

A Mixed-Method Analysis of Persisting Effects Associated with Positive Outcomes Following Ibogaine Detoxification

Alan K. Davis, Ph.D. ^a, Elise Renn, B.S.^b, Austin-Marley Windham-Herman, B.S.^{b,c}, Martin Polanco, M.D.^b, and Joseph P. Barsuglia, Ph.D. ^b

^aBehavioral Pharmacology Research Unit, Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD, USA; ^bCrossroads Treatment Center, Rosarito, Mexico; ^cYale School of Medicine, Yale University, New Haven, CT, USA

ABSTRACT

We examined persisting effects, self-perceived challenges, and potential benefits associated with positive outcomes following ibogaine detoxification using data collected as part of a larger online retrospective study of 73 patients who received treatment for chronic opioid use in Mexico between 2012 and 2015. A mixed-methods design was used comparing treatment responders versus non-responders, as well as content coding of themes from open-ended questions. Most participants reported positive persisting effects of ibogaine detoxification (e.g., enhanced personal sense of gratitude and authenticity, and meaning and appreciation for life). Compared to non-responders, treatment responders endorsed greater persisting changes in their ability to tolerate difficult/painful feelings, capacity for coping with stress, and reduced unhealthy anger. Treatment responders reported greater change in subjective levels of inner peace, joy, feelings of love/openheartedness, and experiences of sacredness in life. Qualitative analyses revealed that treatment responders reported a heightened sense of spiritual awareness and greater connection to their intra-/interpersonal relationships after ibogaine detoxification. Notable challenges of ibogaine detoxification included psychological and health-related difficulties during treatment and challenges with post-treatment integration. Findings highlight the persisting effects associated with positive response to ibogaine detoxification and possible post-treatment needs (i.e., more integration/aftercare resources). Future research using rigorous experimental designs is needed.

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Introduction

Opioid use disorder is now a public health epidemic in the United States (U.S.) and Europe (Degenhardt et al. 2014). Approximately 12% of individuals diagnosed with a substance use disorder are addicted to some form of opioid (Substance Abuse and Mental Health Services Administration 2015), and rates are higher among vulnerable populations (e.g., U.S. military veterans, chronic pain patients; Samoylenko et al. 2010; Sehgal, Manchikanti, and Smith 2012). The U.S. president recently declared the opioid crisis to be “a public health emergency,” with estimates that more than 59,000 lives were lost in 2016 due to opioids (Davis 2017; Johnson and Wagner 2017), making overdose the primary cause of accidental death in the U.S. (Centers for Disease Control and Prevention 2016). Opioid maintenance therapies (OMTs) are the standard treatment for detoxification and managing withdrawal in the U.S. OMTs often require long-term administration and have hazardous long-term effects (Andersen et al.

2011; Tennant 2013; Upadhyay et al. 2010), perpetuate dependency, demonstrate limited efficacy (Ling and Compton 2005; Nielsen et al. 2016; Stotts, DODrill, and Kosten 2009; Veilleux et al. 2010; Weiss et al. 2011), and there is a shortage of providers to meet current demand (National Council on Alcoholism and Drug Dependence 2016; Saloner and Karthikeyan 2015).

One potential treatment for this population is detoxification with ibogaine. Ibogaine hydrochloride is a plant-derived compound that attenuates opioid withdrawal and reduces drug use and craving to opioids, as well as other addictive substances (Schenberg et al. 2014). Ibogaine improves mood (Brown and Alper 2017) and appears to engender novel psychological insights through its dream-like properties, often bringing users through a half-day immersion in visual imagery and autobiographical memories (Schenberg et al. 2017). Ibogaine’s mechanism of action appears to foster adaptive changes in the opioid and dopamine pathways, antagonism of NMDA and nicotinic

acetylcholine receptors, and an increased expression of glial-derived neurotrophic factor (GDNF) (Brown and Alper 2017).

Despite the Schedule I status of ibogaine in the U.S., international studies have documented its efficacy in treating opioid dependence in clinical populations (e.g., Alper et al. 1999; Bastiaans 2004; Brown and Alper 2017; Davis et al. 2017; Mash et al. 2001; Noller, Frampton, and Yazar-Klosinski 2017). In recent observational and longitudinal studies, patients who received one course of ibogaine treatment demonstrated rapid reductions in withdrawal symptoms and durable improvements in drug use and legal and social functioning (Brown and Alper 2017; Noller, Frampton, and Yazar-Klosinski 2017). In earlier studies, a single ibogaine treatment was associated with acute reductions in substance use and improvements in psychosocial domains, including depression, anxiety, and interpersonal functioning (Bastiaans 2004; Mash et al. 2001).

Although these studies have demonstrated positive clinical outcomes associated with ibogaine detoxification, little is known about the acute and persisting subjective effects of ibogaine treatment. For example, qualitative reports from patients in Brazil revealed that ibogaine treatment led to long-term improvements in family and social relationships, increased engagement in academic and professional activities, improved quality of life, self-efficacy, and coping (Schenberg et al. 2016). Moreover, a phenomenological analysis showed that the long-term effects were associated with accounts of the ibogaine experience which included enhanced memory retrieval connected to substance use, perception of the future, including simulations of the future with or without drug use, cognitive effects of “brain resetting,” and spiritual phenomena such as connecting with deceased ancestors and spiritual entities (Schenberg et al. 2017). These reports highlight aspects of the qualitative and visionary aspects of the acute ibogaine experience and its subsequent effects. However, the small sample sizes of these investigations, coupled with the possible heterogeneity of ibogaine patients across cultures, and the lack of examination of whether treatment-response is associated with persisting effects of ibogaine, limit understanding of this topic and thus warrant further investigation.

Identifying differences in perceived benefits/challenges and persisting effects associated with ibogaine between individuals with positive treatment responses (i.e., abstinence and reduction of use) versus negative treatment response (i.e., no change in use or use increased) could assist clinicians and researchers in designing more effective adjunctive psychosocial or environmental interventions. Therefore, the present

study addresses these questions by evaluating the persisting psychosocial effects associated with ibogaine treatment and comparing the differences in persisting effects between those with and without a positive treatment response among people with chronic opioid use. The second aim of this study is to evaluate patients' self-reported perceptions of the benefits, and the personal changes resulting from, and challenges associated with, ibogaine detoxification. We also examine differences in subjective reports as a function of whether participants had a positive or negative treatment response (based on post-detoxification patterns of opioid use).

Method

Recruitment procedure

The present study is a secondary data analysis from a larger retrospective study evaluating the subjective effectiveness of ibogaine treatment among a sample of chronic opioid users who received treatment at an inpatient clinic in Mexico (Davis et al. 2017). Details regarding recruitment and procedures are provided elsewhere (see Davis et al. 2017). Past patients were contacted via phone and email to participate in an anonymous web-based survey. Of the 285 people who were contacted, 134 (47%) responded to this contact, consented to participate, and began filling out the survey. However, 33 did not complete all measures and 13 reported seeking treatment for problems associated with another substance (e.g., alcohol). Of the 88 participants included in the main outcome publication (Davis et al. 2017), 15 did not complete our measures of the persisting psychosocial effects of ibogaine and were excluded from the present study. Thus, the final sample was comprised of 73 participants. All procedures were approved from an independent Institutional Review Board (Solutions IRB).

Treatment setting and content

All participants received one week of detoxification treatment with ibogaine on a fee-for-service basis at a clinic in Mexico. This residential setting provided care for adults (18–60) with substance use disorders and co-occurring mental health problems. Patients at this clinic undergo a physical examination with a staff physician. Each patient is administered ibogaine hydrochloride (*Voacanga*-derived), which is imported from Phytostan Enterprises, Inc., and is Good Manufacturing Practice (GMP) certified. All patients received cardiac monitoring, intravenous saline and electrolytes, and medical

monitoring during their ibogaine session. Further details about the setting can be found in the main outcomes manuscript (Davis et al. 2017).

Measures

Opioid consumption before and after ibogaine detoxification

Participants were asked about their primary substance use (i.e., prescription opioids or heroin), whether there was a secondary substance for which they were seeking treatment, how many years of consumption they had prior to treatment, the number of days using primary substance in the 30 days prior to treatment, their patterns of consuming opioids after ibogaine detoxification compared to pre-treatment patterns (i.e., abstinent, increased, decreased, stayed the same), and whether any opioids had been consumed during the six months prior to this survey.

Persisting effects of ibogaine

Persisting subjective effects of ibogaine were assessed using a modified version of the Persisting Effects Questionnaire (Doblin 1991; Griffiths et al. 2006; Pahnke 1969). This questionnaire was originally used to measure changes in attitudes, moods, behavior, and spiritual experience in several studies that evaluated the lasting effects of psilocybin (Griffiths et al. 2008, 2011). We modified the 145-item questionnaire used by Griffiths et al. (2006) to reduce response burden and eliminate item redundancy. Specifically, the original questionnaire included items that have similar content but are measured in two ways as a function of valence (i.e., whether an item being measured has increased and whether the item being measured has decreased). Therefore, we collapsed all of these pairs of opposite valence items into one item each with a response option that captured whether the item being measured had decreased or increased (from -2 “Significantly decreased” to +2 “Significantly increased”) since the participant’s ibogaine treatment. This reduced the item pool from 145 to 70 items. An additional 24 items were excluded from the questionnaire because they were ambiguous (e.g., “Your life has a diminished dynamic quality”) or redundant with other items (e.g., “Your experience of sacredness in daily life has increased” and “You experience profound sacredness more frequently”). The remaining 46 items comprised the modified version of the questionnaire (see Table 2 for items).

Qualitative items regarding ibogaine treatment

We asked three open-ended questions examining participants’ perceptions of their treatment experiences:

(1) “Describe any personal changes that you believe occurred as a direct result of your ibogaine treatment experience (e.g., emotional health, identity, substance use, addictive behaviors, relationships, spirituality, physical health, etc.)”; (2) “What is the greatest benefit that you received from ibogaine treatment?”; and (3) “What was the most challenging part of your ibogaine treatment experience?”

Demographics

Participants reported demographic information, including age, gender, sexual orientation, ethnicity, and relationship status.

Data analyses

We conducted frequency counts of demographic characteristics, and primary substance use and treatment history variables using the entire sample ($n = 73$). For the quantitative analysis of responses to items from the persisting effects of ibogaine questionnaire, we evaluated means and standard deviations. Next, the sample was split into two subgroups based on treatment response following ibogaine treatment (i.e., treatment responder = never used primary substance again, decreased use; treatment non-responder = no change in use, use increased). Using treatment response as an independent variable, we then conducted a series of t -test analyses and effect size (Cohen’s d) calculations to evaluate whether there were differences in mean ratings of persisting effects of ibogaine treatment between subgroups. Only those items where both the t -test was significant at a conservative cutoff ($p < .01$) and the effect size was large ($>.80$) were interpreted as meaningfully different between subgroups in order to reduce the likelihood of Type I error. All quantitative analyses were conducted using SPSS version 23.

For the qualitative analysis of open-ended questions examining the personal changes, greatest benefits, and challenges associated with ibogaine treatment, we conducted a content analysis (Casterle et al. 2012; Miles and Huberman 1994) to allocate each participant’s response to a list of themes that were derived from each set of responses from the open-ended questions. We started with the Preparation for Coding Process described by Casterlé et al. (2012), which consisted of reading all open-ended responses, generating a list of potential themes, and refining themes when they were not initially supported by the responses. Following this, in the Actual Coding Process, we used a list of themes for each open-ended question to generate a list of concepts used to define each theme and then assigned each theme a numerical code (e.g., 1, 2, 3, 4, etc.) to

link a participant comment to the associated theme. Absolute number of utterances that were coded into each theme within each open-ended question were then calculated. Last, we used the same independent variable (i.e., treatment response) in the quantitative analysis to separate utterances for comparison by qualitative responses.

Results

Characteristics of sample and pre-treatment substance use and treatment history

Most participants were male (70%), approximately one-half (49%) were between the ages of 18 and 34, and 90% reported that they were White/Caucasian (Table 1). Almost equal proportions reported that they sought treatment for problematic prescription opioid (52%) or heroin (48%) consumption. Most participants (71%) had been using heroin or prescription opioids for at least four years, many of whom (21%) had been using for at least 10 years prior to treatment, and most (58%) reported that it had been at least one year since their ibogaine treatment. Overall, 26 (36%) reported never using opioids again, 33 (45%) reported decreased

use, 11 (15%) reported no change in their opioid use, and three (4%) reported increased use following ibogaine treatment. Thus, 81% were classified as treatment responders (i.e., never used opioids again or use decreased after treatment) and 19% were classified as non-responders (i.e., use stayed the same or increased after treatment). Furthermore, 58% of the sample reported that it had been at least one year since treatment, and one-quarter of them indicated that it had been more than two years since treatment (Table 1).

Persisting attributions of the effects of ibogaine treatment and differences in functioning by treatment responder subgroup

Item means of the persisting effects of ibogaine questionnaire in the total sample indicate that most participants believed that they had experienced positive changes in psychological, behavioral, and social functioning after ibogaine treatment (Table 2). For the sample overall, participants reported the greatest positive changes in psychosocial functioning, which included changes in their sense of gratitude, ability to be a more authentic person, sense of meaning in life, appreciation for

Table 1. Demographic history, pre-ibogaine substance use for full sample, and treatment responder and non-responder subgroups.

Characteristic	Full sample (n = 73)	Treatment responders (n = 59) ^a	Treatment non-responders (n = 14) ^a	χ^2
	%	%	%	Statistic
Age				6.472
18–24	8	7	14	
25–34	41	36	64	
35–54	38	42	21	
55+	12	15	0	
Gender				2.067
Male	70	66	86	
Female	30	34	14	
Ethnicity				1.837
White/Caucasian	90	88	100	
Non-White/Other	10	11	0	
Relationship Status				1.264
Single/Divorced	66	63	79	
Married/Partnered	34	37	21	
Time Since Ibogaine Treatment				1.281
Less than 1 year	43	43	43	
1–2 years	33	31	43	
2 years or more	25	27	14	
Primary Substance				3.827*
Heroin	48	42 [^]	71 [^]	
Prescription Opioids	52	58 [^]	29 [^]	
Number of years using primary substance prior to ibogaine treatment				1.445
Less than 1 year	6	5	7	
1–3 years	24	22	36	
4–6 years	32	32	29	
7–9 years	18	19	14	
10 or more years	21	22	14	

* $p < .05$

Note. Totals may not sum to 100% due to rounding.

[^]Values marked with this superscript within a row are significantly different from one another.

^aResponder categories were created by combining treatment response subgroups. Participants were considered Responders if they reported that they never returned to using or if their use had decreased, and Non-responders were those participants who reported that there was no change in their substance use following treatment or that their use had increased.

Table 2. Item means and standard deviations of the persisting effects of ibogaine questionnaire, and comparison of item means between treatment response groups (responders vs. non-responders).

Item (in Descending Order of Overall Mean Score)	Overall Sample	Treatment Responders	Treatment Non-responders	t-Value	Cohen's d
	(N = 73) M(SD)	(N = 59) M(SD)	(N = 14) ^a M(SD)		
Your gratitude or sense of gratefulness has...	1.04 (1.15)	1.24 (1.06)	0.21 (1.19)	-3.18**	.91[†]
Your ability to be a more authentic person has...	1.00 (1.05)	1.17 (0.29)	0.29 (1.07)	-2.97**	1.12[†]
The sense of meaning in your life has...	0.99 (1.09)	1.19 (0.99)	0.14 (1.10)	-3.47**	1.27[†]
Your appreciation for life has...	0.96 (1.07)	1.14 (1.01)	0.21 (1.05)	-3.05**	.90[†]
Your sense of life being interconnected has...	0.88 (0.95)	0.97 (0.95)	0.46 (0.88)	-1.76	.56
The quality of your relationships has...	0.86 (1.09)	0.98 (1.04)	0.31 (1.18)	-2.07*	.60
The importance of spirituality in your life has...	0.86 (0.97)	0.95 (0.99)	0.46 (0.78)	-1.66	.55
Your sense of values (e.g., what is important in your life) has...	0.85 (0.92)	0.97 (0.93)	0.36 (0.75)	-2.28*	.72
Your acceptance of others has...	0.85 (0.84)	0.90 (0.85)	0.64 (0.84)	-1.02	.31
Your mental flexibility/open-mindedness has...	0.78 (0.98)	0.88 (1.00)	0.31 (0.75)	-1.94	.64
Your desire for serving others has...	0.78 (1.00)	0.90 (0.85)	0.29 (0.99)	-2.10*	.66
Your interpersonal empathy (e.g., sharing others' feelings) has...	0.78 (0.93)	0.88 (0.93)	0.36 (0.84)	-1.93	.59
Your connection to the God of your understanding/ultimate reality/higher power has...	0.78 (0.94)	0.86 (0.96)	0.38 (0.77)	-1.69	.55
The degree of intimacy with your loved ones has...	0.77 (1.03)	0.86 (1.04)	0.36 (0.93)	-1.67	.51
Your experience of inner peace (i.e., centeredness, serenity, calmness, contentment) has...	0.77 (1.11)	0.95 (1.06)	0.00 (1.04)	-3.03**	.90[†]
Your feelings of love and openheartedness have...	0.75 (1.13)	0.97 (1.02)	-0.14 (1.17)	-3.57**	1.01[†]
Your sense of inner authority in your life has...	0.73 (1.23)	0.86 (1.20)	0.14 (1.23)	-2.02*	.59
Your feelings of certainty about the reality of unconditional love (also called divine love, metta, or grace) have...	0.72 (1.00)	0.81 (0.99)	0.31 (0.95)	-1.68	.52
Your degree of mental clarity has...	0.70 (1.09)	0.81 (1.09)	0.21 (0.98)	-1.88	.58
The degree to which your spiritual practice has provided you with a sense of emotional support has...	0.69 (0.97)	0.78 (0.97)	0.31 (0.95)	-1.60	.49
Your ability to be more at home in the present moment has...	0.65 (1.09)	0.76 (1.04)	0.15 (1.21)	-1.86	.54
Your sensitivity to the needs of others has...	0.65 (0.86)	0.73 (0.85)	0.31 (0.86)	-1.62	.49
Your level or sense of hopefulness has...	0.64 (1.36)	0.83 (1.33)	-0.14 (1.23)	-2.50*	.76
Your experience of joy or bliss has...	0.63 (1.12)	0.83 (1.04)	-0.21 (1.12)	-3.34**	.96[†]
Your belief in some form of continuance after death has...	0.62 (1.04)	0.69 (1.07)	0.31 (0.86)	-1.22	.39
Your self-confidence/self-assurance has...	0.60 (1.18)	0.76 (1.09)	-0.07 (1.33)	-2.47*	.68
Your feelings of being inspired or having inspiration have...	0.53 (1.11)	0.68 (1.09)	-0.07 (1.00)	-2.35*	.72
Your capacity to be playful has...	0.47 (1.09)	0.61 (1.03)	-0.14 (1.17)	-2.39*	.68
The impact past traumas have on your current emotional well-being has...	0.47 (0.94)	0.54 (0.92)	0.14 (1.03)	-1.43	.41
Your ability to focus your attention has...	0.47 (1.12)	0.58 (1.05)	0.00 (1.30)	-1.76	.49
Your experience of sacredness in daily life has...	0.47 (1.15)	0.68 (1.12)	-0.46 (0.78)	-3.48**	1.18[†]
Your ability to tolerate difficult or painful feelings has...	0.44 (1.14)	0.66 (1.08)	-0.54 (0.88)	-3.75***	1.22[†]
Your decision-making ability has...	0.42 (1.08)	0.49 (1.07)	0.14 (1.10)	-1.09	.32
Your level of impulsivity has...	0.42 (0.91)	0.46 (0.92)	0.29 (0.91)	-0.63	.19
Your capacity for coping with stress has...	0.41 (1.05)	0.59 (0.97)	-0.36 (1.08)	-3.23**	.93[†]
Time spent in quiet meditation or prayer has...	0.39 (1.07)	0.47 (1.10)	0.00 (0.82)	-1.46	.48
Your ability to access helpful forms of therapy (e.g., counseling, yoga, recovery groups, etc.) has...	0.38 (0.97)	0.47 (1.01)	0.00 (0.68)	-1.67	.55
Your ability to have healthy sleep and rest has...	0.37 (1.22)	0.54 (1.21)	-0.36 (1.09)	-2.58*	.78
Your creativity has...	0.30 (1.02)	0.42 (0.99)	-0.21 (1.05)	-2.15*	.62
Your level of interpersonal conflict has...	0.30 (1.02)	0.42 (0.99)	-0.21 (1.05)	-2.15*	.62
Your concern with thoughts and feeling about your body has...	0.15 (0.95)	0.14 (0.90)	0.21 (1.19)	0.28	.07
Your apprehensiveness about your own death has...	-0.25 (1.10)	-0.29 (1.10)	-0.08 (1.12)	0.63	.19
Your feelings of anxiety or nervousness have...	-0.42 (1.20)	-0.56 (1.19)	0.14 (1.10)	2.01*	.61
Your feelings of unhealthy anger (e.g., bitterness, hostility, scorn) have...	-0.62 (1.15)	-0.81 (1.04)	0.21 (1.25)	3.19**	.89[†]
Your feelings of unhealthy or unhelpful guilt have...	-0.62 (1.15)	-0.85 (1.10)	0.00 (1.18)	2.57*	.75
Your feelings of sadness or depression have...	-0.63 (1.18)	-0.78 (1.16)	0.00 (1.11)	2.28*	.69

Note. Items in bold text were both statistically significant at $p < .01$ and had an effect size $> .80$.

* $p < .05$; ** $p < .01$; *** $p < .001$.

[†]Large effect size (> 0.80).

^a Ns range from 13–14 due to missing data.

life, sense of life being interconnected, quality of relationships, importance of spirituality in life, sense of values, and acceptance of others (highest endorsed items with $M > 0.84$). Further, statistically significant differences in positive effects were associated with ibogaine treatment. Specifically, compared to participants in the non-responder subgroup, those in the treatment responder

subgroup had significantly greater positive changes in their sense of gratitude, ability to be a more authentic person, sense of meaning in life, appreciation for life, experience of inner peace, feelings of love and openheartedness, experience of joy or bliss, experience of sacredness in daily life, ability to tolerate difficult or painful feelings, and capacity for coping with stress, and they experienced a

significant decrease in feelings of unhealthy anger ($d > 0.80$, $p < .01$).

Qualitative analysis of persisting subjective ibogaine experiences and challenges related to treatment

Regarding persisting experiences related to personal changes, treatment responders reported a total of 106 utterances and treatment non-responders reported a total of 17 utterances. Table 3 (top half) reveals that the most frequently mentioned themes across both groups were psychological changes (32% of utterances by treatment responders and 35% of utterances by treatment non-responders; “it gave me a new outlook on life,” “increase in clarity, drive, pursuit of happiness, freedom”) and SUD symptom relief (32% of treatment responders; “decreased craving,” “I am not an addict anymore”). Treatment non-responders made no utterance regarding changes in spirituality or one’s relationship to self and others, compared to approximately 17%

of the utterances made by treatment responders (Table 3).

Regarding the greatest benefits associated with ibogaine treatment, treatment responders provided a total of 90 utterances and treatment non-responders provided a total of 14 utterances. Table 3 (lower half) shows that the most frequently mentioned themes were psychological benefit (41% of utterances by treatment responders and 64% of utterances by treatment non-responders; “felt alive finally,” “depression and anxiety gone”) and SUD symptom relief (44% of treatment responders and 29% of treatment non-responders; “no more heroin,” “rapid detox from opiates,” “no more cravings, drug dreams”). Treatment non-responders did not mention any emotional and spiritual benefits; however, these themes comprised 11% of the utterances in the treatment responder group.

Last, when reporting the greatest challenge of one’s ibogaine detoxification, treatment responders provided a total of 121 utterances and treatment non-responders provided a total of 29 utterances (Table 4). The most frequently expressed challenges occurred post-

Table 3. Open-ended responses to two questions regarding the long-term effects of ibogaine detoxification by treatment response group (i.e., responder versus non-responder).

Theme Exemplar Quote	Number of Utterances (% of Group)	
	Treatment Responders (N = 59)	Treatment Non-Responders (N = 14)
Long-Term Effects: Personal Changes		
Emotional	9 (8%)	2 (12%)
“I am no longer afraid of death”		
“I have a great deal less fear in my life”		
Spiritual	9 (8%)	0 (0%)
“...more in tune spiritually”		
Psychological	34 (32%)	6 (35%)
“it gave me a new outlook on life”		
“increase in clarity, drive, pursuit of happiness, freedom”		
Health-related	10 (9%)	6 (35%)
“able to sleep better at night”		
“practice yoga daily, changed diet”		
SUD Symptom Relief	34 (32%)	3 (17%)
“decreased craving”		
“I am not an addict anymore”		
Relationship to Self and Others	10 (9%)	0 (0%)
“reconnected to my true self”		
“my relationship with my wife improved”		
Long-Term Effects: Greatest Benefit		
Emotional	4 (4%)	0 (0%)
“self love”		
Spiritual	7 (9%)	0 (0%)
“put me on a path to spiritual awareness”		
Psychological	37 (41%)	9 (64%)
“felt alive finally”		
“depression and anxiety gone”		
Health-Related	2 (2%)	1 (7%)
“(ibogaine) ended my digestive problems”		
SUD Symptom Relief	40 (44%)	4 (29%)
“no more heroin”		
“rapid detox from opiates”		
“no more cravings, drug dreams”		

Table 4. Open-ended responses to one question regarding the challenges associated with ibogaine detoxification by treatment response group (i.e., responder versus non-responder).

Theme Exemplar Quote	Number of Utterances (% of Group)	
	Treatment Responders (N = 59)	Treatment Responders (N = 59)
Pre-treatment		
Psychological "the unknown"	5 (4%)	0 (0%)
Emotional "being afraid... to do something illegal"	3 (2%)	0 (0%)
Health-related "finding a vein for an IV"	1 (1%)	0 (0%)
During treatment		
Ibogaine Itself "the treatment itself"	10 (8%)	2 (7%)
Psychological "being committed to the process"	14 (12%)	4 (14%)
Health-Related "being without cannabis"	13 (11%)	6 (21%)
Post-treatment		
Integration "the 4 weeks after..."	28 (23%)	6 (21%)
Staying off Opiates "adjusting to a new and sober life"	10 (8%)	3 (10%)
Exhaustion/Fatigue "sleeping after treatment"	7 (6%)	2 (7%)
Emotional "uncomfortable and raw feelings"	11 (9%)	1 (3%)
Health-Related "the restlessness afterward"	14 (12%)	4 (14%)
Cost-Related "paying for it"	5 (4%)	1 (3%)

treatment (61% of all utterances). Among the utterances associated with post-treatment challenges, the most frequently mentioned theme was difficulty with incorporating their ibogaine experience into their daily lives (i.e., integration; 23% of treatment responders and 21% of treatment non-responders). The challenges that occurred during treatment comprised 33% of all utterances, with the most frequently reported themes being psychological challenges (12% of treatment responders) and health-related problems (21% of treatment non-responders). Pre-treatment challenges were mentioned the most infrequently (less than 1% in both groups) and included psychological, emotional, or health-related problems.

Discussion

To our knowledge, this is the largest published sample of opioid users' persisting effects following ibogaine detoxification. Qualitative and quantitative analyses yielded an array of subjective changes, as well as challenges, following ibogaine

administration. Our findings are consistent with several studies (Bastiaans 2004; Mash et al. 2001; Schenberg et al. 2016, 2017), documenting cessation and reduction of chronic substance use and reductions in craving and withdrawal (Davis et al. 2017), and also a spectrum of reported changes in emotional, spiritual, social, and health-related outcomes following ibogaine detoxification. This study builds upon prior work by examining a larger variety of psychosocial changes using a modified questionnaire of persisting effects and examining differences in these effects as a function of treatment response. Taken together, the results support the notion that ibogaine patients experience persisting benefits associated with a change in gratitude, authenticity, and sense of meaning in life, although those who are able to decrease or quit using opioids (i.e., treatment responders) reported the most benefit in these areas.

The results also revealed that treatment responders endorsed comparatively greater persistent increases in positive affect (peace, love, joy), affective coping ability (stress, painful feelings), and reductions in negative

affect (anger, stress). These findings are consistent with behavioral theory wherein negative reinforcement (i.e., substance use helps one avoid a negative affective state) is itself an important predictor of the development and maintenance of a substance use disorder (Blume 2001). It is possible that ibogaine detoxification has secondary benefits associated with emotional regulation, which would be consistent with the theoretical implication that improving emotional regulation enhances recovery from a substance use disorder (Yi-Yuan, Tang, and Posner 2016). However, these temporal associations are speculative, given the cross-sectional nature of the data, and future research should examine this hypotheses using a longitudinal design.

In addition to affect regulation and other persisting psychological benefits, participants indicated that they experienced persisting effects related to social and interpersonal relationships (e.g., quality of relationships, acceptance of others). Consistent with evidence suggesting that isolation from social relationships predicts future substance use (Baarendse, Limpens, and Vanderschuren 2014; Lesscher et al. 2015), this study demonstrates that ibogaine detoxification is associated with increased sense of interpersonal and social connection, which were experienced to a greater degree by treatment responders compared to non-responders. We speculate that the benefits of ibogaine detoxification (reductions in craving and withdrawal) are, in part, maintained by pre-existing social supports that the patient is able to re-engage with following treatment. However, it could also be that persisting changes associated with interpersonal connections are a result of enhanced ability to make new social connections. Either of these hypotheses, if supported, suggest that ibogaine treatment may be enhanced when families and significant others are included in the process of preparation or recovery/integration, or by connecting patients to mutual support groups or assisting them in developing new social connections following treatment.

Our results also highlight the importance of persisting psychological and spiritual insights gained during the ibogaine session, which were reported to a higher degree in treatment responders compared to non-responders. This raises the question of whether the insightful or mystical effects engendered by ibogaine are a necessary component of the experience, similar to the mystical experience found to be associated with persisting changes following psilocybin administration in clinical trials (e.g., Griffiths et al. 2006, 2011), and thus required to catalyze a therapeutic outcome. Although research

using non-psychedelic congeners of the ibogaine molecule (e.g., 18-methoxycoronaridine; Rezvani et al. 2016) supports the potential of this substance in reducing substance use in animal models, these endeavors may limit the therapeutic role of the acute psychedelic experience in humans. For example, research on the applications of LSD and psilocybin in the treatment of addiction demonstrates that their efficacy is, in part, due to their ability to occasion mystical experiences, which in turn have lasting effects on personality and outlook (Bogenschutz and Johnson 2016). Thus, the role of the psychedelic experience can be one of visions and breakthrough psychological insights that are not merely an unwanted side-effect but are a primary therapeutic mechanism. This hypothesis awaits future research using rigorous experimental designs.

Study limitations should be considered when interpreting these results. First, we recruited participants who received ibogaine detoxification from only one facility, most of whom were White and male, and individuals who received treatment elsewhere or who are from diverse backgrounds may have experienced different persisting effects. Our response rate was 47% of all possible patients with contact information from this clinic, and it is possible that patients who were not reached or who declined to participate differed in their persisting experiences associated with ibogaine detoxification. Our results are also dependent upon factors associated with retrospective recall and social desirability. Similarly, although participants were asked about their experiences in relation to ibogaine, it is possible that their attributions are better accounted for by other aspects of their residential detoxification experience, such as the social support experienced by the staff of the treatment facility or the cumulative effects of the multiple psychosocial and medical treatments attempted by patients prior to this treatment. Moreover, we used a modified version of a measure assessing the persisting effects associated with ibogaine detoxification and, due to our small sample size, we were unable to examine the psychometric properties of this modified questionnaire. Consequently, the reliability and validity of this scale should be examined in future studies.

These limitations notwithstanding, the study findings have several implications. For example, future analyses should include prospective measures of multiple domains of emotional, social, and spiritual functioning following ibogaine interventions in order to develop predictive models for assessing factors associated with efficacy of the ibogaine detoxification experience. Further,

continuing to examine patient experiences using qualitative or mixed methods in research on ibogaine can be useful in developing more robust theoretical models surrounding short- and long-term ibogaine outcomes, as the data in humans are still negligible. Grounded qualitative approaches (Strauss and Juliet 1994) could be used to capture the phenomenology of this under-researched compound. Last, we recommend that researchers continue to elucidate what aspects of treatment appear to be beneficial or challenging for patients, which could inform current treatment practices in international jurisdictions where ibogaine is an available treatment option. In terms of clinical applications, clinicians who provide this intervention should know that the most frequently mentioned challenge in our sample was difficulty with integrating the acute effects of their ibogaine experience into their daily lives following treatment, for both treatment responders and non-responders. Therefore, such integration/aftercare needs could come in the form of connecting patients to some form of residential or outpatient psychological support (e.g., therapist, addiction recovery coach) in their home environment or to maintain such supports with patients via telemental health by providers associated with their treatment facility. Providing such services, especially to those with low levels of family or other social support, may contribute to a positive treatment response.

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ORCID

Alan K. Davis  <http://orcid.org/0000-0003-4770-8893>
Joseph P. Barsuglia  <http://orcid.org/0000-0001-7337-9486>

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