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Treating drug dependence with the aid of ibogaine: A qualitative study

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Background: Substance use disorders are important contributors to the global burden of disease, but current treatments are not associated with high rates of recovery. The lack of approved and effective treatments is acutely problematic for psychostimulants like cocaine and crack cocaine. One promising alternative in the treatment of drug dependence in general and psychostimulants in particular is the use of the psychedelic alkaloid ibogaine combined with psychotherapy. This was recently shown to induce prolonged periods of abstinence in polydrug users, including psychostimulants. However, drug dependence treatments cannot be comprehensively evaluated with reductions in consumption alone, with current recommendations including secondary outcome measures like craving, family and social relationship, quality of life, and self-efficacy. *Methods:* We therefore employed a directed approach to qualitative content analysis to evaluate the outcomes of a treatment combining ibogaine with cognitive-behavioral therapy based on data gathered from patient's reports obtained in semi-structured interviews. *Main findings:* The results revealed that patients benefited from the treatment in all the secondary outcomes, reporting decreases in craving and improvements in personal relationships, quality of life, and self-efficacy, thus supporting existing notions that treatments combining ibogaine and psychotherapy do have a therapeutic potential in the treatment of substance use disorders.

Keywords: ibogaine, cocaine, crack, addiction, treatment, dependence

INTRODUCTION

Recent estimates suggest that 149–271 million people used illicit drugs worldwide in 2009 (Degenhardt & Hall, 2012). This illicit drug use causes considerable morbidity and mortality in many countries (Degenhardt, Chiu, Sampson, & Kessler, 2008) and is an important contributor to the global burden of disease, directly accounting for 20 million disability-adjusted life years (DALYs) in 2010, representing a 52% increase since 1990 (Degenhardt et al., 2013; Whiteford et al., 2013). This illicit drug use is estimated to cause 10.9% of the DALYs in mental disorders (Whiteford et al., 2013). This scenario is aggravated using the legal drugs such as tobacco and alcohol reaching nearly one and three billion people, respectively (Degenhardt & Hall, 2012; Ng et al., 2014). This legal drug use significantly contributes to DALYs in more than 20 countries, with tobacco smoking increasing from third to second largest risk factor in the global burden of disease between 1990 and 2010, while alcohol drinking increased from eighth to fifth in the same period (Lim et al., 2012), alone contributing to 9.6% of mental health DALY (Degenhardt et al., 2013; Whiteford et al., 2013). A minority of these users develop substance use disorders such as drug dependence, but this is still a serious problem affecting 15–39 million people for illicit drugs, 76 million for alcohol, and more than a billion for tobacco (Degenhardt & Hall, 2012).

The search for effective drug dependence treatments is therefore paramount. Current available options include behavioral therapies (Carroll & Onken, 2005), pharmacotherapies (Vocci, Acri, & Elkashef, 2005), and combinations of both approaches (Potenza, Sofuoglu, Carroll, & Rounsaville, 2011; Stead & Lancaster, 2012). However, differences in treatments apply for different drugs abused, for example, opioids and stimulants (Badiani, Belin, Epstein, Calu, & Shaham, 2011). Alarmingly, for stimulants like cocaine and crack cocaine, effective pharmacotherapies are still lacking and the effectiveness of current behavioral and psychotherapeutic approaches is generally low (Karila et al., 2011; Nutt & Lingford-Hughes, 2008; Phillips, Epstein, & Preston, 2014; Shorter & Kosten, 2011). One possible route in the development of a new therapeutic approach for drug abuse and dependence is the use of ibogaine, an alkaloid extracted from the root bark of *Tabernanthe iboga* (Alper, 2001; Alper, Beal, & Kaplan, 2001; Brown, 2013). Ibogaine induces a prolonged state of modified consciousness with changes in perceptions, emotions, and cognition that makes it hard to be classified, but the most adequate categories seem to be hallucinogen or psychedelic (Alper & Lotsof, 2007).

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This is a class of substances including lysergic acid diethylamide (LSD) and psilocybin that is increasingly recognized as having important therapeutic potentials in the treatment of substance use disorders (Bogenschutz, 2013; Johnson, Garcia-Romeu, Cosimano, & Griffiths, 2014; Krebs & Johansen, 2012; Sessa & Johnson, 2015; Tupper, Wood, Yensen, & Johnson, 2015; Winkelman, 2014). Evidence of ibogaine efficacy in the treatment of drug addiction spans a wide variety of methods, from anecdotal evidences (Alper, 2001; Brown, 2013) to small clinical trials (Alper, Lotsof, Frenken, Luciano, & Bastiaans, 1999; Mash et al., 2001), also including improvements in some pre-clinical animal models of drug addiction (Benwell, Holtom, Moran, & Balfour, 1996; Dzoljic, Kaplan, & Dzoljic, 1988; Glick, Rossman, Rao, Maisonneuve, & Carlson, 1992; Glick, Rossman, Steindorf, Maisonneuve, & Carlson, 1991; Leal, Michelin, Souza, & Elisabetsky, 2003; Maisonneuve, Keller, & Glick, 1991; Parker, Burton, McDonald, Kim, & Siegel, 2002; Parker & Siegel, 2001; Rezvani, Overstreet, & Lee, 1995; Sharpe & Jaffe, 1990).

Physiologically, ibogaine is metabolized to noribogaine by CYP2D6 enzymes in the liver. Noribogaine has a much longer half-life, being detected in blood after 15 min from ingestion of ibogaine and remaining in relevant concentrations even days after ingestion and clearance of the parent compound. Both compounds are lipophilic, cross the blood–brain barrier, and interact with different receptors in the brain, including N-methyl-D-aspartate, opioid receptors (κ and μ), and sigma-2 receptor sites (Litjens & Brunt, 2016). Ibogaine also increases the levels of glial cell line-derived neurotrophic factor, a result related to its anti-addictive properties (He et al., 2005). Ibogaine may have important cardiotoxic effects mediated by its action at hERG potassium channels, resulting in prolongation of the QTc interval (Alper et al., 2016; Koenig, Kovar, Boehm, Sandtner, & Hilber, 2014; Koenig et al., 2013; Thurner et al., 2014), an effect related to fatalities after ingestion of the ibogaine or other materials, such as plant extracts (Alper, Stajic, & Gill, 2012).

In previous research with retrospective methodology, it was shown that a treatment combining ibogaine with cognitive therapy facilitated prolonged periods of abstinence (median of 5.5 months with one ibogaine session and 8.4 months with multiple ibogaine sessions) in drug-dependent patients who were considered as polyusers of alcohol, cannabis, cocaine, and crack (Schenberg, de Castro Comis, Chaves, & Da Silveira, 2014). This is the first evidence of efficacy of administering ibogaine in a sample whose drug problem was not majoritarily related to opiates, and therefore, it constitutes an alternative form of psychostimulant dependence treatment.

However, drug dependence is a chronic condition involving mental and physical health, social relationships, and quality of life. Therefore, a comprehensive evaluation of treatments for substance use disorders cannot be completely achieved by measuring only quantity and frequency of drug use (Dodge, Krantz, & Kenny, 2010; Tiffany, Friedman, Greenfield, Hasin, & Jackson, 2012). According to recent proposals, secondary outcome measures that should be considered in the evaluation of drug dependence treatments include craving, family relationships, network support, changes in self-efficacy, and quality of life (Tiffany et al., 2012). In this study, we employed a directed approach to qualitative content analysis (Hsieh & Shannon, 2005), also termed deductive content analysis (Elo & Kyngäs, 2008), to test the hypothesis that an ongoing treatment in Brazil combining ibogaine administration in a hospital with pre- and post-ibogaine cognitive therapy is beneficial to patients with substance use disorders.

MATERIALS AND METHODS

Sampling and recruitment

The study sample consisted of 22 drug-dependent patients, diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR, American Psychiatric Association, 2000) criteria. Recruiting was done by a staff at the clinic where the cognitive therapy was done. Patients participated in the research voluntarily and signed an informed consent agreement before starting the interview.

Sample characteristics

There were 7 women and 15 men in the sample. Participants ranged in age from 22 to 53 years, with an average of 33 years. The age of first drug use ranged from 10 to 30 years, with an average of 15 years. Drug use in life most commonly started with alcohol, cigarettes, and cannabis. The time since the ibogaine session ranged from 4 weeks to 4 years, with an average of 17 months. For 10 patients (45%), the primary drug was cocaine, and for 9 patients (41%), the primary drug was crack cocaine. Alcohol, cannabis, and heroin were the primary drug for one patient each. Other substances mentioned by some patients included “acid” (LSD), “ecstasy” (MDMA), mushrooms, solvents/inhalants, and amphetamines. Only one patient had previous experience with opioids. All participants were white and all but one were Brazilians. Twenty participants (91%) previously failed in drug treatments with sixteen (73%) having previously undergone treatments as inpatients at other clinics, in some cases against their own will. Only two patients (9%) had ibogaine with cognitive therapy as their first treatment for drug dependence. Six participants were unemployed (27%) at the time of the interview, nine resided with parents (41%), ten with the spouse (45%), one was living with the aunt, one with parents-in-law, and for one participant this information was missing in the transcripts. None of the participants had ever been in jail. Ten participants had university degrees, ten were enrolled in university studies, and two had never started a university degree. Eight patients self-referred as socioeconomic class A and fourteen as class B. Eleven participants were single and the other half were married. Six participants identified themselves as Catholics, one as Spiritist Catholic, two as Spiritists, one as Presbyterian, one as Atheist, one as Baptist, one as Theist, one as Christian, four as having spiritual beliefs unrelated to any specific religion, and for four participants this information was missing in the transcripts. To protect participant’s privacy, pseudonyms were adopted for this publication.

Therapeutic procedure

All the therapeutic procedures were conducted as private practice before the research was conducted. The treatment included cognitive therapy (Beck, Wright, Newman, & Leise, 1993; Beck & Liese, 1993) and relapse prevention (Larimer, Palmer, & Marlatt, 1999) and was provided in a private clinic in Brazil with psychotherapy sessions conducted both before and after administration of ibogaine, which took place in a hospital. Patients were psychologically and physically evaluated at the clinic by a multiprofessional team, including psychiatrists, psychologists, nurses, physiotherapists, and music therapists. Drug dependence diagnostics was reportedly established by the clinic staff using the diagnostic criteria from the DSM-IV-TR. The inclusion criteria for the ibogaine treatment were general conditions of good health, as measured by routine clinical exams (electrolyte levels, aspartate aminotransferase, alanine aminotransferase, bilirubin and fractions, gamma glutamyl transferase, creatinine, blood sugar, and hemogram), an absence of psychiatric comorbidities, strong psychological motivation to remain abstinent, and willingness to participate in the psychotherapy before and after ibogaine administration, with familial support. Exclusion criteria were pregnancy, surgery in the last 6 months, uncontrolled high blood pressure, uncontrolled diabetes, cardiac arrhythmias, renal insufficiency, hepatic insufficiency, Alzheimer's disease, and Parkinson's disease. Patients were required to stay abstinent at least 30 days at the clinic before ibogaine administration to prevent any unwanted pharmacological interactions between ibogaine and any other drug. They were advised to stay at the clinic or at home after the ibogaine session, away from other people, duties, or any kind of social activity for at least 7 days. Participants were only accepted into the ibogaine treatment if they agreed to comply with the psychological treatment.

Ibogaine hydrochloride was legally imported from a Canadian provider (Phytostan Enterprises, Inc.) and was orally administered in a private hospital with an average dose of 15 mg/kg for men and 12 mg/kg for women in a single administration early in the morning, as described in detail elsewhere (Schenberg et al., 2014). Patients were continuously monitored and accompanied by a physician during the whole duration of ibogaine's acute effects that lasted at least 8 hr, as previously described in detail (Schenberg et al., 2014).

Qualitative interviews

Semi-structured one-to-one interviews were conducted personally by a trained psychologist (MACC). Interviews were audio-recorded and later transcribed verbatim for analysis using UCLA's Center for Culture and Health cross-platform software for qualitative and mixed-methods research (Dedoose, 2014). Patients were reassured of anonymity and that the informations provided would be protected at all times to encourage them to speak honestly and openly. Interviews lasted about 1 hr and were conducted in the cognitive therapy clinic where patients had previously been treated. Issues covered at the interviews include basic sociodemographic data, previous drug use patterns (including drugs previously used), main drug of choice (if any), age of onset, reasons to start using drugs, first drug used in life (including alcohol and cigarettes), number of previous treatments attempted, family issues, professional issues, and a description of the subjective features during ibogaine acute effects as well as on their perceptions if and how ibogaine helped them recover from drug abuse.

Content analysis

To test the hypothesis that this treatment combining cognitive therapy with ibogaine sessions in a hospital helps patients overcome problems related to drug abuse and dependence, we employed a directed approach to qualitative content analysis. This methodology starts from a previous knowledge or from a present theory to orient the creation of relevant categories to better understand the data (Hsieh & Shannon, 2005). This methodology is very similar to, if not identical with, deductive content analysis, which aims to test a theory in a new situation (Elo & Kyngäs, 2008). Therefore, we hypothesized that patients benefited from this treatment centered on the use of the psychedelic alkaloid ibogaine, further supported with cognitive therapy sessions before and after ibogaine administration in a hospital. We started from a recent comprehensive proposal listing clinical outcomes that should be considered as secondary outcomes in drug dependence treatments, in addition to the primary outcome of abstinence. These outcomes include psychosocial functioning, changes in self-efficacy, craving, family support, network/social support, and quality of life (Tiffany et al., 2012). Therefore, we created a structured matrix of analysis based on these six categories and carefully studied the data choosing only the contents that fitted into the categorization frame (Sandelowski, 1993; Sandelowski, Docherty, & Emden, 1995). Selected quotes were translated to English by the authors for the sole purpose of this publication, and all names used are pseudonyms to protect privacy.

Ethics and confidentiality

All procedures for the interviews were previously approved by the Ethical Committee of Universidade Federal de São Paulo (UNIFESP) in Brazil. Participants signed informed consent stating that their participation was voluntary and that confidentiality would be kept at all stages of the research including any publication resulting from it.

RESULTS

Most patients were explicit about the importance of the experience with ibogaine in their recovery processes, mentioning that without the ibogaine session they would hardly had achieved the improvements they did. On the other hand, many were also keen to reinforce that without the accompanying cognitive therapy, the ibogaine session might not have been very useful. Because they felt in need of help to interpret and make sense of the contents of their subjective experience under the influence of ibogaine. Some were emphatic to say that this treatment was very different, and better, than many other treatments they had tried previously,

with ibogaine speeding up their psychological process and allowing them to achieve insights that seemed would take many years in different treatment modalities, as in the examples below:

Ibogaine speeds up the process of acceptance and [personal] growth that sometimes with conversation and knowledge it will take years, [and] ibogaine does it within hours (Paulo, 34)

I have never had any benefit from any treatment. The only one to which I truly commit myself, that I felt a big change with it, was this treatment I did with ibogaine (Ricardo, 25)

Family support

Patients reported visualizations, or perception of images with eyes-closed, during the acute effects of ibogaine, containing or related to childhood memories, with parents quarrelling and fighting. This was especially prominent for a patient who had problems related to alcohol consumption. Through these memories rendered in imagery and emotions, the patient achieves an insight of how his alcohol abuse habit was learned in the family and how the problem extended beyond his own behavior, involving a whole dynamics of family malfunctioning:

Mostly from my childhood, related to my parents quarrelling. I saw a lot of bad things. I saw my father bribing my mother with jewelry, flattering her with leisure activities, with superfluous things. I saw him drinking, falling down where he stored his drinks. [. . .] I could realize through these images that the origin of my chemical dependency mostly related to alcohol. This dependence has initiated with my grandparents (Pedro, 28)

In another direction, other patients reported gaining awareness of how they had failed to properly care for their children. Through the memories evoked during the ibogaine experience and the imagery experienced related to these memories, these patients realized how much they were suffering by not being close and caring for their children. Most felt regret toward this issue, or reported acquiring the capacity to assume their parenting role after the ibogaine experience, thus improving their family relationship and at the same time receiving more care and attention from the family:

Actually I really blame myself for not having spent more time with my son, you know? (Caio, 35)

. . . the courage to accept my role as a father, because I had not done it yet (Paulo, 34)

Other patients emphasized insights related to the emotional aspects of their familial relationships. Anger, hatred, fear, distrust, and unacceptance toward family behavior regarding the patient and his habits related to drugs were in some cases transformed into acceptance, trust, sadness, and forgiveness. These emotional processes resulted in improvements in feelings toward, and relation with, parents and the family as a whole:

I blamed my parents for everything and [pause] [now I] accept they're humans, they make mistakes, and value the life I have (Tiago, 26)

I could feel again my family acceptance, from my family towards me, you know? I regained trust to be a good father for my children, a good husband (Rodrigo, 35)

I did not accept my family, you know? This was something scaring to me, because I never saw it from this angle. And it came in a very strong way, a certainty came, to recover my family. I got very emotional, cried a lot (Lucas, 23)

Some of the family-related issues were felt as so intense, and the positive consequences so profound, that the patient wished for the whole family to undergo a similar process as he/she found with ibogaine:

I would like for everybody I love to do ibogaine, you know? My father, my mother, I would really like that, like a gift to themselves, I would really like to see them having the experience I had with ibogaine (Jonas, 29)

Network/social support

In addition to the issues of close relationships as in family issues, participants also referred that ibogaine helped them to be aware of problematic issues in friendships and social interactions during their period of using drugs. They got insights on how the friendships around drug use have particular dynamics, most of the time characterized by negative emotions and drug-reinforcing habits and group behaviors. Through these insights, they were able to compare the social relationships during drug use with social relationships outside of the drug use periods or outside of the circles of people they knew who used drugs. These comparisons, sometimes appearing as visualization of memories full of emotional content, clarified some patients on how people can behave toward them in constructive or destructive ways, wishing them well or not caring for them. This led to some benefits, insights and behavioral change in their friendship circles, helping them to stay away from drug use and drug reinforcing groups:

Relating to friends I think I got a new concept about people, I realized that they could damage me (Pedro, 28)

It's unmistakable, it is very clear, the change I had about the quality of people I relate to nowadays (Jonas, 29)

After taking it we start seeing who are the people that really make part of our life, who is really important [. . .] If I meet these people today, I greet them and go away. The friends I have today are my wife and my family, of course. I [also] have some acquaintances, they know about my problem, they respect me, they help me (Silvio, 32)

Psychosocial functioning

Through visualizations of memories and imagination of possible future scenarios in their life, some patients achieved important insights pertaining to their role in society, the job they would like to do, a business they would like to have, or how they should and really wanted to go back to school or university studies. Through this process of imagination and memory visualization, some patients realized how their drug abuse behaviors were severely keeping them away from activities they considered more important and rewarding in life than abusing drugs a lot of their time, and how they could have pleasure and rewarding activities doing more productive activities. One patient explicitly referred to what was perceived as some type of cognitive improvement in

reading, paying attention, focusing, and understanding of texts:

I saw myself in a Psychology university, I saw myself restarting from the beginning, I really saw myself slowly creating a solid foundation. Whenever I thought about working, I saw myself at the university. I realized I need to study, if I want to do this, this ibogaine showed to me, showed me in between lots of books, showed me in the corridor of a university (Cesar, 35)

I couldn't study anymore, I couldn't have pleasure anymore, couldn't understand things. I read an article but it took me three, four times to get into something. And after ibogaine, this was very clear to me, I could understand things much easier, I could understand the text, I could read it faster and with more clarity, with better discernment (João, 39)

Other patients, especially those that managed to keep a job despite drug abuse, reported improved functioning and more responsible behavior at work after the ibogaine treatment. They felt an increased willingness to do their jobs, more motivation to strive for progress in their professional careers:

On a professional level, I started to dedicate myself much more, I started making changes, wishing to . . . to evolve, to learn. Now I am studying restaurant management, I have other aims, you know? I want someday to have my own business, my place, to have my own restaurant, to have a goal (Joana, 26)

Things out there are now working better than ever, mainly in the development of my professional activities (Pedro, 28)

Leisure was also mentioned as an area where improvements could be felt after the treatment, with increased diversity of activities practiced and enjoyed. They referred to these activities as more rewarding than before the treatment, with an increased and intensified perception of the pleasure they can have while at leisure and how monotonous and repetitive their leisure activities were during their drug abuse periods. Enjoying some activities with family and friend also got a refreshed meaning and more profound significance:

I attend my soccer team games, I go with my wife, with my godfather, or I go out with my wife, my dog, or to exercise, to run. I developed a way of going on living (Silvio, 32)

I used to say I was free, that I did different sorts of things, that I was always innovating in my life. Then after stop using [drugs] I passed by my friends house, my friends from the times I used, [. . .] and they were in the same house, having barbecue in the same way with the same people. Then I said Fuck! I am here feeling great, I got out of that routine. This was the day I realized I did nothing new, my life was stuck always in the same thing, the same way (Joaquim, 34)

Quality of life

Overall improvements in quality of life following ibogaine sessions were mentioned, including the solution of previous unfavorable mood and lack of will to engage in activities and increased attention to the activities done at the present moment. Patients referred to a perception of general loss of desire to engage in things during drug abuse and an impoverished capacity to enjoy life and its activities during the time they were heavily abusing drugs. Through the imagery and feelings evoked by ibogaine, they gained a genuine interest in being alive and doing healthy activities and feel alright at the present moment:

I had lost desire to do anything, I lacked will to go to the gym, to the park, the cinema, I only wanted to stay home. After ibogaine the first thing I wanted to do was going to the park, to the movies (Ricardo, 25)

I enjoy every moment, every instant, you know? It doesn't matter if I make the same route everyday to work, I pay attention to the details, I look at a tree, at other things, and it makes me feel all right (Jonas, 29)

Another important aspect related to quality of life refers to better nutritional habits and enjoyment of food. Patients realized how poor was their nutrition and how they were not paying attention to what they ate, how fast they did it, and how these mechanic habit toward nutrition was taking away the pleasure that can be achieved with healthy foods and natural products, such as juices, fruits, and salad, things they hardly thought about while abusing drugs:

Now I'm looking at this again, [avoiding] drinking sodas, greasy food, and I am trying to adapt, to readapt. Trying to make it right with it (Paulo, 34)

Wanting to enjoy, eating fruits, salad, you know, drinking water [. . .] Healthy things, they're good. Water has a different taste, an apple is tasty, not that it wasn't, but it's more, has a fragrance like perfume (Felipe, 45)

I ate very fast, you know? I did not chew properly, I did not ate salad, and I started desiring these things (Ricardo, 25)

In parallel with this increased and improved attention toward nutrition, patients also mentioned gaining general health improvements through a refreshed willingness to practice sports and stay fit. Some patients referred to a renewed perception of respiration and of how much it is important and pleasurable to simple breathe fresh air and feel fit and healthy:

Things like sports and nutrition came very strongly in the following week, a need to do sports (Felipe, 45)

My breath improved, my nutrition changed, everything was now 100% (Joaquim, 34)

Other participants reported profound gains in general quality of life related to their basic and fundamental desire to stay alive and enjoy life itself more deeply and truthfully. They mentioned improvements in connecting with feelings of joy, happiness, to want to live and feel free, beautiful and smile for life, with deep feelings of gratitude toward the good things they can enjoy:

I came back in pure joy, the first days were even strange because it was so much joy. I came back and everybody said go look yourself in the mirror, look at your happy face (Luanda, 25)

Ibogaine brought back to me the desire to live. It brought back many sensations that were dead, so to speak. And, indirectly, with an intense emotional balance (Pedro, 28)

Very good, 1000% in well-being. Like if some chains had been removed, I used to be chained, arrested, then I was free, feeling free, you know? It is a very intense purity (Rosa, 33)

Craving

Reduced craving after the ibogaine sessions were mentioned for different drugs, either mentioning episodes that happened after the ibogaine treatment when patients again confronted drug use near them, or as stating how their feelings toward drug use and their effects had dramatically changed. Reduced craving to cigarettes included strong nausea and disgust toward tobacco smell. The reported changes are characterized as being very strong and sudden, to the point of surprising the patients on how their feelings toward drug consumption changed from a compulsive style to a repulsive and disgusting feeling after the ibogaine treatment, as if all the rewarding aspects of drug use and abuse were suddenly gone and substituted by a negative framework where the smells, taste, somatic feelings, and psychic effects were all of a sudden perceived almost entirely in its negative aspects:

It's unbelievable because you pass by on the street, you smell the cigarette, and I still get nauseated, I get sick, it's bad, I look those people and my god, they are killing themselves [. . .] I look, I can smell cigarettes from far, I can't stand those [people] who are smoking you know? It is not that I turned that boring former smoker, but it really makes me sick (Rosa, 33)

The action of ibogaine in cigarettes is something I am still living with. It makes me so nauseated. My wife smokes but no matter how much she brushes her teeth or whatever, the smell is there and it is terrible, yes it is terrible (Ricardo, 25)

Reduced craving were also mentioned by the only participant whose primary drug of choice was alcohol:

It eliminates craving, I don't want to drink (Robson, 53)

For patients whose primary drug was cocaine, there seemed to be a change in how they emotionally relate to the memories of their cocaine use, which seemed to change from a compulsory need to do it again toward a memory from something which was not interesting or attractive anymore:

The memory exists, but not the craving (Rosa, 33)

when I had craving, something in my head quickly thought about the good part, the taste, the feeling, the high, right? But if I think of drug now, when I think, I quickly think about the down side. It changed the perception I have regarding the drug (Ricardo, 25)

Similar to cocaine patients, participants whose primary drug of abuse was crack cocaine referred to an increased capacity to stay away from the drug and its users. This seemed to them to be true even if this required intense effort, anxiety, and distress, which was not mentioned as intensely and frequently by patients whose primary drug of choice was cocaine:

I walked with my father at the center of the city, saw people using crack, I felt disgusted, a very strange feeling [. . .]

The thought can come to you, you remember the drug but you can't take it. You can fight yourself, it is an inner struggle (Danilo, 28)

Others felt reductions in craving as an important outcome of their treatment, but even more fundamental and crucial was their feeling of recovering the ability to make choices regarding drug use:

Ibogaine eliminates craving, decrease craving, but it is your choice, it's all about choice. In life there is only choice (Julia, 26)

The main thing is to be able to choose again if you want to use or not, instead of using because of a need. That's the main thing (Tiago, 26)

Changes in self-efficacy

Participants also mentioned having insights and improvements about how they relate to their own strengths and weaknesses. They reported becoming aware of what they can and what they cannot do, including the planning of goals and objectives, the decisions of what is important to them, awareness of the reasons of their own actions, and how to cope with daily challenges, stress, and emotional discomfort. They refer to concepts closely related to personality, awareness, and consciousness, as if the ibogaine experience had allowed them to increasingly introspect and reason about themselves and their place in the world:

Table 1. Summary of the answers of drug dependence patients who have undergone combined treatment with ibogaine and psychotherapy. Categories were based on a directed qualitative content analysis approach using key elements in the evaluation of treatment of addiction according to Tiffany et al. (2012)

Category	Content
Family support	–Visions of childhood memories of family life
	–Acceptance of the parenting role by the patient
	–Improvement of feelings regarding family relationships
	–Desire that relatives also undergo ibogaine treatment
Network/social support	–Changes in social circles for more positive relationships
Psychosocial functioning	–The establishing of new roles as professionals or students
	–More responsible behavior at work
	–Improvement in leisure activities
	–Attention to citizenship and responsible role in society
Quality of life	–Increased willingness to engage in activities
	–Better nutritional habits
	–Willingness to practice sports and stay fit
	–Desire to enjoy life more deeply and truthfully
Craving	–Reduced tobacco craving
	–Reduced alcohol craving
	–Memories of cocaine use with the absence of craving
	–Increased capacity to stay away from drug and from drug users
	–Increased ability in making choices
Changes in self-efficacy	–Insight into relating to one's own strengths and weaknesses

Ibogaine acts directly in the person consciousness, in the mind, the ideas, the objectives, goals, in the actions and thinking. This is a fundamental thing [. . .] because it is still acting with great strength, making me take the right decisions at the right time and the right place (Pedro, 28)

You relate with the reason for your actions, like, why do I do this, and why do I do that? And so, you can change what you want to change (Tiago, 26)

Ibogaine makes you value what has value. It makes you consider what is important and to discard what's not important (Marcio, 48)

Though my problems obviously have not stopped to happen and appear, I changed in the face of them. So, I get to the end of my day very grateful, very happy (Jonas, 29)

The results of the selected categories and the emerging discourses are summarized in Table 1.

DISCUSSION

The psychological experiences elicited by acute ingestion of ibogaine HCL in high doses were interpreted by patients as having positive impacts in aspects of their lives currently considered important secondary measures in the evaluation of drug dependence treatments (Tiffany et al., 2012). Corroborating previous literature on ibogaine (Alper, 2001; Brown, 2013), patients reported decreased craving after therapeutic ibogaine sessions. However, while most of the literature reports ibogaine to decrease craving for opioids, the present data shows that this effect can also happen in alcohol, tobacco, cocaine, and crack cocaine users, suggesting this effect is not specific to opioid craving. Furthermore, according to the patients' experiences, ibogaine helped them to improve family and social relationship, engaging in study and professional activities, engaging in healthy nutrition, practicing sports and therefore generally improving their quality of life. The data also support positive changes in self-efficacy, with patients reporting increased capacity to make important decisions, to establish goals and aims, and to better cope with life difficulties and challenges through improvements in their capacity and willingness to introspect.

Overall, these results support the hypothesis that ibogaine can be helpful in the treatment of drug abuse and dependence. However, limitations must also be highlighted. The given sampling and recruitment were done by a staff where the cognitive therapy treatment was done, it is hard to discard biases in the selection procedure. However, once it is hard to get a random sample, given the illegality of ibogaine treatments in some countries and the low number of professionals doing it in Brazil, where ibogaine is currently unscheduled, we interpret that the data are still meaningful even if some selection bias might be present. Another limitation is that the treatment also included extended sessions of cognitive therapy and other therapeutic practices, such as music therapy, yoga, and group meetings. Therefore, not all those improvements can be uniquely and exclusively attributed to ibogaine sessions, and in fact some patients emphasized the importance of the combination of pharmacotherapy and psychotherapy to help them fully recover. Cognitive therapy in particular may have influenced the content of the patient's reports according to the therapeutic principles and goals. However, it is important to note that in the interviews and during the analysis process, we aimed to focus on aspects related to the ibogaine sessions and not to cognitive therapy or any other aspect of the treatment. Furthermore, most patients had previously failed other psychotherapeutic treatments, leading us to consider an important role ibogaine sessions may have played. Indeed, some reports sustain this interpretation, with patients stating that ibogaine was highly important and that without it they would not have recovered. However, it is also important to emphasize that the path to recovery involves actual changes in behavior, and therefore ibogaine should not be simply seen as a cure for drug dependence, in the sense that willingness to recover seems fundamental to truly achieve and implement long-standing changes in behavior and lifestyle. In this regard, it is also important to consider that patients had high socioeconomic status and educational levels, factors shown to influence the outcomes in drug dependence treatments (Wahler & Otis, 2014).

Given the series of fatalities related to ibogaine ingestion and its cardiotoxic effects, some safety caution is needed. This is especially important because the first fatality after ibogaine ingestion for the treatment of cocaine and crack dependence was reported in Brazil in June 2016 (Rede Agora Valinhos, 2016). The fatality was totally unrelated to this study, the clinic and the hospital where these patients were treated and, as far as we know, did not involve the use of ibogaine HCL from Phytostan Inc. The deceased was a 29-year-old man who had a cardiac arrest in a second ibogaine treatment that was done in a private clinic. Therefore, it is important to emphasize that all the patients who participated in this study had previously taken medical grade ibogaine HCL with dose precisely calculated for each patient, under constant medical supervision in a hospital, in a legal environment, thus increasing safety and patient trust in the process and in the therapeutic team.

In conclusion, the data support the notion that ibogaine can be therapeutically useful in a treatment combining both pharmacotherapy and psychotherapy among polydrug users. Given the current lack of effective treatments for drug abuse, especially for psychostimulants, new research should aim to better explore ibogaine's therapeutic potential, with caution to avoid adverse or serious adverse events like fatalities due to its cardiotoxic effects.

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Conflict of interest: BDRC has a financial interest in this work given that the ibogaine treatment is part of his private practice. All other authors declare no conflict of interest.

REFERENCES

Alper, K., Bai, R., Liu, N., Fowler, S. J., Huang, X. P., Priori, S. G., & Ruan, Y. (2016). hERG blockade by iboga alkaloids. *Cardiovascular Toxicology, 16,* 14–22. doi:10.1007/s12012-015-9311-5

Alper, K. R. (2001). Ibogaine: A review. *The Alkaloids: Chemistry and Biology, 56,* 1–38.

Alper, K. R., Beal, D., & Kaplan, C. D. (2001). A contemporary history of ibogaine in the United States and Europe. *The Alkaloid: Chemistry and Biology, 56,* 249–281.

Alper, K. R., & Lotsof, H. S. (2007). The use of ibogaine in the treatment of addictions. In T. Roberts (Ed.), *Psychedelic medicine: New evidence for hallucinogenic substances as treatments* (Vol. 2, pp. 43–66). London, England: Praeger Publishers.

Alper, K. R., Lotsof, H. S., Frenken, G. M., Luciano, D. J., & Bastiaans, J. (1999). Treatment of acute opioid withdrawal with ibogaine. *The American Journal on Addictions, 8,* 234–242. doi:10.1080/105504999305848

Alper, K. R., Stajic, M., & Gill, J. R. (2012). Fatalities temporally associated with the ingestion of ibogaine. *Journal of Forensic Sciences, 57,* 398–412. doi:10.1111/j.1556-4029.2011.02008.x

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text rev.). Washington, DC: American Psychiatric Association.

Badiani, A., Belin, D., Epstein, D., Calu, D., & Shaham, Y. (2011). Opiate versus psychostimulant addiction: The differences do matter. *Nature Reviews Neuroscience, 12,* 685–700. doi:10.1038/nrn3104

Beck, A. T., Wright, F. D., Newman, C. S., & Leise, B. S. (1993). *Cognitive therapy of substance abuse*. New York, NY: Guilford Press.

Beck, J. S., & Liese, B. S. (1993). Cognitive therapy. In R. J. Frances & S. L. Miller (Eds.), *Clinical textbook of addictive disorders* (2nd ed., pp. 547–573). New York, NY: Guilford Press.

Benwell, M. E., Holtom, P. E., Moran, R. J., & Balfour, D. J. (1996). Neurochemical and behavioural interactions between ibogaine and nicotine in the rat. *British Journal of Pharmacology, 117,* 743–749. doi:10.1111/j.1476-5381.1996.tb15253.x

Bogenschutz, M. P. (2013). Studying the effects of classic hallucinogens in the treatment of alcoholism: Rationale, methodology, and current research with psilocybin. *Current Drug Abuse Reviews, 6,* 17–29. doi:10.2174/15733998113099990002

Brown, T. K. (2013). Ibogaine in the treatment of substance dependence. *Current Drug Abuse Reviews, 6,* 3–16. doi:10.2174/15672050113109990001

Carroll, K. M., & Onken, L. S. (2005). Behavioral therapies for drug abuse. *The American Journal of Psychiatry, 162,* 1452–1460. doi:10.1176/appi.ajp.162.8.1452

Dedoose. (2014). *Dedoose Version 5.0.11, web application for managing, analyzing, and presenting qualitative and mixed method research data*. Los Angeles, USA: SocioCultural Research Consultants.

Degenhardt, L., Chiu, W. T., Sampson, N., & Kessler, R. C. (2008). Toward a global view of alcohol, tobacco, cannabis, and cocaine use: Findings from the WHO World Mental Health Surveys. *PLoS Medicine, 5,* 1053–1067. doi:10.1371/journal.pmed.0050141

Degenhardt, L., & Hall, W. (2012). Extent of illicit drug use and dependence, and their contribution to the global burden of disease. *Lancet, 379,* 55–70. doi:10.1016/S0140-6736(11)61138-0

Degenhardt, L., Whiteford, H. A., Ferrari, A. J., Baxter, A. J., Charlson, F. J., Hall, W. D., Freedman, G., Burstein, R., Johns, N., Engell, R. E., Flaxman, A., Murray, C. J., & Vos, T. (2013). Global burden of disease attributable to illicit drug use and dependence: Findings from the Global Burden of Disease Study 2010. *Lancet, 382,* 1564–1574. doi:10.1016/S0140-6736(13)61530-5

Dodge, K., Krantz, B., & Kenny, P. J. (2010). How can we begin to measure recovery? *Substance Abuse Treatment, Prevention, and Policy, 5,* 31. doi:10.1186/1747-597X-5-31

Dzoljic, E. D., Kaplan, C. D., & Dzoljic, M. R. (1988). Effect of ibogaine on naloxone-precipitated withdrawal syndrome in chronic morphine-dependent rats. *Archives Internationales de Pharmacodynamie et de Thérapie, 294,* 64–70.

Elo, S., & Kyngäs, H. (2008). The qualitative content analysis process. *Journal of Advanced Nursing, 62,* 107–115. doi:10.1111/j.1365-2648.2007.04569.x

Glick, S. D., Rossman, K., Rao, N. C., Maisonneuve, I. M., & Carlson, J. N. (1992). Effects of ibogaine on acute signs of morphine withdrawal in rats: Independence from tremor. *Neuropharmacology, 31,* 497–500. doi:10.1016/0028-3908(92)90089-8

Glick, S. D., Rossman, K., Steindorf, S., Maisonneuve, I. M., & Carlson, J. N. (1991). Effects and aftereffects of ibogaine on morphine self-administration in rats. *European Journal of Pharmacology, 195,* 341–345. doi:10.1016/0014-2999(91)90474-5

He, D. Y., McGough, N. N., Ravindranathan, A., Jeanblanc, J., Logrip, M. L., Phamluong, K., Janak, P. H., & Ron, D. (2005). Glial cell line-derived neurotrophic factor mediates the desirable actions of the anti-addiction drug ibogaine against alcohol consumption. *The Journal of Neuroscience, 25,* 619–628. doi:10.1523/JNEUROSCI.3959-04.2005

Hsieh, H. F., & Shannon, S. E. (2005). Three approaches to qualitative content analysis. *Qualitative Health Research, 15,* 1277–1288. doi:10.1177/1049732305276687

Johnson, M. W., Garcia-Romeu, A., Cosimano, M. P., & Griffiths, R. R. (2014). Pilot study of the 5-HT_{2A}R agonist psilocybin in the treatment of tobacco addiction. *Journal of Psychopharmacology, 28,* 983–992. doi:10.1177/0269881114548296

Karila, L., Reynaud, M., Aubin, H. J., Rolland, B., Guardia, D., Cottencin, O., & Benyamina, A. (2011). Pharmacological treatments for cocaine dependence: Is there something new? *Current Pharmaceutical Design, 17,* 1359–1368. doi:10.2174/138161211796150873

Koenig, X., Kovar, M., Boehm, S., Sandtner, W., & Hilber, K. (2014). Anti-addiction drug ibogaine inhibits hERG channels: A cardiac arrhythmia risk. *Addiction Biology, 19,* 237–239. doi:10.1111/j.1369-1600.2012.00447.x

Koenig, X., Kovar, M., Rubi, L., Mike, A. K., Lukacs, P., Gawali, V. S., Todt, H., Hilber, K., & Sandtner, W. (2013). Anti-addiction drug ibogaine inhibits voltage-gated ionic currents: A study to assess the drug's cardiac ion channel profile. *Toxicology and Applied Pharmacology, 273,* 259–268. doi:10.1016/j.taap.2013.05.012

Krebs, T. S., & Johansen, P. O. (2012). Lysergic acid diethylamide (LSD) for alcoholism: Meta-analysis of randomized controlled

trials. *Journal of Psychopharmacology, 26,* 994–1002. doi:10.1177/0269881112439253

Larimer, M. E., Palmer, R. S., & Marlatt, G. A. (1999). Relapse prevention. An overview of Marlatt's cognitive-behavior model. *Alcohol Res Health, 23*(2):151–160.

Leal, M. B., Michelin, K., Souza, D. O., & Elisabetsky, E. (2003). Ibogaine attenuation of morphine withdrawal in mice: Role of glutamate N-methyl-D-aspartate receptors. *Progress in Neuro-Psychopharmacology & Biological Psychiatry, 27,* 781–785. doi:10.1016/S0278-5846(03)00109-X

Lim, S. S., Vos, T., Flaxman, A. D., Danaei, G., Shibuya, K., Adair-Rohani, H., Amann, M., Anderson, H. R., Andrews, K. G., Aryee, M., Atkinson, C., Bacchus, L. J., Bahalim, A. N., Balakrishnan, K., Balmes, J., Barker-Collo, S., Baxter, A., Bell, M. L., Blore, J. D., Blyth, F., Bonner, C., Borges, G., Bourne, R., Boussinesq, M., Brauer, M., Brooks, P., Bruce, N. G., Brunekreef, B., Bryan-Hancock, C., Bucello, C., Buchbinder, R., Bull, F., Burnett, R. T., Byers, T. E., Calabria, B., Carapetis, J., Carnahan, E., Chafe, Z., Charlson, F., Chen, H., Chen, J. S., Cheng, A. T., Child, J. C., Cohen, A., Colson, K. E., Cowie, B. C., Darby, S., Darling, S., Davis, A., Degenhardt, L., Dentener, F., Des Jarlais, D. C., Devries, K., Dherani, M., Ding, E. L., Dorsey, E. R., Driscoll, T., Edmond, K., Ali, S. E., Engell, R. E., Erwin, P. J., Fahimi, S., Falder, G., Farzadfar, F., Ferrari, A., Finucane, M. M., Flaxman, S., Fowkes, F. G., Freedman, G., Freeman, M. K., Gakidou, E., Ghosh, S., Giovannucci, E., Gmel, G., Graham, K., Grainger, R., Grant, B., Gunnell, D., Gutierrez, H. R., Hall, W., Hoek, H. W., Hogan, A., Hosgood, H. D., Hoy, D., Hu, H., Hubbell, B. J., Hutchings, S. J., Ibeanusi, S. E., Jacklyn, G. L., Jasrasaria, R., Jonas, J. B., Kan, H., Kanis, J. A., Kassebaum, N., Kawakami, N., Khang, Y. H., Khatibzadeh, S., Khoo, J. P., Kok, C., Laden, F., Lalloo, R., Lan, Q., Lathlean, T., Leasher, J. L., Leigh, J., Li, Y., Lin, J. K., Lipshultz, S. E., London, S., Lozano, R., Lu, Y., Mak, J., Malekzadeh, R., Mallinger, L., Marcenes, W., March, L., Marks, R., Martin, R., McGale, P., McGrath, J., Mehta, S., Mensah, G. A., Merriman, T. R., Micha, R., Michaud, C., Mishra, V., Mohd Hanafiah, K., Mokdad, A. A., Morawska, L., Mozaffarian, D., Murphy, T., Naghavi, M., Neal, B., Nelson, P. K., Nolla, J. M., Norman, R., Olives, C., Omer, S. B., Orchard, J., Osborne, R., Ostro, B., Page, A., Pandey, K. D., Parry, C. D., Passmore, E., Patra, J., Pearce, N., Pelizzari, P. M., Petzold, M., Phillips, M. R., Pope, D., Pope, C. A., Powles, J., Rao, M., Razavi, H., Rehfuess, E. A., Rehm, J. T., Ritz, B., Rivara, F. P., Roberts, T., Robinson, C., Rodriguez-Portales, J. A., Romieu, I., Room, R., Rosenfeld, L. C., Roy, A., Rushton, L., Salomon, J. A., Sampson, U., Sanchez-Riera, L., Sanman, E., Sapkota, A., Seedat, S., Shi, P., Shield, K., Shivakoti, R., Singh, G. M., Sleet, D. A., Smith, E., Smith, K. R., Stapelberg, N. J., Steenland, K., Stöckl, H., Stovner, L. J., Straif, K., Straney, L., Thurston, G. D., Tran, J. H., Van Dingenen, R., van Donkelaar, A. Veerman, J. L., Vijayakumar, L., Weintraub, R., Weissman, M. M., White, R. A., Whiteford, H., Wiersma, S. T., Wilkinson, J. D., Williams, H. C., Williams, W., Wilson, N., Woolf, A. D., Yip, P., Zielinski, J. M., Lopez, A. D., Murray, C. J., Ezzati, M., AlMazroa, M. A., & Memish, Z. A. (2012). A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: A systematic analysis for the Global Burden of Disease Study 2010. *Lancet, 380,* 2224–2260. doi:10.1016/S0140-6736(12)61766-8

Litjens, R. P. W., & Brunt, T. M. (2016). How toxic is ibogaine? *Clinical Toxicology, 54,* 297–302. doi:10.3109/15563650.2016.1138226

Maisonneuve, I. M., Keller, R. W., & Glick, S. D. (1991). Interactions between ibogaine, a potential anti-addictive agent, and morphine: An in vivo microdialysis study. *European Journal of Pharmacology, 199,* 35–42. doi:10.1016/0014-2999(91)90634-3

Mash, D. C., Kovera, C. A., Pablo, J., Tyndale, R., Ervin, F. R., Kamlet, J. D., & Hearn, W. L. (2001). Ibogaine in the treatment of heroin withdrawal. *The Alkaloids: Chemistry and Biology, 56,* 155–171. doi:10.1016/S0099-9598(01)56012-5

Ng, M., Freeman, M. K., Fleming, T. D., Robinson, M., Dwyer-Lindgren, L., Thomson, B., Wollum, A., Sanman, E., Wulf, S., Lopez, A. D., Murray, C. J. L., & Gakidou, E. (2014). Smoking prevalence and cigarette consumption in 187 countries, 1980–2012. *Journal of the American Medical Association, 311,* 183–192. doi:10.1001/jama.2013.284692

Nutt, D. J., & Lingford-Hughes, A. (2008). Addiction: The clinical interface. *British Journal of Pharmacology, 154,* 397–405. doi:10.1038/bjp.2008.101

Parker, L. A., Burton, P., McDonald, R. V., Kim, J. A., & Siegel, S. (2002). Ibogaine interferes with motivational and somatic effects of naloxone-precipitated withdrawal from acutely administered morphine. *Progress in Neuro-Psychopharmacology & Biological Psychiatry, 26,* 293–297. doi:10.1016/S0278-5846(01)00268-8

Parker, L. A., & Siegel, S. (2001). Modulation of the effects of rewarding drugs by ibogaine. *The Alkaloids: Chemistry and Biology, 56,* 211–225. doi:10.1016/S0099-9598(01)56015-0

Phillips, K. A., Epstein, D. H., & Preston, K. L. (2014). Psychostimulant addiction treatment. *Neuropharmacology, 87,* 150–160. doi:10.1016/j.neuropharm.2014.04.002

Potenza, M. N., Sofuoglu, M., Carroll, K. M., & Rounsaville, B. J. (2011). Neuroscience of behavioral and pharmacological treatments for addictions. *Neuron, 69,* 695–712. doi:10.1016/j.neuron.2011.02.009

Rede Agora Valinhos. (October, 2016). *Paciente morre durante tratamento com ibogaína em Paulínia [Patient dies during treatment with ibogaine in the city of Paulínia]*. Retrieved from http://agoravalinhos.com.br/arquivos/noticias/paciente-morre-durante-tratamento-com-ibogaina-em-paulinia/

Rezvani, A. H., Overstreet, D. H., & Lee, Y. W. (1995). Attenuation of alcohol intake by ibogaine in three strains of alcohol-preferring rats. *Pharmacology, Biochemistry, and Behavior, 52,* 615–620. doi:10.1016/0091-3057(95)00152-M

Sandelowski, M. (1993). Theory unmasked: The uses and guises of theory in qualitative research. *Research in Nursing and Health, 16,* 213–218. doi:10.1002/nur.4770160308

Sandelowski, M., Docherty, S., & Emden, C. (1995). Focus on qualitative methods. Qualitative metasynthesis: Issues and techniques. *Research in Nursing and Health, 20,* 365–371. doi:10.1002/(sici)1098-240x(199708)20:460;365::aid-nur962;3.0.co;2-e

Schenberg, E. E., de Castro Comis, M. A., Chaves, B. R., & Da Silveira, D. X. (2014). Treating drug dependence with the aid of ibogaine: A retrospective study. *Journal of Psychopharmacology, 28,* 993–1000. doi:10.1177/0269881114552713.

Sessa, B., & Johnson, M. W. (2015). Can psychedelic compounds play a part in drug dependence therapy? *The British Journal of Psychiatry, 206,* 1–3. doi:10.1192/bjp.bp.114.148031

Sharpe, L. G., & Jaffe, J. H. (1990). Ibogaine fails to reduce naloxone-precipitated withdrawal in the morphine-dependent rat. *Neuroreport, 1,* 17–19. doi:10.1097/00001756-199009000-00005

Shorter, D., & Kosten, T. R. (2011). Novel pharmacotherapeutic treatments for cocaine addiction. *BMC Medicine, 9,* 119. doi:10.1186/1741-7015-9-119

Stead, L. F., & Lancaster, T. (2012). Combined pharmacotherapy and behavioural interventions for smoking cessation. *Cochrane Database of Systematic Reviews, 10,* CD008286. doi:10.1002/14651858.CD008286

Thurner, P., Stary-Weinzinger, A., Gafar, H., Gawali, V. S., Kudlacek, O., Zezula, J., Hilber, K., Boehm, S., Sandtner, W., & Koenig, X. (2014). Mechanism of hERG channel block by the psychoactive indole alkaloid ibogaine. *The Journal of Pharmacology and Experimental Therapeutics, 348,* 346–358. doi:10.1124/jpet.113.209643

Tiffany, S. T., Friedman, L., Greenfield, S. F., Hasin, D. S., & Jackson, R. (2012). Beyond drug use: A systematic consideration of other outcomes in evaluations of treatments for substance use disorders. *Addiction, 107,* 709–718. doi:10.1111/j.1360-0443.2011.03581.x

Tupper, K. W., Wood, E., Yensen, R., & Johnson, M. (2015). Psychedelic medicine: A re-emerging therapeutic paradigm. *Canadian Medical Association Journal, 187,* 1054–1059. doi:10.1503/cmaj.141124

Vocci, F. J., Acri, J., & Elkashef, A. (2005). Medication development for addictive disorders: The state of the science. *American Journal of Psychiatry, 162,* 1432–1440. doi:10.1176/appi.ajp.162.8.1432

Wahler, E. A., & Otis, M. D. (2014). Social stress, economic hardship, and psychological distress as predictors of sustained abstinence from substance use after treatment. *Substance Use & Misuse, 49,* 1820–1832. doi:10.3109/10826084.2014.935789

Whiteford, H. A., Degenhardt, L., Rehm, J., Baxter, A. J., Ferrari, A. J., Erskine, H. E., Charlson, F. J., Norman, R. E., Flaxman, A. D., Johns, N., & Burstein, R., Murray, C. J. L., & Vos, T. (2013). Global burden of disease attributable to mental and substance use disorders: Findings from the Global Burden of Disease Study 2010. *Lancet, 382,* 1575–1586. doi:10.1016/S0140-6736(13)61611-6

Winkelman, M. J. (2014). Psychedelics as medicines for substance abuse rehabilitation: Evaluating treatments with LSD, peyote, ibogaine and ayahuasca. *Current Drug Abuse Reviews, 7,* 101–116. doi:10.2174/1874473708666150107120011