstract

Modern rituals based on the use of shamanic plants are becoming more popular in the European countries and in the USA since the last decades. *Salvia divinorum* (SD) is such a plant, for ages and still used by the Mazatec shamans for initiation purposes. SD contains a great number of diterpenes of which Salvinorin A is quite remarkable, as to date it is the strongest psychedelic plant compound we know of. Its high affinity to the kappa opioid receptor (KOR) however does not explain all of its effects. We will highlight a special effect related to the sudden and drastic changes in body schema after administering SD extracts, metamorphic symptoms, especially macro-somatognosia, in which one feels that the body or its parts are growing taller or larger, which resemble one of the key symptoms of the Alice in Wonderland syndrome. We will discuss these phenomena in the light of the neurophenomenological concepts of our body schema and cortical spreading depression.

## Introduction

Following the synthesis of LSD by Albert Hoffmann in 1938, the pharmaceutical company Sandoz introduced the compound as a commercial drug under the trade-name 'Delysid' for various psychiatric indications in 1947, and psychiatrists started using it to better understand the mind of the schizophrenic patient.

We discovered that Salvinorin A (methyl (2S,4aR,6aR,7R,9S,10aS,10bR)-9-acetyloxy-2-(furan-3-yl)-6a,10b-dimethyl-4,10-dioxo-2,4a,5,6,7,8,9,10a-octahydro-1H-benzo[f]isochromene-7-carboxylate), a strong psychedelic diterpene in SD, might be of use in better understanding the genesis of aura's in migraine, but especially the metamorphic symptoms of the Alice in Wonderland syndrome. For a cluster of certain SD effects, the focus of this paper, we introduce the term 'metamorphic', from 'morph' (meaning form), and 'meta' (meaning change). These metamorphic experiences induced by SD are extremely haptic, interfering with and redefining our body schema, and we suggest referring to these haptic effects as metamorphemes. The SD effects are remarkably similar to the metamorphemes reported in the Alice in Wonderland syndrome, and the genesis of the changing haptic sensations of the body follows a pattern which also points to cortical spreading depression in the somatosensory areas of our cortex. Haptic sensations are those relating to the sense of touch and proprioception, as in the sense of the relative position and shape of one's own parts of the body.

*Salvia divinorum* (SD), an ancient sacred plant for Mexican shamans, since some decades has found its way into the global world as a psychoactive and legal food supplement [1].

Since the first description of its active constituent, Salvinorin (or Divinorin) A, a highly selective kappa-opioid receptor (KOR) agonist based on a unique diterpene structure (not an alkaloid-opioid structure), many pharmacological findings have been published. Some

papers warned for abuse, although this proved to be extremely rare, and mostly only in case of multi-dependent users. Frequent users may have a dependent personality structure, and nearly always co-use Cannabis or stronger drugs [2]. As often, these rare cases however induced legislation, and some countries started to criminalize SD, without objective reasons related to a thorough analysis of its effects and risks [3]. Most people who experiment with SD however do not transition to frequent or long-term use [4]. Already as early as in 2004 in a sample of 500 users it was found that SD was used most often to explore altered consciousness or to have a spiritual/mystical (transpersonal) experience [5]. Tranacchi (2018) pointed out that since the early 1990s a new paradigm emerged among people experiencing with psychedelic compounds, and these substances were re-defined as entheogens, compounds which facilitate the experience of divinity [8]. Entheogens users engages with sacred plants, or 'plant-teachers', in order to grow spiritually. SD is regarded as a sacred plant, and it enables the user to enter the 'Salvia Space', resulting in accounts of experiences in narratives of neoshamanistic peak-experiences [8]. In a previous paper, we discussed a neo-shamanic ritual using the Blue Nile Lilly extract as an example of a modern ritual created in the Western world and the putative relevance of one of its compounds, nuciferine for psychiatry [7]. The value of Salvinorin A for psychiatry is still unknown, but it seems important to us to highlight in this paper the fact that many users of SD report strange haptic sensations of the body,

\*Correspondence to: Jan M Keppel Hesselink, Institute for Neuropathic Pain, Bosch en Duin, Netherlands, E-mail: jan@neuropathie.nu

**Key words:** body schema, cortical spreading depression, migraine, macro-somatognosia, Salvinorin A

**Received:** December 10, 2018; **Accepted:** January 16, 2018; **Published:** January 21, 2018

sometimes leading to total morphing into other shapes, and sometimes ending in a bodiless awareness.

We will especially focus on these specific haptic experiences related to a changed awareness of our body and the impressive metamorphic changes in the perceived body schema up to the vanishing of all bodily sensations in the light of modern neuropsychology and related to the aura symptom in migraine, and to the symptoms occurring in the Alice in Wonderland syndrome.

### Body schema in the Alice in wonderland syndrome

What in general is referred to as ‘body schema’ codes the position of body parts in space for the guidance of action and is mainly based on tactile input combined with proprioceptive information [8]. The body schema is continuously updated as our body moves around. The cerebral basis of the body schema remains unclear, in general it is thought that the superior part of the posterior parietal cortex plays an important role. The experiences after intake of SD mimics the effects of incongruent visuo-tactile stimulation on the body which also results in feelings of dis-ownership and being out of ones’ own body. Such experiences might perhaps shed some light on body representation disorders, mysterious disorders involving the anatomical substrate that underlies our mental representation of the body and syndromes such as the Alice in Wonderland syndrome. Certain higher cortical pathologies such as asomatognosia result in body parts which are ‘missing’ or disappearing from corporal awareness, from the body schema. Such disorders of the body schema are often a result of premotor, parietal and posterior insular area lesions [9].

Lippman was the first in 1952 to describe a migraine equivalent defined by the feeling that certain parts of the body became distorted in size and shape and called it a distortion of the body image [10]. The second patient he described experienced moments where the left ear was ballooning out 6 inches and more. The third patient of Lippman described her head becoming big and bigger and very light, so that it floated upwards to the ceiling. One of his patients referred to the odd body sensations as a Tweedledum and Tweedledee feeling, referring to the characters in Lewis Carroll’s *Through the Looking-Glass*. Lippman pointed out that Lewis Carroll himself was a migraineur.

### Haptic and body morphing experiences after the use of SD

We will present some narratives, easily accessible via the Erowid Experience Vaults, coordinated by a non-profit educational organization that provides information about psychoactive plants and chemicals [11]. The name ‘Erowid’ refers to ‘Earth Wisdom’ (er meaning ‘earth,’ exist,’ and ‘be born’ and wid meaning ‘knowledge’ / ‘wisdom’ or ‘to see’) [12].

A central experience reported by many users of SD is related to the haptic realm: physical experiences of transformations of the own body and massive shifts in our body scheme, as in our internal awareness of our body and the relationship of body parts to one another. These haptic experiences are so profound, that one can at the end lose all sense of being a body, and subsequently totally dissolves in a state of bodiless consciousness. The latter is also quite common in experiences using ketamine, often this experience is referred to as becoming a ‘disembodied entity’. However, the SD experience is much more intense, as one feels the entire transformation of the natural state of the body, the known body schema into all kinds of weird states of body awareness. The psychopharmacological phenomenology has not yet recognized that these metamorphemes are playing a central role in many SD experiences: fragmentation and the dissolving of

the internally perceived body schema. We explicitly chose the term body schema rather than body image, as body image is based on our cognitions (our image how we look like), while body schema is more linked to vital haptic experiences and the modus operandi of our body.

### Experiences: morphing of the body schema

Due to modern technologies, everyone is familiar with morphing phenomena: the smooth change from one image to another via small gradual steps using computer animation techniques. But not only visual images can morph from one shape into another, our body schema can also morph, as it clearly does under the influence of SD use. The writer himself experienced a number of such haptic morphing experiencing after exploring the effects of extracts of SD on himself and this triggered a further exploration into the phenomenology of these effects and its neurophysiological base related to the metamorphic experiences as described in the Alice in Wonderland syndrome. We now present a number of experiences related to haptic changes in body awareness.

1. I was trapped into the spiral, and, ironically enough, I was also trapped into thinking this, over and over, and over again. I could feel my face decomposing into layers, and I could feel this infinity of layers melting into the flow that fed the spiraling patterns. It was a physical sensation, not just thoughts popping up at the right time, but I could have sworn that I was back in my physical body, and that it was actually decomposing into layers, towards my right, and into the spiraling flow [13].

2. At first, after holding in the smoke for about 30 seconds, I just breathed out and felt a little stoned. There was a sensation of pressure around me, and then I kind of felt like I was being smeared sideways. I lay down, and suddenly the effects hit me very strongly. I was lying on a Persian carpet, and I had very strong sensations of merging with it. It is hard to explain, but I felt as if I was being pulled apart by very harsh waves that were cutting through my being. I no longer had a normal body, but instead had a sliced-up consciousness that felt both confused and fearful. As the effects came on even stronger, I started to lose my thoughts and my sense of where I was. It was a very physical sensation, not just a mental one. I can’t stress enough how real it felt, like I was actually physically being rearranged, and disassembled.

Then, after about a minute, I lost all sensation of having a body or mind. Whereas a few moments ago I felt like I was being cut apart, I now felt that all my molecules had somehow been spread evenly over infinite space. Whilst it may sound ridiculous now to say that I felt I was touching the edges of space, at the time it was a very real and very powerful experience [14].

3. I felt gravity’s pull, but it was pulling me sideways. I felt an extremely strong tug downward, and this intensified as the trip became more and more intense. Suddenly, I felt like I couldn’t grasp what I was seeing anymore. This inability to grasp the I trip, coupled with unbearable pins and needles and an extreme downward pull, started to create some sensation of self (or a body) – but I felt like it was stretched out over the entire field of my vision: I had become the 2-dimensional image of this warped and constantly moving alternate dimension. Suddenly it began to fall apart, and I felt like I was freefalling through this picture... while I was the picture... The only way I can honestly describe how I felt falling was down and to the right, the 3-dimensional world fell apart and I could only perceive things in a 2-dimensional light [15].

4. After a few seconds I felt like I had an electrical current running through my entire body, as numb and painful as pins and needles. I

also felt very aware of gravity, but it wasn't pulling me down, it was like something in my bowel was pulling me down and to the left. Like I had an imaginary electrified rope pulling on every muscle in my body at once [16].

5. My own experience was induced by the inhalation of one puff of a 10x extract of SD, and within seconds I felt my body change – from above a great number of small silver hands grabbed my body and from below the same number of green-black hands did the same, and slowly all these hands pulled me, my body extended and extended, till the experience of having a body vanished totally. In a subsequent experience, I felt as if the feet were elongated in a slow pace, and the elongation process crept up from feet – knees – pelvic area – further to chest and finally the head – after which there was no bodily sensation left. The entire process was like a wave of elongation moving from toes up to the top of my head. This experience I directly understood as an induced migraine aura, but not of the visual cortex, but of the somatosensory cortex. I had experienced auras before, as in migraine sans migraine (experiencing visual aura without headache), and the way an aura moved was directly comparable to this somatosensory experience.

All these experiences seem to match totally with the experience Alice had, in Wonderland (Figures 1 and 2):

'Curiouser and curiouser' cried Alice. She was so much surprised that for the moment she forgot how to speak good English. 'Now I am opening out like the largest telescope that ever was! Goodbye feet!' For when she looked down at her feet, they seemed to be almost out of sight they were getting so far off. 'Oh, my poor feet, I wonder who will put on your shoes and stockings for you now, dears? I'm afraid I shan't be able!'"

Many salvia users report something which is referred to as the 'Salvia Gravity effect' after using SD. This effect is 'a feeling of being pulled, twisted, kneaded or a feeling of intense cosmic gravitational effects far greater than those of Earth' [17]. Hand in hand with this



Figure 1. 1866 The experience of Alice in Wonderland where her body morphs

## CHAPTER II.

### THE POOL OF TEARS.

"Curiouser and curiouser!" cried Alice (she was so much surprised, that for the moment she quite forgot how to speak good English); "now I'm opening out like the largest telescope that ever was! Good-bye, feet!" (for when she looked down at her feet, they seemed to be almost out of sight, they were getting so far off) "Oh, my poor little feet, I wonder

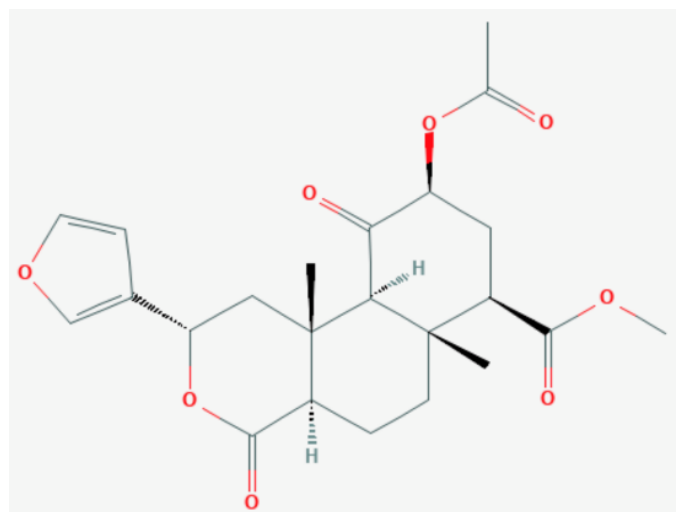


Figure 2. The diterpene salvinorin A from Salvia divinorum (C<sub>23</sub>H<sub>28</sub>O<sub>8</sub>): a non-opioid molecule with high affinity for the KOR receptor (PubChem open chemistry database)

phenomenon is what users refer to as 'changes in felt bodily form' described as 'non-painful sensations of being stretched horizontally or vertically into infinity, splitting into two halves, and a variety of other sudden changes' [18].

### Pharmacology of Salvinorin A

The psychoactive effects are quite amazing and there is consensus that these psychedelic effects are quite different from those induced by other psychoactive compounds, such as Cannabis, LSD, DMT etc. Salvinorin A is a highly selective KOR agonist (Figure 1) [19]. It also has influences directly or indirectly on the functionality of the endocannabinoid system, the dopaminergic system and possibly affinity to the muscarinic acetylcholine receptor [20-21]. KOR receptor activation via Salvinorin A leads to the inhibition of dopamine turnover in the nucleus accumbens, leading to transient feelings of depression [22]. However, it has also dopaminergic activity on its own, independent of the KOR mechanism [23]. Most probably it has D2 agonistic properties [24]. The described neurotransmitter systems based on the KOR and the dopaminergic and cannabinoid systems however cannot totally explain the in general classified as 'weird' somatosensory sensations of morphing, resembling the Alice in Wonderland syndrome. Salvinorin A in this context remains a mystery, and future PET scanning may shed light on the remarkable rimple of metamorphic effects induced shortly after using SD.

### Discussion

Due to modern psychophysiology research related to our body schema, its perceived modifications as in the phantom phenomena and morphisms, it is hypothesised that our central nervous system not only supports the normal body-awareness, based on the sensorimotoric cortical homunculus, but also support a more primitive and global neural representation that is responsible for mapping not only the body schema but also the space around it as well, the so called 'peripersonal space' [25]. From recent neurophysiological studies, we know that bimodal neurons in the posterior parietal and dorsal premotor areas respond both to tactile stimuli on the skin as well as to visual stimuli. It is this interaction which defines the peripersonal space [26]. The ventrolateral occipito-temporal cortex may play an important role here, as it is an area capable of detailed visuo-haptic shape processing [27].

In various epileptic disorders as well as in migraine, body dysmorphic symptoms occur, the most well-known is described as the Alice in Wonderland syndrome. Here patients experience bizarre perceptual sensations such as the morphing of an ear into something of giant ear [28]. Migraine not only leads to migrating visual aura's, but the same cortical spreading depression can of course also influence other cortical areas where our body schema resides. The migration of a visual aura has clearly phenomenological resemblances to the migration of haptic sensations after the use of SD, which also propagates like a slow sort of rimpling effect over the entire body. The fact that the body schema starts to morph, mostly elongate, at one specific part, for instance the feet, and subsequently, step by step starts to involve ankle, under leg, knee, upper leg, pelvis, abdomen, creeping up to the head, and at the end resulting in the total vanishing of the body awareness is indicative for a cortical spreading depression. Therefore, we postulate that the Alice in Wonderland syndrome is based on the same mechanism, a cortical spreading depression, whereby the exact neurotransmitter involvement is not clear, but may be related to interactions between the MOR system and the endocannabinoid system.

## References

- Heinrich M, Casselman I (2018) Ethnopharmacology—From Mexican Hallucinogens to a Global Transdisciplinary Science. In *Ethnopharmacologic search for psychoactive drugs: 50th anniversary symposium* 2: 316-224.
- El-Khoury J, Baroud E (2018) Case series: Salvia divinorum as a potential addictive hallucinogen. *Am J Addict* 27: 163-165. [Crossref]
- Babu KM, McCurdy CR, Boyer EW (2008) Opioid receptors and legal highs: Salvia divinorum and Kratom. *Clin Toxicol (Phila)* 46: 146-152. [Crossref]
- Croff JM, DeJong W (2018) Predictors of Salvia divinorum Use Among a National Sample of Entering First-year US College Students. *The International Journal of Alcohol and Drug Research* 7: 10-15.
- Baggott, MJ, Erowid E, Erowid F, Mendelson JE (2014) Use of Salvia divinorum, an unscheduled hallucinogenic plant: a web-based survey of 500 users. *Clinical Pharmacology and Therapeutics* 75: 72.
- Tramacchi D (2018) Entheogens, elves and other entities: Encountering the spirits of Shamanic plants and substances. In *Popular Spiritualities - Chapter 8* in Hume L (ed) *Popular Spiritualities: The Politics of Contemporary Enchantment*, Routledge. 91-104.
- Keppel Hesselink JM (2008) Blue Nile flower rituals from the perspective of transpersonal psychology- the role of nuphar and its putative value as an antipsychotic drug. *Edelweiss Psysi Open Access* 1: 22-24.
- van Stralen H, Dijkerman C (2011) Central Touch Disorders. *Scholarpedia* 6: 8243.
- Vallar G, Ronchi R (2009) Somatoparaphrenia: A body delusion. A review of the neuropsychological literature. *Exp Brain Res* 192: 533-551. [Crossref]
- Lippman C W (1952) Certain hallucinations peculiar to migraine. *J Nerv Ment Dis* 116: 346-351. [Crossref]
- Psychoactive Plants and Drugs. Available from: <https://erowid.org/psychoactives/psychoactives.shtml>.
- Erowid. Available from: <https://en.wikipedia.org/wiki/Erowid>
- The Scary Life of a Cell in an Astral Body by dqr. <https://erowid.org/experiences/exp.php?ID=111977>
- An Intense Lesson in Respect for Life by Yosh. Available from: <https://erowid.org/experiences/exp.php?ID=33014>
- Goodbye Reality, Goodbye Universe by Hubert Cumberland. Available from: <https://erowid.org/experiences/exp.php?ID=86484>
- The Fire in Plato's Cave by s david. Available from: <https://erowid.org/experiences/exp.php?ID=102590>
- The Salvia Gravity Phenomenon. Available from: [https://www.reddit.com/r/Salvia/comments/3qwkj3/the\\_salvia\\_gravity\\_phenomenon/](https://www.reddit.com/r/Salvia/comments/3qwkj3/the_salvia_gravity_phenomenon/)
- Salvinorin A. Available from: [https://psychonautwiki.org/wiki/Salvinorin\\_A](https://psychonautwiki.org/wiki/Salvinorin_A)
- Roth BL, Baner K, Westkaemper R, Siebert D, Rice KC, et al. (2002) Salvinorin A: a potent naturally occurring nonnitrogenous kappa opioid selective agonist. *Proc Natl Acad Sci U S A* 99: 11934-11939. [Crossref]
- Xu X, Ma S, Feng Z, Hu G, Wang L, et al. (2016) Chemogenomics knowledgebase and systems pharmacology for hallucinogen target identification-Salvinorin A as a case study. *J Mol Graph Model* 70: 284-295. [Crossref]
- Kivell B, Uzelac Z, Sundaramurthy S, Rajamanickam J, Ewald A, et al. (2014) Salvinorin A regulates dopamine transporter function via a kappa opioid receptor and ERK1/2-dependent mechanism. *Neuropharmacology* 86: 228-240. [Crossref]
- Ebner SR, Roitman MF, Potter DN, Rachlin AB, Chartoff EH (2010) Depressive-like effects of the kappa opioid receptor agonist salvinorin A are associated with decreased phasic dopamine release in the nucleus accumbens. *Psychopharmacology (Berl)* 210: 241-252. [Crossref]
- Phipps SM, Butterweck V (2010) A new digitized method of the compulsive gnawing test revealed dopaminergic activity of salvinorin A in vivo. *Planta Med* 76:1405-1410. [Crossref]
- Seeman P, Guan HC, Hirbec H (2009) Dopamine D2 High receptors stimulated by phencyclidines, lysergic acid diethylamide, salvinorin A, and modafinil. *Synapse* 63: 698-704. [Crossref]
- Moseley GL, Gallace A, Spence C (2012) Bodily illusions in health and disease: physiological and clinical perspectives and the concept of a cortical 'body matrix'. *Neurosci Biobehav Rev* 36: 34-46. [Crossref]
- de Haan AM, Smit M, Van der Stigchel S, Dijkerman HC (2016) Approaching threat modulates visuotactile interactions in peripersonal space. *Exp Brain Res* 234: 1875-1884. [Crossref]
- Lee MH, Bulte J, Op de BHP, Wallraven C (2016) Visual and Haptic Shape Processing in the Human Brain: Unisensory Processing, Multisensory Convergence, and Top-Down Influences. *Cereb Cortex* 26: 3402-3412. [Crossref]
- Evans RW, Rolak LA (2004) The Alice in Wonderland Syndrome. *Headache* 44: 624-625. [Crossref]

**Copyright:** ©2019 Hesselink JMK. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.