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Traditional Amazonian Medicine

Adapted To Treat Substance Use Disorder

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Abstract

Pathological substance use is amongst the most persistent and costly ills of global modern society. In spite of advances made in therapeutic possibilities over the past decades, long-term treatment responses remain relatively discouraging, with relapse rates higher than for most other psychiatric disorders. The chronic disease course of substance use disorder (SUD) has led to debate whether illness management strategies from somatic chronic care may also be suitable for SUD. In particular, traditional or alternative medicines, a common present-day adjunct to conventional somatic chronic care, may offer benefits for SUDs as well.

The current work consists of three empirical studies exploring the therapeutic potential of traditional Amazonian medicine as applied in an integrative addiction treatment program, using a multimodal and cross-disciplinary research approach. The investigation was conducted at the *Takiwasi Center for Addiction Treatment and Rehabilitation* in the Peruvian Amazon, an integrative healthcare center that implements a combination of traditional Amazonian medicine and conventional psychotherapy. As a first step, Study 1 aimed to investigate how SUD is understood in traditional Amazonian medicine and which kinds of treatment methods are used in this context, also aiming to identify the main therapeutic technique used for SUD. For this purpose, we conducted interviews with 13 practicing experts of Amazonian medicine, asking them about their underlying conceptions of disease etiology and treatment of SUD. A qualitative content analytic approach was adopted for data analysis, which revealed an array of conceptual categories. Some of the concepts regarding disease etiology showed similarity to Western scientific views proposing a biopsychosocial model for SUD. Amazonian treatment concepts however differed markedly from Western ones. Instead of identifying a main treatment constituent, the experts emphasized the importance of an integral, combined application of Amazonian methods.

Study 2 then aimed to investigate who the people are that seek out the Amazonian medicine based treatment for SUDs, assessing clinical and socio-demographic characteristics of 50 SUD-diagnosed patients enrolling in the Takiwasi treatment by means of structured clinical interviews and psychological self-report measures. We additionally were interested to know the participants' motivations for selecting this particular therapy program, which we assessed via qualitative analysis of patient motivation letters. Our results showed that most Takiwasi patients were young or middle-aged, unmarried males living with their relatives in urban areas in Peru or other Latin American countries. Polydrug use was the most common diagnosis, with cannabis, alcohol, cocaine and cocaine base paste as the most prevalent substances. Common comorbid psychopathologies included anxiety and mood disorders as well as antisocial personality disorder. Compared to norms from patients entering conventional psychiatric treatment, severity was elevated in the Takiwasi sample on several addiction and well-being indicators. The motives behind individuals' choices to initiate treatment at this center are described.

Finally, Study 3 aimed to explore short-term treatment effects of the overall Takiwasi therapy program. About one-third of the initial sample abandoned treatment prematurely, which resulted in a final sample of n = 36 SUD-diagnosed patients that completed the treatment. We found significant improvements of addiction severity from baseline assessment to treatment completion on indicators of drug use, alcohol use, psychiatric status, and social and familial relationships. Overall substance craving decreased significantly after treatment, as did overall emotional distress. Quality of life scores increased significantly at treatment completion. Taken together, these findings point to a substantial improvement of key symptomatic features of SUD after completing this alternative SUD treatment. At the same time it is important to note that these results are preliminary and need to be confirmed by further, randomized-controlled studies including follow up assessments.

In summary, findings from this research point to a promising novel treatment approach for SUD, which invites further investigation. We propose two parallel lines of research to be followed: One is qualitative, involving a detailed and systematic inquiry into the conceptual underpinnings of Amazonian medicine, and a thorough analysis of its characteristics and specifics for safe and efficacious application. The second line of research should involve quantitative studies on treatment effects, using progressively more controlled research designs adapted to a traditional medicines paradigm, while also assessing the transferability of Amazonian therapeutic methods to other cultural contexts. Results from the current work serve as a basis for future research and may in the long term open new treatment possibilities for SUD on a large scale.

Zusammenfassung

Schädlicher Substanzgebrauch gilt als eines der wesentlichsten Gesundheitsprobleme weltweit, welches auf individueller sowie gesellschaftlicher Ebene mit erheblichen Kosten und Leidensdruck verbunden ist. Substanzgebrauchsstörungen gelten heute als chronische Erkrankung, für deren Versorgung noch nach langfristig wirksamen Lösungen gesucht wird. Heutzutage wird für die Behandlung somatischer chronischer Erkrankungen zunehmend zu alternativ- bzw. traditionell-medizinischen Verfahren gegriffen, oftmals zusätzlich zu herkömmlichen medizinischen Behandlungen. Eine solche Behandlungsstrategie könnte auch für Substanzgebrauchsstörungen Chancen bergen.

Die vorliegende Arbeit untersucht in drei empirischen Studien mittels multimodalem Forschungsdesign, interdisziplinärem Rahmen und kulturübergreifender Perspektive die therapeutischen Potentiale einer spezifischen alternativen Suchtbehandlung, welche auf traditionellen Heilmethoden aus dem Peruanischen Amazonasgebiet basiert. Die Untersuchung wurde im *Takiwasi Center* (Tarapoto, Peru) durchgeführt, ein Suchtbehandlungszentrum, dessen Therapieangebot westliche psychotherapeutische Methoden mit traditioneller Amazonasmedizin kombiniert.

Studie 1 ermittelte Krankheits- und Behandlungskonzepte aus traditionell-medizinischer Sicht mittels qualitativer Forschungsmethoden. Es wurden halbstrukturierte Interviews mit 13 praktizierenden Experten/innen der traditionellen Amazonasmedizin durchgeführt und inhaltsanalytisch ausgewertet. Die Ergebnisse wiesen auf ein vielschichtiges Krankheitsverständnis hin. Der Experten ätiologische Erklärungen zeigten Ähnlichkeit mit aktuellen wissenschaftlichen Ansätzen welche ein biopsychosoziales Modell für Substanzgebrauchsstörungen postulieren. Die traditionellen Behandlungsmethoden hingegen, welche die komplexe Anwendung von Medizinalpflanzen mittels rituellen Techniken umfassen, sind mit westlichen Therapien schwer vergleichbar. Die Experten betonten in

diesem Zusammenhang die Bedeutsamkeit der traditionellen Techniken und des ganzheitlichen Einsatzes der verschiedenen Interventionen.

In Studie 2 wurden die Merkmale der Patienten, die das peruanische integrative Therapiezentrum aufsuchen, untersucht. Zu diesem Zweck wurden soziodemographische sowie klinische Merkmale von 50 Patienten anhand von klinischen Interviews und psychologischen Fragebogen erfasst. Zusätzlich wurde der motivationsbezogene Hintergrund der Entscheidung, sich in dieser Klinik behandeln zu lassen, mittels qualitativem Verfahren erfasst. Ergebnisse zeigten, dass die meisten Takiwasi-Patienten unverheiratete Männer jungen oder mittleren Alters sind, welche in städtischen Regionen Perus und anderer lateinamerikanischen Länder leben. Die meisten Patienten wiesen einen Mischkonsum auf, wobei Cannabis und Alkohol die meistgebrauchten Substanzen waren, gefolgt von Kokain und deren Vorläuferprodukt (Kokainbasispaste). Komorbide psychische Störungen umfassten insbesondere affektive und Angststörungen sowie antisoziale Persönlichkeitsstörung. Vergleiche mit Normwerten wiesen bei einigen klinischen Indikatoren auf einen stärkeren Beeinträchtigungsgrad der Stichprobe hin. Ergebnisse bezüglich Behandlungsmotivation werden im Detail beschrieben.

Studie 3 ermittelte anhand eines naturalistischen Forschungsdesigns die Kurzzeiteffekte der Takiwasi-Therapie insgesamt. Die Baseline-Messung klinischer und soziodemographischer Merkmalen erfolgte bei Eintritt vor Beginn der Behandlung(T1). Die Indikatoren die als Outcome-Kriterien dienten wurden nach Beendigung der Therapie erneut gemessen (T2). Etwa ein Drittel der Studienteilnehmer verliess die Behandlung frühzeitig, so dass die finale Stichprobe aus 36 Teilnehmenden bestand. Es konnten signifikante Verbesserungen des Schweregrads bei folgenden klinischen Indikatoren festgestellt werden: Drogenkonsum, Alkoholkonsum, psychiatrische Beeinträchtigung, soziale/familiäre Beeinträchtigung, Substanzcraving, allgemeine emotionale Beeinträchtigung sowie

Lebensqualität. Aufgrund des naturalistischen Designs und der fehlenden Kontrollgruppenbedingung sollten diese Ergebnisse allerdings als präliminär verstanden werden; sie stellen erste Hinweise für positive Outcomes dieser Therapie dar.

Insgesamt deuten die Ergebnisse der vorliegenden Untersuchung auf einen vielversprechenden integrativen Behandlungsansatz für Substanzgebrauchsstörungen hin. Weitere vertiefende wissenschaftliche Studien sind notwendig, um endgültige Aussagen machen zu können. Hierfür sollten zwei Forschungsrichtungen weiterverfolgt werden: Zum einen sollte durch weitere qualitative Studien ein vertieftes Verständnis der Therapiemethoden und der Amazonasmedizin zugrundeliegender Konzepte erarbeitet werden. Zum anderen sollte weitere quantitative Forschung mittels kontrollierter randomisierter Studien die Langzeiteffekte der Behandlung untersuchen und deren Anwendung in verschiedenen Kulturen erproben. Die vorliegenden Befunde bilden die Grundlage für weiterführende Studien, welche längerfristig zu neuen Behandlungsmöglichkeiten für Substanzgebrauchsstörungen auf internationaler Ebene führen könnten.

List of abbreviations

AA/NA	Alcoholics Anonymous / Narcotics Anonymous
APA	American Psychiatric Association
ASI	Addiction Severity Index
BF	Bonferroni-corrected
CBT	Cognitive-Behavioral Therapy
CEQ	Craving Experience Questionnaire
CI	Confidence Interval
DSM	Diagnostic and Statistical Manual of Mental Disorders
HADS	Hospital Anxiety and Depression Scale
ICD	International Classification of Diseases
NIDA	National Institute on Drug Abuse
M	Mean
MINI	Mini International Neuropsychiatric Interview
RCQ	Readiness to Change Questionnaire
SD	Standard deviation
SMD	Standardized Mean Difference
SPSS	Statistical Package for the Social Sciences
SUD	Substance use disorder

SWBS	Spiritual Well-Being Scale
TSF	Twelve-Step Facilitation
UNODC	United Nations Office on Drugs and Crime
WHO	World Health Organization
WHOQOL	World Health Organization Quality of Life Questionnaire

Table of Contents

1. Introduction

The pathological usage of psychoactive substances represents one of today's largest public health problems worldwide. It is associated with extensive impairments to health and early death, contributing substantially to the overall global burden of disease (Lim et al., 2012; Mathers, Stevens, & Mascarenhas, 2009).

1.1. Global prevalence of pathological substance use

Global estimates assess that 4.9% of the 2012 adult world population suffered from alcohol use disorders in the previous year (Gowing et al., 2015). The past-year prevalence of alcohol consumption in general (pathological or not) was estimated to be 43% worldwide, with large geographic variations ranging from 88.2% in western Europe to 9.8% in certain parts of Asia (Gowing et al., 2015). For illegal psychoactive substances, such as cocaine, heroin, or cannabis, past-year prevalence worldwide was estimated to range between 3.5 and 9.0%, again with considerable between-country differences (Gowing et al., 2015). The globally most prevalently used illegal substance was cannabis, followed by cocaine-type and amphetamine-type stimulants (Gowing et al., 2015). Past-year prevalence estimates in Europe also identified cannabis as the most frequent illicit substance (Mounteney et al., 2016; 15-34 years aged population), ranging from 22.1% in France to 0.4% in Turkey, followed by cocaine (from 4.2% in the United Kingdom to 0.2% in Greece and Romania), and ecstasy (from 3% in the Czech Republic and the United Kingdom to 0.1% in Italy and Turkey). The World Drug Report of the United Nations Office on Drugs and Crime (UNODC, 2016) estimates 29 million people in the world to suffer from drug use disorders.

1.2. Individual and societal impact

Pathological substance use has deleterious consequences, not only because of direct physical harm caused by toxic substance intake or overdose, but also indirectly, due to dangerous or risky behaviors in the intoxicated states, accidents, violence (linked for instance to drug trafficking), infectious diseases from injecting drugs or sexually transmitted, etc. (Lim et al., 2012; Mounteney et al., 2016). For example, more than 60 types of diseases and injuries have been linked to alcohol consumption (Mathers et al., 2009). In the latest repetition of the Global Burden of Disease Study 2013 (Forouzanfar et al., 2015), alcohol, tobacco, and drug use featured prominently among the top ten risk factors to health and mortality in the world. While tobacco smoking was the number one risk factor in most high-income countries, alcohol use was the leading one in most of Latin America (Forouzanfar et al., 2015). The number of deaths in the world attributable to alcohol and drug use encompassed 3.2 million individuals in 2013 (Forouzanfar et al., 2015).

Direct and indirect consequences of harmful substance use come with high costs, both for individuals as well as on a societal level (UNODC, 2016). Economic analyses have attempted to express these costs in monetary terms (e.g., Collins & Lapsley, 2008; Garcia-Altes, Olle, Antonanzas, & Colom, 2002; Gonçalves, Lourenço, & da Silva, 2014; Healey et al., 1998), combining expenses arising from health care, accidents, loss of productivity and work incapacity, criminality and law enforcement, and so on. To give an example, the United States National Institute on Drug Abuse (NIDA) assesses the abuse of tobacco, alcohol, and illicit drugs to cost their nation more than $700 billion annually (NIDA, 2017). However, non-tangible costs, like loss of life or affliction experienced by the concerned individuals, are masked in such quantifications (UNODC, 2016).

1.3. Gap in service provision

In spite of the international concern and magnitude of the issue, there is a continuing gap in service provision for substance use problems worldwide, with only 1 in 6 persons requiring treatment actually receiving it (UNODC, 2016). For example, a study reviewing community-based psychiatric epidemiology studies estimated the treatment gap (assessed as median rate of untreated cases) for different mental health disorders, for example major depression (56.3%), schizophrenia and other psychoses (32.2%), panic disorder (55.9%), or obsessive-compulsive disorder (59.5%), and found the largest treatment gap (78.1%) for alcohol abuse and dependence (Kohn, Saxena, Levav, & Saraceno, 2004). What prevents the affected individuals from obtaining help is most likely a large-scale lack of access to acceptable treatments, besides the characteristic fear of stigmatization and often denial that the consumption is problematic (Volkow & Li, 2005). There is thus a critical need for treatments that are accessible, acceptable, and affordable for the wider public (Kohn et al., 2004; Pullen & Oser, 2014; UNODC, 2016).

Local traditional medicines seem to suggest themselves as a potential answer to this gap (Bill et al., 1993). Such treatments tend to be considerably more cost-effective than Western biomedical interventions, more accessible to the larger population (especially in rural regions), and, depending on the context, also more culturally familiar (Bill et al., 1993; Bodeker & Kronenberg, 2002). This is particularly the case in developing countries, where the majority of the population relies on traditional medicines for primary health care (Shanley & Luz, 2003)

1.4. The present work

In light of this situation and the identified gap, the present work aims to explore therapeutic potentials of an integrative addiction treatment based on traditional medicine. The

following Chapter 2 will provide a literature-based overview of relevant theoretical concepts and state of the art research. Chapter 3 will outline the empirical work of the current investigation, describing its context, research questions, goals, and methodologies. Chapters 4, 5, and 6 subsequently describe in detail the three empirical studies that represent the core of this work. They are presented here in the form of preliminary manuscript versions; their final versions have been published as original research papers in three international peer-reviewed scientific journals. The concluding Chapter 7 then provides a general discussion of the empirical work conducted, including a summary of key findings, discussion of results, study limitations, outlook with recommendations for future research, and conclusions.

2. Theoretical background

2.1. Substance use disorder: Current scientific views and treatments

2.1.1. Terminology and diagnostic criteria

The WHO Lexicon of Alcohol and Drug Terms (Babor, Campbell, Room, & Saunders, 1994) points to the varied usage of the term *drug*. Whereas in pharmacology it designates any chemical agent that modifies the physiology of an organism, the medical context generally reserves this term for substances with curative properties, or conversely, it is used colloquially to refer to substances that are psychoactive and illicit, such as cocaine or heroin (Babor et al., 1994). A *psychoactive substance* may refer to a chemical or natural substance, licit or illicit, which, when ingested, effects changes in cognitive, affective, or behavioral functioning (Babor et al., 1994; Bühringer & Behrendt, 2011; Shadel, Shiffman, Niaura, Nichter, & Abrams, 2000).

The pathological usage of psychoactive substances (subsequently abbreviated as *substance/s*) was historically called *addiction*, a term the WHO however abandoned in the 1960ies (Babor et al., 1994). The addiction term was exchanged for *dependence*, defined as a state of psychological and/or physiological reliance on a substance, arising in a person following recurrent usage of that substance (Eddy, Halbach, Isbell, & Seevers, 1965). Physiological dependence was conceptualized to involve *tolerance*, a natural bodily response in which repeated or prolonged exposure to a substance leads to a lessening of its experienced effects and therefore necessity for higher dosages to achieve comparable effects (Heit, 2003). If after sustained usage, the consumption of certain substances (e.g., opiates, alcohol) is discontinued, *withdrawal* symptoms may develop, i.e., unpleasant behavioral, physiological, or cognitive responses to the disequilibrium induced by the decline of substance concentration in the body (APA, 2000; Schmidt & Rist, 2006; Shadel et al., 2000). Withdrawal symptoms

are substance-specific and are usually alleviated with the renewed ingestion of the substance (Eddy et al., 1965). Another relevant concepts is *craving* or the strong desire or urge to use a substance (Skinner & Aubin, 2010). Although there is controversy as to the precise nature and definition of the craving concept, there is a general agreement that craving represents a central aspect of all pathological substance use (Pickens & Johanson, 1992).

The former version of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM–IV–TR; American Psychiatric Association [APA], 2000) defined diagnostic criteria for *Substance Dependence* as follows:

> A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring at any time in the same 12-month period: (1) tolerance, as defined by either of the following: (a) a need for markedly increased amounts of the substance to achieve intoxication or desired effect, (b) markedly diminished effect with continued use of the same amount of the substance; (2) withdrawal, as manifested by either of the following: (a) the characteristic withdrawal syndrome for the substance (refer to Criteria A and B of the criteria sets for Withdrawal from the specific substances), (b) the same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms; (3) the substance is often taken in larger amounts or over a longer period than was intended; (4) there is a persistent desire or unsuccessful efforts to cut down or control substance use; (5) a great deal of time is spent in activities necessary to obtain the substance (e.g., visiting multiple doctors or driving long distances), use the substance (e.g., chain-smoking), or recover from its effects; (6) important social, occupational, or recreational activities are given up or reduced because of substance use; (7) the substance use is continued

> despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance (e.g., current cocaine use despite recognition of cocaine-induced depression, or continued drinking despite recognition that an ulcer was made worse by alcohol consumption). (p. 181)

A somewhat less severe but still pathological substance use pattern was reflected in the DSM–IV–TR (APA, 2000) diagnostic category labeled *Substance Abuse*:

> [A.] A maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by one (or more) of the following, occurring within a 12-month period: (1) recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home (e.g., repeated absences or poor work performance related to substance use; substance-related absences, suspensions, or expulsions from school; neglect of children or household); (2) recurrent substance use in situations in which it is physically hazardous (e.g., driving an automobile or operating a machine when impaired by substance use); (3) recurrent substance-related legal problems (e.g., arrests for substance-related disorderly conduct); (4) continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance (e.g., arguments with spouse about consequences of intoxication, physical fights). [B.] The symptoms have never met the criteria for Substance Dependence for this class of substance. (p. 182-183)

Similarly, the *International Classification of Diseases* (ICD–10; World Health Organization [WHO], 2004) uses two categories labeled *dependence syndrome* and *harmful use*, which are equivalent to the *dependence* and *abuse* categories, respectively, from the

DSM–IV–TR (APA, 2000). Since the empirical part of the present work was based on the DSM (mainly on the corrected 4th version; APA, 2000) rather than on the ICD–10 (WHO, 2004), we refrain from describing the ICD categories in further detail.

The last revision of the DSM resulting in its 5th version (DSM–V; APA, 2013) led to structural changes and modifications of criteria in the chapter on substance-related disorders (Hasin et al., 2013). Dependence and abuse criteria were merged into a single diagnostic category labeled *Substance Use Disorder* (subsequently: *SUD*) made of 11 criteria, out of which 2 need to be present within a 12-months period in order to assign the SUD diagnosis (APA, 2013; Hasin et al., 2013). Furthermore, *craving* was added as a diagnostic criterion, and the former criterion concerning legal problems (nr. 3 of the DSM–IV–TR abuse criteria; APA, 2000) was omitted (Hasin et al., 2013). Overall severity in the DSM–V (APA, 2013) can now be estimated using a criteria count, with 2–3 symptoms being classified as *mild*, 4–5 symptoms as *moderate*, and 6 or more symptoms as *severe*. According to the DSM–V (APA, 2013), SUD can be developed for the following classes of drugs: alcohol; caffeine; cannabis; hallucinogens; inhalants; opioids; sedatives, hypnotics, and anxiolytics; stimulants (including cocaine and amphetamine-type substances); tobacco; and other (or unknown) substances.

In the scope of this work, we use the term *SUD* (or its plural *SUDs*) in an inclusive manner, unless otherwise stated, to denote a pathological substance use in terms of any of the abovementioned diagnostic categories of the 4th and 5th DSM (APA, 2000; 2013), as well as of the ICD–10 (WHO, 2004).

2.1.2. Etiological models

Current scientific views of SUD postulate a *biopsychosocial model*, in which psychosocial factors interact with genetic and physiological predispositions and together contribute to the propensity for developing SUD (Küfner & Metzner, 2011; Lindenmeyer,

2011; Martin-Soelch, 2010, 2013; Wallace, 1990; Zucker & Gomberg, 1986). Diverse sources of vulnerability have been identified, among them adverse life experiences (especially early stressors), temperament and personality traits (such as impulsivity), developmental factors (e.g., initiating substance use during early developmental stages), psychopathological comorbidities, socioeconomic environment, and the presence and ease of access to drugs (Koob & Le Moal, 2008; Martin-Soelch, 2013; Volkow & Li, 2005).

A large number of etiological models, focusing on different aspects of SUD and classifiable along differing parameters, have been proposed (Anderson, 1998; Küfner & Metzner, 2011; Miller & Kurtz, 1994; Petraitis, Flay, & Miller, 1995). While a comprehensive overview of such models is beyond the scope of this work, some central theoretical concepts will be outlined here for each of the three components of the biopsychosocial framework:

Behavioral-biological approaches based on classical and operant conditioning explain the initiation and persistence of drug use in terms of a complex interplay of positive and negative reinforcement (Martin-Soelch, 2010, 2013). Pleasant drug-induced states act as positive reinforcement and are what drives drug-seeking initially. A shift to negative reinforcement tends to gradually occur, insofar as aversive physical and affective states develop when substance use is discontinued (i.e., withdrawal); since drug intake tends to alleviate these states, those behaviors are further strengthened (Koob, 2009). On a neurophysiologic level, the dysregulation of the cerebral dopamine system, which is linked to motivation and reward, is believed to be key in the acquisition and maintenance of SUDs across substances (Martin-Soelch, 2013). Moreover, the development of a drug-related memory is believed to play an important role in these processes (Martin-Soelch, 2013); drug-related stimuli become conditioned with the hedonic, reinforcing effects of the substance, gain excessive motivational value, and may act as cues that subsequently trigger the drug-seeking

behavior independently (Di Chiara, 1999; Martin-Soelch, 2013). These characteristic neuroadaptive changes are observed to be long-term and to date appear to be irreversible, suggesting that once acquired, SUD may present a chronic condition (Le Moal & Koob, 2007).

Cognitive approaches focus on underlying belief systems of individuals suffering from SUDs, which are typically biased and associated with alterations in decision-making processes (Marlatt & George, 1984; McCusker, 2001). Characteristically, this involves positive outcome expectancies (i.e., expecting benefits from substance use), coupled with a diminished self-efficacy (an internalized view of low personal capacity for coping), that together propel pathological consumption (Marlatt & George, 1984; Shadel et al., 2000; Skinner & Aubin, 2010). Minimization of expected negative outcomes is seen to play a role in the maintenance of substance use behaviors as well (McCusker, 2001). Similar to behavioral approaches, cognitive models also refer to learning mechanisms and reinforcement, but elucidate particularly the manner in which inner cognitions translate into addictive behaviors (Shadel et al., 2000). Wright, Beck, Newman, and Liese (1993) point to three types of dysfunctional beliefs (i.e., cognitive tendencies that are relatively stable and resistant to change) that contribute to SUD: anticipatory beliefs (e.g., "life is more enjoyable when I smoke"), relief-oriented beliefs (e.g., "I can't stand this sensation any longer"), and facilitative/permissive beliefs (e.g., "cannabis is not so harmful after all"). Such underlying drug-related beliefs are said to become active in high-risk situations, i.e., circumstances which may be external (e.g., social pressure, interpersonal conflict) or internal (e.g., negative emotional states) and involve tension (Beck, Wright, & Newman, 1992; Marlatt & George, 1984). Automatic thoughts get triggered by those underlying beliefs and result in craving, which in turn activates permissive beliefs, decreases awareness for potentially negative consequences, and induces a shift of attention to concrete behaviors for obtaining the substance (Wright et al., 1993).

Sociocultural approaches for SUD are based on the acknowledgement that social values and political action exert a strong influence on the patterns and manners in which psychoactive substances are used in a given society (Bühringer & Behrendt, 2011; Lindenmeyer, 2011). Such models map how those influences contribute to SUD on different levels of social functioning –from macro, i.e., socio-political and economic factors on national and international levels, to micro, e.g., family or school (Anderson, 1998). Primary socialization theory (Oetting & Donnermeyer, 1998) for example, highlights the importance of a youth's sources of socialization for his or her potential drug use, socialization being defined as the "process whereby individuals learn to interact within their environment using behaviors that are acceptable and/or not acceptable" (p.986; Leukefeld & Leukefeld, 1999). Family, peers, and schools are seen as the primary influences of socialization, which directly transmit norms; secondary socialization factors, such as government institutions (e.g., health care or criminal justice systems), media, religious institutions, etc., are said to indirectly influence the socialization process and determine tendencies for prosocial and antisocial behaviors (Leukefeld & Leukefeld, 1999). Similarly, social control theory (Elliott, Ageton, & Huizinga, 1982) states that "weak conventional bonds", i.e., a lack of commitment to conventional society, its values, institutions, role models, and religions, causes individuals to form associations with substance using peers. Strong conventional bonds to society are argued to be what usually prevents people to act out latent deviant impulses, but when such bonds are missing (i.e., feeling detached or alienated from society), individuals tend to associate with deviant/drug using peers and engage in deviant behaviors themselves (Petraitis et al., 1995). According to this theory, causes for lacking commitment to society are found on different levels, including disorganized families, lack of occupational opportunities, disorganized neighborhoods, or a more general breakdown of social systems and establishments (Elliott et al., 1982).

2.1.3. Psychosocial treatments for SUD

Most of currently existing psychosocial interventions for SUD directly draw on some of the above theoretical concepts, implementing one or a combination of the following paradigms:

Treatments grounded in *cognitive-behavioral therapy (CBT)* are common in contemporary clinical practice (Carroll & Onken, 2005). Such treatments focus on identifying and modifying the dysfunctional belief systems underlying the drug-seeking behavior, challenging positive outcome expectancies, and often also training of skills or alternative behaviors (McCusker, 2001; Wright et al., 1993). *Relapse prevention* is a common example for CBT in this context, where drug use cessation and/or maintenance after cessation is encouraged by teaching and training strategies for averting relapse or the return to usage (Irvin, Bowers, Dunn, & Wang, 1999; Marlatt & George, 1984). This intervention specifically targets the identification of high-risk situations, in which drug use is likely to occur, and the development of effective coping in them (Marlatt & George, 1984).

A strongly behavior-oriented intervention is *contingency management* (e.g., voucher-based therapy; Higgins, Alessi, & Dantona, 2002), in which desirable behaviors that are incompatible with drug use are reinforced by means of incentives and the mechanisms of operant conditioning (Prendergast, Podus, Finney, Greenwell, & Roll, 2006). Contingency management treatments are rarely applied in current practice (Kiluk & Carroll, 2013) although they are considered an effective method (Carroll & Onken, 2005). This may be due to the high costs because of the incentives, the difficulty for applying it in groups, and a tendency of patients to fall back to baseline rates of consumption when incentives are removed (Kiluk & Carroll, 2013).

Motivational enhancement therapy or *motivational interviewing* is a widely-adopted type of brief intervention for SUD, which uses an empathic, person-centered approach and

directive counseling style to support the development of responsibility and self-efficacy, while avoiding confrontational methods (Miller, 1996). Eliciting "change talk" (i.e., the verbalization of arguments for change; Miller & Rose, 2009) is hypothesized to be an active mechanism of this treatment (Kiluk & Carroll, 2013).

Another prevalent approach for SUD therapy are *alcoholics/narcotics anonymous (AA/NA)* and the related *twelve-step facilitation (TSF)* interventions, which through 12 sequential steps encourage self-acceptance, engagement in community activities, and the endorsement of a spiritual orientation (Galanter, 2007; Kelly & White, 2012; Ouimette, Finney, & Moos, 1997). Treatments like AA/NA or TSF are popular the world over (Galanter et al., 2007), but a certain controversy exists due to its reliance on and particular usage of the concept of "Higher Power" and spirituality (Sussman et al., 2013).

Finally, *therapeutic community* or *milieu therapy* is based on the idea that living in close association with people who cope with similar problems may bring about therapeutic benefits (Almond, Keniston, & Boltax, 1968). Such treatments are usually long-term, aiming to aid the individual to return to a healthy life in society, and are inherently delivered in a residential or inpatient setting (Rosenthal, 1984).

In general, inpatient treatments for SUD usually also offer pharmacotherapy in conjunction with psychosocial interventions (Schmidt & Rist, 2006). The current work will not further elaborate on pharmacological therapies for SUD but, in brief, such treatments tend to involve substitution therapy (e.g., prescription opiates like Methadone for heroin users), anti-craving agents (e.g., Acamprosat for alcohol users), hypnotics (e.g., benzodiazepines for amphetamine users), aversive agents (e.g., Disulfiram/Antabuse for alcohol users), and/or other psycho-pharmaceuticals like antidepressants or anxiolytics (Gerada, 2005; Schmidt & Rist, 2006).

In general, the decision of whether an individual is treated in an inpatient (residential, stationary) or in an outpatient (ambulatory, day-care) context depends on both economic and clinical considerations, including an individual's somatic condition, presence or absence of suicide risk, other psychiatric comorbidities, as well as a person's general living situation (Küfner & Metzner, 2011). Arguments favoring the residential setting usually stress the benefit of removing patients from their usual context linked to substance use, the capacity of such settings to direct patients' attention and efforts to the treatment, as well as an increased access to medical care and emotional support otherwise unavailable to most patients (Finney, Hahn, & Moos, 1996). Those in favor of outpatient settings on the other hand argue that it is more cost-effective, and that in an outpatient context patients may more realistically assess their behavior and directly apply newly acquired coping skills (Annis, 1985; Lindenmeyer, 2011). With regard to its success, research comparing the inpatient and outpatient setting (beyond the specific SUD intervention/s used) has so far produced inconsistent results and no indication of superiority for either of the two (Berglund et al., 2003; Finney et al., 1996).

2.1.4. Treatment outcomes and relapse

Meta-analyses examining CBT in the context of SUD point to small but statistically significant effects (Kiluk & Carroll, 2013): A meta-analysis of randomized controlled trials found a significant effect (Hedges' g as effect size estimate) of $g = 0.154$, $p < .005$ at the initial outcome assessment, which after 6-9 months follow-up was $g = 0.115$, $p < .005$, and at 12-months follow-up $g = 0.096$, $p < .05$ (Magill & Ray, 2009). Alcohol users, cannabis users, cocaine users with comorbid depression, as well as female participants tended to respond particularly well to this type of treatment (Carroll & Onken, 2005; Magill & Ray, 2009). Poor cognitive functioning, on the other hand, has been linked to less favorable treatment outcomes, which may be indicative of high cognitive demands in CBT as an intervention (Kiluk & Carroll, 2013). As for relapse prevention, a meta-analysis reported reductions in

substance use with an effect size of *r* = .14 (Irvin et al., 1999), and a narrative review suggests evidence to be strongest for smoking cessation (Carroll, 1996). A meta-analysis on contingency management interventions points to good overall effects initially (*d* = 0.42) which diminish over time (Prendergast et al., 2006). Largest effect sizes were found for opiate users (*d* = 0.65) and for cocaine users (d = 0.65; Prendergast et al., 2006). A meta-analysis specifically on the voucher-based variant of contingency management reported an effect size of *r* = .32 (Lussier, Heil, Mongeon, Badger, & Higgins, 2006). With regard to motivational interviewing, a Cochrane review found significant post-treatment effects on substance use (standardized mean difference [*SMD*] of 0.79, 95% CI 0.48 to 1.09), which diminished substantially after a short follow-up (*SMD* = 0.17, 95% CI 0.09 to 0.26) and disappeared after a long follow-up (Smedslund et al., 2011). Motivational interviewing has been found particularly effective for younger age groups, and relatively more suited for tobacco and alcohol-related interventions (Kiluk & Carroll, 2013). Evidence for AA/NA and TSF treatments is mixed at this stage. A literature review on the effectiveness of AA concluded there to be strong evidence for increased abstinence rates and for more frequent attendance to predict higher rates of abstinence (Kaskutas, 2009), as well as the effects not being due to self-selection (Humphreys, Blodgett, & Wagner, 2014). However, a Cochrane review concluded that the efficacy of AA or TSF could not unambiguously be demonstrated (Ferri, Amato, & Davoli, 2006). Finally, available studies for SUD treatment in the therapeutic community are limited, but one meta-analysis reports an effect size of *d* = 0.25, and suggests the intervention to be particularly apt for patients with more severe drug use (Prendergast, Podus, Chang, & Urada, 2002; Prendergast et al., 2006). In sum, for most of the above SUD therapies, evidence points to significant, but not overly large effect sizes (Dutra et al., 2008; Hubbard, Craddock, & Anderson, 2003; Miller & Wilbourne, 2002). However, a tendency for initial benefits to lessen over time can also be observed (Magill & Ray, 2009; Prendergast et

al., 2006; Smedslund et al., 2011), pointing to a general high likelihood for relapse, i.e., the return to substance use following a period of cessation (Lustyk, 2013).

High relapse rates remains an important challenge in the field (Brownell, Marlatt, Lichtenstein, & Wilson, 1986). Brandon, Vidrine, and Litvin (2007) report post-treatment relapse rates for different substances, ranging between 80–92% for alcohol use (after one year), 86% for heroin use (after one year), 75% for non-specific intravenous drug use (after varying follow-up periods up to 10 years), and 84–98% for tobacco use (after 6–12 months of follow-up). Other authors mention relapse rates across different substances and time frames between 60–80% (O'Brien & McLellan, 1996), 50–90% (Brownell et al., 1986), or somewhat more moderately between 40–60% (McLellan, Lewis, O'Brien, & Kleber, 2000), but, nonetheless, well above what can be considered desirable.

In an attempt to find out how to improve treatment success, researchers have thus turned to studying potential moderating or mediating factors rather than focusing on overall efficacy (Kiluk & Carroll, 2013). An exhaustive description of the research literature in this context would be beyond the present scope. Suffice it to say that the most commonly reported person-related predictors of treatment outcomes relate to levels of pre-treatment dependence severity, psychiatric severity, coping and self-efficacy, as well as motivational aspects (Adamson, Sellman, & Frampton, 2009; Brewer, Catalano, Haggerty, Gainey, & Fleming, 1998; McKay & Weiss, 2001).

Treatment motivation is a particularly important concept in this context, ascribed with a central role not only for treatment initiation, but also for retention, engagement and outcomes (Longshore & Teruya, 2006). In addiction research, the motivational concept is often articulated via the *stages of change* or *transtheoretical model* (Prochaska, DiClemente, & Norcross, 1992). This widely-adopted model describes a series of motivational stages that are said to characterize intentional changes in addictive behaviors, whether they are

therapeutically assisted or individually attempted (Prochaska et al., 1992). The stages of change construct involves five stages, through which people are said to progress in a spiral-like pattern: *pre-contemplation* (no or little interest for change), *contemplation* (analyzing potential costs and benefits of change), *preparation* (committing and planning), *action* (concrete acts are carried out), and finally *maintenance* (changed behavior becomes normative), but different variants of the model exist (DiClemente, Schlundt, & Gemmell, 2004). Besides its utility for assessing treatment motivation as a predictor for therapeutic success, the stages of change model is also frequently used in clinical practice to explain change processes to SUD patients (Küfner & Metzner, 2011).

2.1.5. SUD as a chronic illness

SUD is often conceptualized as a chronic disease, whereby the persistent tendency for recurrence is seen as a behavioral expression of the aforementioned drug-related memory and neuroadaptations that have been detected in substance users' brains (Koob & Le Moal, 2008; Volkow & Li, 2005). The DSM–V (APA, 2013) has consolidated this view in their manual, by describing as an important feature of SUD

> an underlying change in brain circuits that may persist beyond detoxification, particularly in individuals with severe disorders. The behavioral effects of these brain changes may be exhibited in the repeated relapses and intense drug craving when the individuals are exposed to drug-related stimuli. (p. 483)

In consideration of the observed long-term treatment responses and the manifestly chronic nature of SUDs, seminal work by McLellan and colleagues (2000) suggested that appropriate treatment standards for this disorder should actually be sought among other chronic illnesses, such as hypertension, diabetes, or asthma. Clinical practice however shows a tendency to treat SUD as an acute curable condition (White, Boyle, & Loveland, 2002;

Willenbring, 2014): Many patients receive only detoxification or acute stabilization, and in general, specialized programs often hope to rehabilitate and discharge patients as they would for a person after a simple surgery (McLellan et al., 2000). Exceptions certainly do exist (e.g., maintenences strategies such as relapse prevention; Marlatt & George, 1984), but a general tendency in contemporary addiction treatment remains (Willenbring, 2014). Yet, in keeping with today's prevailing conceptual understanding of SUD, this chronic condition may benefit from more comprehensive and long-winded care strategies, analogous to for instance cancer or diabetes (O'Brien & McLellan, 1996). Treating SUD in such a manner may present a doorway for translating the latest scientific conceptual understanding of this disorder into more effective therapeutic practices.

2.2. Alternative medicines: A potential for SUD treatment?

Alternative or *traditional medicines* play a central role in global health care and are increasingly being integrated into official health care policies (WHO, 2013). They are defined by the WHO (2000) as

> the sum total of the knowledge, skill and practices based on the theories, beliefs and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health, as well as in the prevention, diagnosis, improvement or treatment of physical and mental illnesses. (p. 1)

Traditional medicines are an emerging field particularly in the context of chronic health conditions (Bodeker & Kronenberg, 2002; Falci, Shi, & Greenlee, 2016; WHO, 2013). Individuals suffering from for instance multiple sclerosis (Skovgaard et al., 2012), chronic pain (Rosenberg et al., 2008), musculoskeletal disorders (Rossignol et al., 2011), or cancer (Molassiotis et al., 2005) tend to turn to alternative treatments on an international level, and research in this context is increasing (e.g., a recent Swiss study investigating Maya medicine

for cancer; Berger-Gonzalez, Gharzouzi, & Renner, 2016; Berger-Gonzalez, Stauffacher, Zinsstag, Edwards, & Krutli, 2016; Berger-Gonzalez, Vides-Porras, et al., 2016)

Considering the emergent role of alternative medicines in somatic chronic care, and given SUD's chronic nature, similar applications might be promising also for SUD. Transposing such a care model to SUD could have the advantage of accounting for the disorder's chronic nature, as well as the potential of novel and low-cost treatment possibilities (Bill et al., 1993; WHO, 2013). Indeed, the WHO has identified the potential of traditional therapies for SUD already long ago; a 1993 synopsis of observational evidence led them to conclude that "in the rehabilitation and prevention of chemical substance dependence, therapeutic modalities based on indigenous cultural and religious traditions are found in general to be as successful as, and in some instances more successful than, 'official' treatment and rehabilitation programs" (Bill et al., 1993, p.184).

In spite of the confidence expressed in this statement made over 20 years ago in an international WHO publication, the extent to which research on such methods has been reported in the scientific literature thus far is modest. Heggenhougen (1997) provided a valuable description of indigenous SUD therapies from Thailand, Malaysia, and other countries. A more recent study presented a literature-based overview of remedies from diverse traditions, such as Ayurveda, indigenous American medicines, traditional African medicines, etc., allegedly helpful for SUD (Lu et al., 2009). Further, Khanna and Greeson (2013) describe applications of Indian yoga practices and mindfulness meditation to SUD. Mindfulness-based therapies have recently been integrated into more conventional paradigms as part of the so called third wave CBT (Kahl, Winter, & Schweiger, 2012), and also applications specifically for SUD ("mindfulness-based relapse prevention") are gaining popularity (Kiluk & Carroll, 2013; Witkiewitz & Bowen, 2010). Finally, the use of acupuncture and herbal remedies from traditional Chinese medicine is also reported for SUD

therapy (Min et al., 2007). However, systematic clinical studies analyzing these methods, their effects, underling disease concepts, and therapeutic effectiveness, are still rare.

2.3. Traditional Amazonian medicine and SUD treatment

There are reasons to believe that ancient healing knowledge from the Amazon rainforest could help treat SUD (Mabit, 2007; Thomas, Lucas, Capler, Tupper, & Martin, 2013). Traditional Amazonian medicine is a millennia-old healing science informed by great ecological diversity, a medical system which has survived repeated periods of colonization and exploitation, as have other such systems across Latin America (Finer, Jenkins, Pimm, Keane, & Ross, 2008; Giove Nakazawa, 2016; Montenegro & Stephens, 2006; Pedersen & Baruffati, 1985). It involves a complex usage of local medicinal plants, prepared and applied according to sophisticated rituals and rules (Bussmann & Sharon, 2006; Jovel, Cabanillas, & Towers, 1996; Luna, 1986; Sanz-Biset, Campos-de-la-Cruz, Epiquien-Rivera, & Canigueral, 2009). Indications that the Amazonian healing system holds effective methods specifically for SUD come from the *Takiwasi Center for Addiction Treatment and Rehabilitation* in Peru, a therapeutic institution that has been applying traditional Amazonian medicine to addiction-related problems since 1992 .

2.3.1. The Takiwasi Center for Addiction Treatment and Rehabilitation

In 1980, a French medical doctor went for a primary health care project with Médecins Sans Frontières (MSF) to Peru. He there discovered resourceful local medicinal traditions and, after his work with MSF had ended, began to investigate how these could be put to use more efficiently in order to respond to the local healthcare needs. This was a time of civil riots and drug-traffic in Peru, which pushed many Amazonian farmers to abandon food crops cultivation in favor of coca leaf production and manufacturing of cocaine (Giove Nakazawa,

2002; Sanz-Biset et al., 2009). As a consequence, addiction to cocaine and particularly to its precursor cocaine base paste was gaining incidence in the region (Giove Nakazawa, 2002).

It was against this backdrop that the *Takiwasi Center for Addiction Treatment and Rehabilitation* in the Amazonian highlands of Peru was founded in 1992, supported by the French Ministry of Foreign Affairs (General Delegation For the Fight against Drugs and Drug Addiction) and the European Commission's Directorate-General (DG8). The Takiwasi Center is formally recognized by the Peruvian Health Ministry and is one of very few legally acknowledged institutions treating addictions in Peru in general. It has pioneering character as the first health institution worldwide applying traditional Amazonian medicine to the treatment of substance use problems (Giove Nakazawa, 2002). More precisely, its therapeutic protocol combines traditional Amazonian medicine with contemporary psychotherapeutic approaches (Mabit & Sieber, 2006). The clinical staff at this center consists of specialized health professionals trained in traditional Amazonian medicine, as well as western-trained ones like psychologists, physicians, or nurses.

The Takiwasi Center offers residential treatment for addiction-related problems (maximal capacity of 18 beds) according to a defined therapeutic protocol. The inpatient treatment is restricted to males, in keeping with the Peruvian legal requirement for residential therapies to be gender-specific. The center additionally offers outpatient services for both males and females, regarding varying mental health concerns. Therapeutic activities of the residential SUD program consist of Western treatments on the one hand, such as individual and group psychotherapies, biomedical health checks, cohabitation in a therapeutic milieu, and performance of daily chores guided by an occupational therapist. In parallel to these treatments, traditional Amazonian herbal medicines and ritual interventions are applied as part of the therapy protocol. The Amazonian interventions used at this center may be grouped into three main types: (1) Purging rituals, in which plants that provoke emesis are administered in

a ritualized setting held by a traditional healer; (2) dietary retreats, i.e. weeklong solitary retreats in the forest involving the ingestions of medicinal plants; and (3) healing ceremonies, in which plant medicines are ingested in a ceremonial framework.

Completing the SUD inpatient treatment generally takes between 3 and 12 months, but the duration is adapted to each individual's needs. The program is structured into three stages: an initial detoxification phase of 2-4 weeks, a second stage, during which deeper psychotherapeutic work is aimed for, and a third stage, in which an individual's reintegration to professional and social life is prepared. Informal testimonies and statistics from the Takiwasi Center suggest promising results (Giove Nakazawa, 2002). However, no scientific clinical research has yet systematically studied this SUD treatment and its effects.

2.3.2. Recent developments around traditional Amazonian medicine

Besides the lack of scientific study of this specific SUD treatment based on traditional Amazonian medicine, we also identified a broader lack of clinical research on the Amazonian tradition as a medical system that can potentially treat mental health problems. This in spite of ethnobotanical evidence of vast numbers of plant species and techniques used in this region for the treatment of psychosomatic ailments, including for instance anxiety or stress-related conditions (Bussmann, Glenn, & Sharon, 2010; Shepard, 1998). However, what does exist, currently observable in both scientific and popular literature, is an exponentially rising interest in one specific therapeutic means from Amazonian medicine, namely ayahuasca or *Banisteriopsis caapi* (Tupper, 2009). Research examining psychotherapeutic applications of this plant or of the medicinal brew of the same name, to which *Banisteriopsis caapi* is the central ingredient, is increasing (e.g., Nielson & Megler, 2014; Sanches et al., 2016; Santos, Landeira-Fernandez, Strassman, Motta, & Cruz, 2007), and some studies have specifically focused on substance use problems (Fabregas et al., 2010; Loizaga-Velder & Verres, 2014;

Thomas et al., 2013). Findings suggest promising effects, but evidence at this point is fragmentary (Bouso & Riba, 2014).

However, while there is no doubt that ayahuasca represents a key element in traditional Amazonian medicine, it does not usually seem to be prescribed as a stand-alone treatment; there are numerous other plants and ritual interventions in Amazonian medicine (Bussmann et al., 2010; Elisabetsky, Figueiredo, & Oliveria, 1992; Sanz-Biset et al., 2009), suggesting that an unspecific or exclusive application of ayahuasca may not accurately represent Amazonian healing knowledge, nor necessarily bring about the desired results. Moreover, ill-informed and non-medical types of usages across the world are increasingly being witnessed (Tupper, 2008). In an attempt to protect the traditional usages of ayahuasca and differentiate them from inadequate and decontextualized usages, the Peruvian National Institute of Culture in 2008 declared traditional knowledge and usage of ayahuasca as practiced in Amazonian native communities as a National Cultural Heritage (Giove Nakazawa, 2016).

2.3.3. Twenty-first century Amazonian medicine: Can it be considered traditional?

The use of the term "traditional" in the scope of this work deserves a brief explanation. We refer to Amazonian medicine as "traditional" in accordance with the WHO definition (2000) and in the sense of it being entrenched in an old body of knowledge, similar to other ancestrally-rooted medical systems, such as traditional Chinese medicine. Moreover, we use this term to distinguish such medical systems from modern or conventional ones (biomedicine, contemporary psychology) based on Western sciences (Stoner, 1986). Nevertheless, considering the fundamental dynamism and transformational character of medical systems in general, which are essentially cultural systems (Kleinman, 1978), a clear-

cut distinction of such type may be unrealistic, and the terminology hence somewhat misleading (Janes, 1999; McClatchey, 2005).

The difficulty of correct terminology for these medicines (alternately called *traditional, indigenous, native, alternative, complementary*, etc.) goes beyond it being merely a linguistic challenge. Traditional medicines from around the world are observed to have changed significantly over the past centuries (Frank & Stollberg, 2004; McClatchey, 2005), tending to incorporate elements from biomedicine, which results in a fused medical understanding and practice, a phenomenon referred to as "medical syncretism" (Stoner, 1986; Waldram, 2000). This is particularly relevant for traditional healing systems of Latin America, given the far-reaching colonial and postcolonial influences that have been operative in this region since the 16th century, introducing diverse cosmological and medical belief systems from across the world (Andritzky, 1987; Bussmann, 2013; Luna, 1986; Pedersen & Baruffati, 1985).

In the Amazonian scenario, the situation is further complicated by the recent "globalization" of ayahuasca (Tupper, 2009) resulting in yet another cycle of foreign exchange and modification of Amazonian cultures. As a consequence, a complex hybridization (i.e., recombination of different forms of practices from separate systems into a new form; Pieterse, 1994) of medical knowledge and practice has ensued in the Amazon and in Peru in general (Bussmann, 2013). For these reasons, contemporary "traditional" Amazonian medicine can be expected to diverge from the original native science it historically was in very significant ways, exceptions perhaps still existing among communities living in deep (inaccessible) forest areas. Furthermore, on top of this general phenomenon of sociocultural hybridization and medical cross-pollination, the Takiwasi adaptation of traditional Amazonian medicine, with its combined approach and specific alignment for SUD, undoubtedly introduces an array of additional idiosyncrasies to this

practice. It should therefore be understood as a kind of Third Space (Bhabha, 1994), a construct born from the interaction of different cultural systems, rather than a historically speaking "traditional" construct. It is this Third Space or the adapted hybridized version of traditional Amazonian medicine practiced at the Takiwasi Center, which is of interest in the scope of the present work.

3. Empirical work

3.1. Context and main research questions

To summarize the rationale that lead to the current investigation, 29 million people in the world are estimated to suffer from drug use disorders (UNODC, 2016), with consequences negatively affecting both individuals and global society (Lim et al., 2012; Mounteney et al., 2016). However, despite the international concern and extent of the problem, a large gap in service provision for substance use problems exists worldwide, with only 1 among 6 persons that need treatment actually receiving it (UNODC, 2016). Moreover, individuals which do have access to treatment show a high tendency for relapse, even when treatment was initially successful (Brandon et al., 2007). Therefore, and on account of neurobiological evidence, current scientific views conceive SUD as a chronic type of disease (Le Moal & Koob, 2007). This understanding however has not yet been fully implemented in contemporary health care practice in a general way (McLellan et al., 2000). SUD therapies making use of traditional or alternative medicines have the potential to address a number of these issues. Traditional medicines play an emergent role in health care across the world, particularly for chronic illnesses (WHO, 2013) and could thus serve to enhance SUD therapy as well. Moreover, since treatments based on traditional medicines tend to be more readily available, affordable, and in many instances also more accepted (Bill et al., 1993; Bodeker & Kronenberg, 2002), applying such a framework to SUD could improve global accessibility to treatments.

The present work empirically investigated such an alternative treatment approach to SUD in the Peruvian Amazon. It was conducted as part of a research project supported by the Swiss National Science Foundation (SNSF) entitled *Substance Dependence Treatment: An Exploratory Study of the Psychotherapeutic Potential of Traditional Medicinal Practices of the Peruvian Upper Amazon* (SNSF, Doc.CH, 2013-2017). The primary goal of this project

was thus to investigate therapeutic potentials of traditional Amazonian medicine for SUD as practiced at the integrative *Takiwasi Center for Addiction Treatment and Rehabilitation* in Peru. We intended to explore this treatment approach using multiple data sources, a cross-disciplinary perspective, and combining qualitative and quantitative methodologies. The main research questions that guided this work were:

(1) How is SUD understood in traditional Amazonian medicine and what are the main methods for its treatment?

(2) Who are the treatment-seeking individuals that select this alternative SUD therapy based on traditional Amazonian medicine?

(3) What are the short-term therapeutic effects of the integrative SUD treatment?

Each of these questions was addressed with an empirical study, which will be described in detail in the following sections and chapters. Our central research hypothesis for this investigation was that the treatment approach involving Amazonian medicine will reduce symptoms of SUD and that we will be able to identify relevant underlying concepts.

3.2. Specific aims and rationale per empirical study

3.2.1. Study 1 – Conceptions and practices of an integrative treatment for substance use disorders involving Amazonian medicine: Traditional healers' perspectives

SUD treatments based on Amazonian medicine are already offered in some Latin American therapeutic contexts, including the aforementioned *Takiwasi Center for Addiction Treatment and Rehabilitation* in Peru, whose treatment protocol integrates Amazonian medicine with conventional therapies. Internal statistics of the center suggest favorable results (Giove Nakazawa, 2002), but so far no scientific studies have empirically assessed the effects

of this treatment. However, before we can evaluate this treatment's effectiveness, we need to understand which methods are used and how SUD is conceptualized within this medicinal system (Fønnebø et al., 2007). The overall aim of this study was therefore to identify conceptions and treatments of Amazonian medicine for SUD as applied in the Takiwasi treatment framework. For this purpose we conducted interviews with expert practitioners of Amazonian medicine linked to this center. The specific study aims included an analysis of experts' understanding of SUD disease etiology (Aim 1) and SUD treatment (Aim 2). We further aimed to assess which amongst the Amazonian techniques applied in the Takiwasi protocol was seen as the main constituent for SUD therapy (Aim 3). Finally, we intended to discuss similarities and differences between the adapted Amazonian and current scientific views of SUDs (Aim 4).

3.2.2. Study 2 – Who turns to Amazonian medicine for treatment of substance use disorder? Patient characteristics at the Takiwasi Addiction Treatment Center

The former study provided a basic understanding of the nature of Amazonian SUD treatments and illness concepts underlying the Takiwasi Center's therapeutic framework. The primary goal of this second study was then to understand who the people that seek out this alternative SUD treatment are and what motivated their choice. Guidelines for research on traditional medicine by the WHO (2000) recommend first focusing on patient characteristics when beginning to investigate an unknown treatment. This may help understand who is attracted to the treatment or for whom it is usually indicated, including the identification of subgroups. More specifically, we aimed to describe the socio-demographic and clinical characteristics of SUD patients enrolling in this treatment and identify their specificities compared to norms (Aim 1). Additionally, since motivational factors are known to be crucial for treatment retention and success (Longshore & Teruya, 2006), we also aimed to assess the motivations that led patients to select the alternative treatment at this center (Aim 2).

3.2.3. Study 3 – Short-term treatment effects of a substance use disorder therapy involving traditional Amazonian medicine

The previous two studies provided data on illness and treatment concepts (qualitative) and quantitative data on patient characteristics. The findings from these studies served as the empirical and conceptual basis for the third study, whose main objective it was to explore short-term therapeutic effects of the Takiwasi addiction treatment program. We aimed to assess the short-term effects of this treatment using a naturalistic design, with a particular focus on (a) addiction severity, (b) substance craving, (c) depressive and anxiety symptoms, and (d) quality of life.

3.4. Methods

A multimodal approach was used to address the outlined goals per empirical study: The first study used a qualitative methodology, the second one applied a cross-sectional mixed methods approach, and the third study relied on a quantitative longitudinal methodology.

3.4.1. Samples

The sample of the first study consisted of 13 experts practicing Amazonian medicine, all of which were associated with the Takiwasi Center. The second study was based on a sample of 50 males diagnosed with SUD enrolling in the Takiwasi addiction treatment program. The third study involved a sample of 53 SUD-diagnosed males admitted to the Takiwasi treatment, and focused on a subset of this sample consisting of 36 participants that completed the treatment. A detailed description of each of these samples will be given in Chapters 4, 5, and 6, respectively.

3.4.2. Instruments

For data collection in the qualitative Study 1, a semi-structured interview was used (see Table 1 in Chapter 4), which had been designed in alignment with a health psychology framework for exploring illness concepts (the common sense model of illness representation; Leventhal, Diefenbach, & Leventhal, 1992) and with reference to the interview guidelines of an investigation of illness concepts in traditional Maya medicine (Berger-Gonzalez, Stauffacher, et al., 2016).

Both the second and the third study used the *Mini International Neuropsychiatric Interview* (MINI; Sheehan et al., 1998) to assess psychiatric diagnoses, including affective disorders (major depression, dysthymia, hypo-/mania), anxiety disorders (panic disorder, agoraphobia, social phobia, generalized anxiety disorder, obsessive-compulsive disorder, post-traumatic stress disorder), substance use disorders (dependence, abuse), psychotic disorders (not further specified), eating disorders (anorexia, bulimia), as well as antisocial personality disorder. In both Study 2 and Study 3, the severity of substance dependence was measured by means of the *Addiction Severity Index 5* (ASI; McLellan et al., 1992), a structured interview covering seven areas of functioning (medical, employment, alcohol use, drug use, legal, familial/social, and psychiatric). Both Studies 2 and 3 also employed a set of quantitative self-report measures: The *Hospital Anxiety and Depression Scale* (HADS; Zigmond & Snaith, 1983) was used to assess symptoms of depression, anxiety, and overall emotional distress. Substance craving was measured using the *Craving Experience Questionnaire* (CEQ; May et al., 2014), assessing overall craving frequency as well as intensity, intrusiveness, and imagery of craving. The *World Health Organization Quality of Life-BREF* (WHOQOL-BREF; WHOQOL Group, 1998) was used to assess overall quality of life, as well as quality of life in four specific life domains (physical health, psychological health, social relationships, and environment). Motivation for change was measured using the

Readiness to Change Questionnaire (RCQ; Rollnick, Heather, Gold, & Hall, 1992), its subscales consisting of the pre-contemplation, contemplation, and action stages from the stages of change model (Prochaska et al., 1992). Study 2 additionally assessed treatment motivation in a qualitative manner, using motivation letters written by the participants according to specified guiding questions. Furthermore Study 2 measured facets of well-being that related to spirituality using the *Spiritual Well-Being Scale* (SWBS; Ellison, 1983; Paloutzian, Bufford, & Wildman, 2012), which assessed overall spiritual well-being as well as religious and existential well-being. All of these measures including their psychometric characteristics are described in detail in the methods sections of Study 2 and Study 3 (Chapters 5 and 6, respectively).

3.4.3. General study procedures

Data collection for Study 1 involved interview sessions with participants (expert practitioners of Amazonian medicine) held by a trained psychologist (IB). Data collection was discontinued once saturation occurred, i.e., when the most salient aspects of the subject matter were identified and no fundamentally new material was emerging (Morse, 1995). Interviews were tape-recorded and subsequently transcribed verbatim.

For Study 2, sociodemographic and clinical data were collected from participants (patients sample) within one week of enrolling in the Takiwasi treatment. Data collection for Study 3 involved the same measurement of sociodemographic and clinical variables as Study 2 at clinical admission, which represented the pre-treatment baseline assessment (T1). A second assessment of tests related to the outcome indicators (i.e., ASI, HADS, CEQ, and WHOQOL-BREF) was then conducted at the time of treatment completion (T2).

3.4.4. Data analysis

The qualitative data from Study 1 as well as from Study 2 were analyzed using qualitative content analysis (Mayring, 2008). Quantitative analyses for Studies 2 and 3 were conducted by means of statistical tests, using SPSS version 17.0.1 (SPSS Inc. Released 2008. SPSS Statistics for Windows, Version 17.0. Chicago: SPSS Inc). The analytic methods used will be described in greater detail in the corresponding Chapters 4, 5, and 6.

4. Empirical Study 1

Conceptions and Practices of an Integrative Treatment for Substance Use Disorders Involving Amazonian Medicine: Traditional Healers' Perspectives

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4.1. Abstract

Objective: The harmful use of psychoactive substances represents one of today's largest public health problems. Yet, in spite of its global relevance, current treatment for substance use disorders (SUDs) is still not entirely successful. The purpose of this study was to investigate alternative treatments and conceptions from traditional Amazonian medicine adapted to SUDs. **Methods:** We conducted semi-structured interviews with 13 practicing experts at a well-established addiction treatment center in the Peruvian Amazon and performed qualitative content analysis on the collected data. Main categories were deductively defined and corresponding subcategories inductively developed. **Results:** Our findings revealed characteristic features and consequences, causes and antecedents, and treatment methods of SUDs as the main categories. Overall, concepts of disease etiology bore resemblance with contemporary biopsychosocial models of SUDs. The Amazonian therapeutic means however differed markedly from current Western ones. The main methods involved dietary retreats, healing ceremonies, and purging rituals. The integral application of Amazonian methods, as well as their traditional implementation according to prescribed ritual protocols, were emphasized by the experts as crucial for efficacy and safety of treatment delivery. **Conclusion:** We suggest further scientific attention to these therapies, including clinical studies, for which our results provide conceptual underpinnings. Findings from this research expand the cross-cultural understanding of SUDs and, in the long run, may enhance its treatment options.

Keywords: Substance use disorders; addiction; traditional Amazonian medicine; illness concepts; expert interviews; addiction treatment; alternative medicine; Peru; Amazon

4.2. Background

The harmful use of psychoactive substances is one of today's most substantial public health problems, being amongst the main contributors to the global burden of morbidity (Gowing et al., 2015). It is associated with avoidable health impairments, disabilities, and early death (Mathers et al., 2009), implying both individual suffering and high societal costs, economically amounting to over $600 billion per year in the USA alone (National Institute on Drug Abuse, 2012). However, in spite of the magnitude and international concern of the problem, current treatments for substance use disorders (SUDs) are not yet entirely successful; valuable evidence-based therapies are available (Moos, 2007), but relapse rates remain high (Brandon et al., 2007). This recurrent pattern of SUDs, along with neuroscientific studies showing long-term cerebral changes in this context (Koob & Volkow, 2010), point to the chronic nature of the condition (McLellan et al., 2000).

In an attempt to improve existing treatment options, some research has therefore explored alternative or traditional healing practices for SUDs (Lu et al., 2009), in a parallel way as such therapies are often used for somatic chronic diseases, like cancer (Falci et al., 2016; Molassiotis et al., 2005; Thorne, Paterson, Russell, & Schultz, 2002). Specifically traditional Amazonian medicine, an ancient healing system involving the use of medicinal plants and ritual techniques from the Amazon rainforest (Luna, 1986), ought to be investigated. SUD treatments based on Amazonian medicine are already being offered in some therapeutic contexts in South America, including the pioneering Takiwasi Center for Addiction Treatment and Rehabilitation in Peru, whose treatment protocol combines Western psychotherapy with Amazonian medicine. Internal statistics from the center suggest good results, but so far no scientific studies have assessed the effects of this treatment empirically. However, to evaluate how this treatment works and whether it is effective requires first gaining insight on how SUDs are understood within this medicinal system (Fønnebø et al.,

2007). Once a fundamental conceptual understanding of Amazonian treatment processes has been established, clinical assessment of efficacy can follow at a next stage. The overall objective of our research was therefore to identify conceptions and practices of SUDs as understood in the Amazonian medicinal practice used in the Takiwasi treatment framework.

It is important to note that the illness concepts explored in this study reflect a contemporary adaptation of Amazonian medicine, which may differ from more ancient or traditional versions in significant ways. Amazonian medicine, as it is practiced in Peru today, reflects a blend of traditions, modified by centuries of exposure to colonial and postcolonial influences, rather than the native science it originally was (Bussmann & Sharon, 2006). As such, current Amazonian medical practice and its application in the Takiwasi treatment are understood as a kind of hybrid system (Pieterse, 1994) or Third Space (Bhabha, 1994), i.e., a construct that evolved from the interaction of different cultural systems. Rather than giving an ethnographic account of traditional Amazonian medicine in its most original form, it is this hybrid medical practice, its methods, and its underlying concepts that the present study aimed to investigate. More specifically, our study intended to capture expert practitioners' understanding of the etiology (Aim 1) and treatment (Aim 2) of SUDs. We further aimed to assess which among the Amazonian techniques applied in the Takiwasi protocol is seen as the main constituent in SUD therapy (Aim 3). Finally, we intended to discuss similarities and differences between the adapted Amazonian and current scientific views of SUDs (Aim 4).

4.3. Methods

4.3.1. Participants

Our sample consisted of a group of 13 expert practitioners of traditional Amazonian medicine that presently do or in the past have worked with the Takiwasi Center. Selecting practitioners on the basis of their work association with this institution ensured that all experts

were (a) knowledgeable in Amazonian medicine, (b) experienced with SUDs, and (c) well-acquainted with the standard treatment regime at the center. This also entails that their expertise relates specifically to the aforementioned Third Space (Bhabha, 1994), within which they act as boundary objects (Star & Griesemer, 1989; Trompette & Vinck, 2009) or hybrid actors, bridging the different medical and cultural contexts. Sample size was determined on the basis of recommendations by Morse (Morse, 1995, 2000) concerning data adequacy.

4.3.2. Takiwasi treatment protocol

The Takiwasi Center was originally founded in 1992 by a French medical doctor after a mission with Doctors Without Borders for an unrelated healthcare project in Peru. The Takiwasi Center was the first clinical institution in the world to apply traditional Amazonian medicine to SUDs, and is officially recognized by the Peruvian health department. Its treatment protocol combines Amazonian and Western therapeutic methods. The clinical staff working at the center thus consists of health professionals from both systems (i.e., curanderos/as, psychologists, nurses, etc.). Western therapeutic methods include individual psychotherapy (such as Gestalt or Analytic therapy) and group psychotherapy (e.g., relapse prevention, psychodrama, etc.), milieu therapy, and occupational therapy, as well as occasional biomedical health checks. The center generally does not administer psychopharmacological treatments for SUD (or comorbidities) except in rare cases, in which immediate stabilization is necessary (for instance, by means of tranquilizers). Traditional Amazonian methods essentially involve the use of local medicinal plants in the context of traditional rituals. The duration of the inpatient program varies, but is typically between 3 to 12 months (about 7 months on average; internal statistics), depending on individual clinical requirements. Amazonian medical treatments are administered in a weekly routine and in parallel to Western interventions to all participants throughout the entire program. The exact treatment plan, in terms of which technique is applied at which stage and with which

frequency, is adapted individually and decided on in a case-by-case manner. On a typical day of treatment, a patient may do physical exercises in the morning and perform daily chores (cooking, gardening, cleaning, etc.) with the help of an occupational therapist. Individual therapy sessions may also take place during that time. Afternoons and evenings are dedicated to group interventions, Amazonian or Western, depending on the day and patient. The first weeks tend to focus on the detoxification process, while the remainder of the treatment aims at deeper therapeutic work. In accordance with Peruvian legislative requirements, a therapeutic community such as Takiwasi needs to be gender-specific. The residential treatment program therefore serves exclusively male patients, with a maximal capacity of 18 beds. The majority of treatment seekers use a combination of alcohol and illicit drugs (cocaine-related substances, cannabis, amphetamines, opiates, or tranquilizers) and are from Peru or other Latin American countries, with a minority of European or North American patients (internal statistics). Besides the male-only residential treatment for SUD patients, the center also operates outpatient services for males and females with psychosomatic problems.

4.3.3. Data collection

We conducted semi-structured expert interviews using guiding questions (Table 1) leaning on those developed by Berger-González, Stauffacher, Zinsstag, Edwards, and Krütli (2016) and in alignment with the common-sense model of illness representation (Leventhal et al., 1992), a health psychology framework for exploring dimensions of illness concepts. Our research focused on the following three dimensions: causes, consequences, and management (i.e., treatment). All interviews were conducted by a trained psychologist (IB). Data were collected in the San Martín Province of Peru between October 2013 and September 2014, until saturation occurred. Saturation was defined in terms of data adequacy, i.e., when the most salient information was identified and no fundamentally new categories were emerging, at which point data collection was discontinued (Morse, 1995). Most interviews were held at

the Takiwasi Center facilities (77%), and the rest at the interviewees' home/workplace. Interviews were conducted in Spanish, except for one in English. The average interview length was 70 minutes (range, 35–123 minutes), distributed across one to three sessions per participant, depending on time availability and circumstantial demands. Interviews were tape-recorded and subsequently transcribed verbatim. The study was approved by the relevant ethics committee and conducted in accordance with international regulatory requirements (nr. 88-2013, Fribourg, Switzerland). Participants were carefully informed about the purposes of the study, and their consent was obtained.

Table 1

Interview Guidelines (Condensed Form)

– How do you as a practitioner of traditional Amazonian medicine understand addiction/substance use disorders? Probe: Could you describe the main characteristics of this condition the way you see it?
– What is at the origin of addiction/substance use disorders? What are the main causes, would you say? Probe: What are the reasons for a certain person to develop an addiction, while others may sometimes use substances without becoming addicted? What is the critical difference between these two types?
– When a patient comes to see you and asks for your help to cure his addiction, what are the different components, plants, tools, or techniques of the treatment that you propose? Probe: Could you briefly describe each component and tell me in global terms what this particular tool/technique is used for? – Which of these components is the most central or important one for the treatment process of addiction problems?

4.3.4. Data analysis

We took a conventional approach to content analysis, as is recommended when existing research literature on the subject is limited (Hsieh & Shannon, 2005). We performed qualitative content analysis (Mayring, 2008) by means of a computer-assisted (Microsoft

Office) iterative process: in a first analytic step, main categories were deductively developed on the basis of our research questions and the illness representation model (Leventhal et al., 1992). These categories had initially been defined as 1) characteristics of SUDs, 2) causes of SUDs, and 3) treatment of SUDs, but the preliminary labels were subsequently adjusted to more precisely match the data at hand. Subcategories or coding categories ("codes") within these main themes were then developed from the data in a stepwise inductive procedure, identifying common clusters of themes. The iterative process thus involved a repetitive analysis of the data material, in which the emerging coding system was continuously revised, until a final set of codes was established. To assess the final coding system's reliability, a random sample of 20% of the textual material was re-coded by an independent rater (VA). The independent rater was experienced in qualitative analysis and psychological research but had no prior involvement in our study, as recommended by Krippendorff (1980). In cases of discrepancies between the two ratings, consensus was reached by discussion and adjustment of codes. For each of the three main categories, Cohen's kappa was calculated as a chance-adjusted between-rater agreement measure (McHugh, 2012). In the scope of this study, we specifically focused on the Amazonian treatments applied in the Takiwasi framework. Western methods used at the Takiwasi Center (such as psychotherapy) were therefore not probed for in the interviews, and not considered in the analysis. Similarly, aspects mentioned by expert practitioners as part of their personal medicinal repertoire but never applied at Takiwasi Center were also not considered in this analysis. With regard to identification of the main treatment constituent, participants were asked to indicate which of the Amazonian therapeutic methods they had mentioned was most important for SUD treatment. We encouraged expert practitioners to select one method if possible, but allowed multiple choices if necessary. Preferential choices per method were subsequently summed up and the main method identified on the basis of the majority rule.

4.4. Results

Sample characteristics are shown in Table 2. The age of the expert practitioners ranged between 35 and 86 years, with 15% (*n* = 2) being female. The majority of experts were born (77%, *n* = 10) and lived (93%, *n* = 12) in South America, but there was diversity with respect to the sample's cultural background. All participants had received extensive training in one or several traditional systems of Amazonian medicine (e.g., Asháninca, Quechua-Lamas, Chazuta traditions), reporting an average of 28 years of traditional medical experience. It was not generally possible for respondents to separate the learning period from practice, since, as they explained, in Amazonian medicine the learning process occurs concurrently with and through practice. An extreme case was presented by one participant who had started his career in traditional medicine at age 14, and, during the interview, at age 86, insisted he was still learning. With regard to how they had acquired their expertise in SUDs, participants mentioned as their most important source of knowledge instruction by teacher plants (n=8; see below for the concept of teacher plants), years working at Takiwasi (*n* = 6), instruction by senior practitioners of traditional Amazonian medicine (*n* = 2), years of clinical work in other contexts (*n* = 1), or their personal life experience (*n* = 1). Most participants (69%, *n* = 9) considered themselves to be a *curandero/a* (general practitioner) with one or more areas of specialization within traditional medicine, including the self-given labels of *ayahuasquero* (specializing in the use of medicines based on the ayahuasca plant, *Banisteriopsis caapi*; main alkaloids harmine, harmaline, and tetrahydroharmine), *perfumero/a* (specializing in the use of water-based therapies such as plant baths), *huachumero/a* (specializing in the use of medicines based on the huachuma plant, *Echinopsis pachanoi*; main alkaloid mescaline), *preparador de plantas* (specializing in the preparation of plant remedies), or *curioso/a* (general practitioner considered hierarchically below *curandero/a*).

Table 2

Sample Characteristics (N = 13)

	Mean (range)	*n* (%)
Sex		
Female		2 (15)
Male		11 (85)
Age at time of interview	52.2 (35-86)	
Years of experience in TAM	28 (6-74)	
Years working with Takiwasi	13 (2-22)	
Place of birth		
Peru		8 (61)
Colombia		1 (8)
Argentina		1 (8)
France		1 (8)
New Caledonia		1 (8)
Australia		1 (8)
Place of residence		
Peru		10 (77)
Colombia		1 (8)
Argentina		1 (8)
Australia		1 (8)
Ethnic affiliation, self-identified		
Peruvian mestizo		6 (46)
Indigenous Amazonian		3 (23)
Western		4 (31)
Specific TAM tradition trained in		
Asháninca		1 (8)
Quechua-Lamas		1 (8)
Chazuta		1 (8)
Putumayo		1 (8)
Various		9 (68)
Areas of medical specialization*		
Curandero		9 (69)
Ayahuasquero		9 (69)
Huachumero		2 (15)
Curioso		2 (15)
Perfumero		1 (8)
Preparador de plantas		1 (8)

TAM = Traditional Amazonian medicine.

* Most participants reported various areas of specialization simultaneously.

Besides their training in traditional Amazonian medicine, participants reported additional training and/or work experience in fields such as farming, gardening, nursing, social work, logging/carpentry, bodywork, psychology, and biomedicine.

The presentation of findings is structured along the three main categories defined in the analytic process. We found four codes within the first main category "characteristic features and consequences of SUDs," seven codes in the second main category "causes and antecedents of SUDs," and five codes in the third main category "treatment methods for SUDs." Inter-rater reliability was excellent, with Cohen's kappa values of $\kappa = 0.87$, $\kappa = 0.81$, and $\kappa = 0.93$ (first, second, and third main category, respectively). In the following sections, the codes within each main category are presented by means of a condensed summary of statements per code, including citations that illustrate the thematic content. We followed Meuser & Nagel's (2009) recommendation to stay as close as possible to the original material and wording used by the expert practitioners. The percentage of participants that raised concepts in each coding category and the total number of mentions per code are given in Table 3, the order of presentation reflecting level of prominence in the data per main category.

4.4.1. Main category 1: Concepts regarding characteristic features and consequences of substance use disorders

4.4.1.1. Contextualization/label. Subsumed under this code are conceptual issues in which the health condition was tagged or embedded into a wider context. Most of the expert practitioners (85%, $n = 11$) raised such meta-level aspects, commonly labeling SUD as "a vice," "an illness," or as "a habit." SUDs were further classified as "an illness of the soul," a "spiritual illness," a "cultural illness" rather than an individual affliction, or "primarily a Western problem" not observed in more traditional societies until recently. Addiction or SUD was explained as "one of the most difficult problems."

4.4.1.2. Spiritual-energetic concepts. A majority of expert practitioners (62%, *n* = 8) considered that there is a pronounced spiritual dimension to addictions. Some participants referred to a search for spiritual meaning or "filling an existential void." Experts that mentioned this category generally spoke of spirits or disembodied entities involved in SUDs: entities which are "negative," "malefic" or "unhealthy" were explained as pushing the person toward drug use or other (self-)destructive behaviors. One expert phrased it as follows: "The addict is a person that has lost the connection to his soul, to his spirit, and he is inhabited by a spirit, an entity that leads him to destruction, towards death. [...] Addiction does not just imply the consumption of a substance, but also entering into an entire world – a world of transgressions, a world of lies, a world of pacts and obscure relationships. All of this has an impact on that person on the spiritual level, and the person ends up becoming a kind of marionette, manipulated by spirits."

4.4.1.3. Psychosocial concepts. An equally large portion of expert practitioners (62%, *n* = 8) discussed aspects of SUDs that can be classified as psychosocial in nature. Affective problems were commonly mentioned, and drug use was explained to often be an attempt to alleviate emotional difficulties. A general negativistic outlook was described, in which the person "has lost all motivation and appreciation for life." Practitioners reported that an affected person typically "feels well only when using drugs." Moreover, relational aspects were emphasized by some respondents, explaining that addicts have dysfunctional relationships with drugs, the environment, and themselves. Some experts pointed to irresponsible, deceitful or aggressive behaviors, for instance: "persons with addictions show a lack of ability to respect limits and boundaries."

4.4.1.4. Physical concepts. A number of expert practitioners (38%, *n* = 5) considered it to be a basic feature of SUDs that the person's body is affected, but there were comparatively

Table 3

Percentage of Experts (N = 13) Who Mentioned Each Category & Number of Mentions Per Category

Categories	Experts/category (%, *n*)	Mentions/category (nr.)
Characteristic features and consequences of SUDs	100%, 13	101
Contextualization/label	85%, 11	25
Spiritual-energetic concepts	62%, 8	33
Psychosocial concepts	62%, 8	34
Physical concepts	38%, 5	9
Causes and antecedents of SUDs	100%, 13	156
Familial and immediate social environment	100%, 13	37
Personality and emotional tendencies	85%, 11	30
Life stressors	62%, 8	19
Biological and hereditary factors	62%, 8	15
Spiritual-energetic antecedents	54%, 7	25
Larger sociocultural context	54%, 7	22
General remarks concerning causes	46%, 6	8
Treatment methods for SUDs	100%, 13	252
General treatment process and components	100%, 13	83
Healing ceremonies with teacher plants	100%, 13	54
Dietary retreats with teacher plants	92%, 12	40
Purging rituals with emetic plants	85%, 11	49
Further Amazonian modes of treatment	85%, 11	26

Note. SUDs = substance use disorders.

few mentions in this coding category. Practitioners explained that “the body is contaminated” or that “there is physical deterioration,” and that the condition may ultimately lead to death. It was furthermore suggested that SUD patients usually demonstrate “a lack of connection with their own body.”

4.4.2. Main category 2: Concepts regarding causes and antecedents of substance use disorders

4.4.2.1. Familial and immediate social environment. This code appeared in the causal explanations of all expert practitioners, and accounted for the largest number of mentions in this main category. Familial problems that were named to contribute to SUDs included a lack of love, care, or guidance from one's parents. Moreover, the absence of discipline in the family was suggested to play a role in the etiology of SUDs. Typical patterns of dysfunctional familial relationships were mentioned, as well as living with a person that uses drugs or alcohol, or peer pressure, for instance: "there are many reasons [for developing an addiction]; sometimes it is about choosing a friend, the friend that you don't know but you think he is your friend; the friend that makes you do things you shouldn't do, like drinking alcohol or smoking, or takes you to the discotheques where there is much risk." Another example: "It all depends on one's home, if one's home is well [...]. If a parent also has problems, a disorganized life – that's where it originates."

4.4.2.2. Personality and emotional tendencies. Statements about such tendencies featured prominently in the data, with 85% of experts (n = 11) reporting at least one concept in this context. Emotional antecedents that were mentioned as causally linked to SUDs included anger, anxiety, or grief, but also low self-esteem and feelings of loneliness, separation, or not belonging. Personality traits included tendencies to curiosity, experimentation, looking for intense experiences, a lack of willpower, or a "childish rebelliousness." A disposition labeled as "being weak" was pointed to by several respondents: "some let themselves get carried away more than others; because there are many people that are very weak and allow the vice to dominate them too much."

4.4.2.3. Life stressors. Stressful life events were mentioned by a majority of expert practitioners (62%, n = 8) as contributing to the development of SUDs. Common examples

included traumatic experiences such as sexual violence and childhood abuse, but also disappointing events in the course of one's life: "Addiction sometimes comes because of a disappointment, I believe. [...] Personal problems, a disappointment at work, or disappointments in love life, or possibly also disappointments by ones' relatives."

4.4.2.4. Biological and hereditary factors. A majority of respondents (62%, *n* = 8) suggested that biological factors play a role in the development of SUDs, referred to as "physiological disturbances," a "weak bodily system," "contaminated body," or genetic predispositions. One of the experts explained that heredity played an important role in SUDs which extended beyond the somatic level: "So there is an inheritance, I believe, something cross-generational, with a somatic part and a psychological part and a spiritual part." Another expert explained that "...the body of the person demands the liquor, he feels the need, because the body is contaminated, [the body] is sick."

4.4.2.5. Spiritual-energetic antecedents. Slightly more than half of the expert practitioners (54%, *n* = 7) pointed to energetic or spiritual antecedents of addiction. These were described as "energetic disturbances," "energetic pathogens," or "malefic or unhealthy spirits that can cause or exacerbate addictions." Several ways of acquiring these were proposed, among them "relational imbalances between the human and the spirit world," "spiritual transgressions," "witchcraft," or "the use of sacred plants in an incorrect way." One healer explained this in the following way: "Often the Amazonian healers talk about the plants – because the plants have a spirit, a mother, and if one does not treat them with respect, the plants may punish the person, possess the person, rob the person's spirit."

4.4.2.6. Larger sociocultural context. Sociocultural conditions that contribute to SUDs were brought up by about half of participants (54%, *n* = 7). They included factors such as economic problems, a lack of social cohesion, a lack of future perspective, as well as certain occupational environments inherently associated with consumption (e.g., agricultural labor

and alcohol). The experts explained that there are structures specific to Western society that seem to foster addictive tendencies, in particular the absence of sacred spaces and initiatory or healing rituals, which, according to the experts, are vital for well-being: "[historically,] there had been a deliberate attempt to remove people from their culture and their culture's traditional mechanisms of healing, and that's the reason why in my experience there's subsequently so much addiction, because those methods of maintenance of the soul have been removed, and therefore the impact of this Western malaise of addiction is even greater, because there's no resistive process."

4.4.2.7. General remarks concerning causes. All participants expressed a variety of causal factors for the development of SUD, while mono-causal explanations were absent in the data set. A number of participants (46%, *n* = 6) explicitly addressed this, through statements such as "it is a complex problem," "there's a biological, a spiritual, and an energetic component," or "it's multi-causal.

4.4.3. Main category 3: Concepts concerning treatment methods for substance use disorders

4.4.3.1. General treatment process and components. All participants raised concepts related to the general treatment process and its components. Three components were generally pointed out as main constituents: purging rituals, dietary retreats, and healing ceremonies. The expert practitioners reported the use of a variety of plants: "Some clean, others purify, others open our understanding and knowledge." They emphasized that, to ensure safety and efficaciousness, these plants have to be applied in the correct manner, for which adherence to traditional ritual is critically important. A certain class of plants the healers referred to as "teacher plants" was reported to play a significant role in the treatment. One expert explained that these plants "are teaching individuals to know themselves, to know their strengths and

weaknesses, and to balance those." The plants in general were explained to show their effects slowly: "The processes in traditional medicine are long, the healing occurs slowly."

4.4.3.2. Healing ceremonies with teacher plants. All the respondents mentioned healing ceremonies involving specific teacher plants. The experts explained that the plant preparations used for such ceremonies at Takiwasi are chiefly *ayahuasca* and *purgahuasca* (the central ingredient of both being the vine *Banisteriopsis caapi)*. The experts described such ceremonies as following a prescribed ritual protocol that traditional healers guide by means of "*icaros*" (special healing songs) and other therapeutic measures. The respondents further described several behavioral and food restrictions that need to be observed in the context of such healing ceremonies. Several functions that these ceremonies may serve were mentioned, among them cleansing, becoming aware of previously unconscious aspects of self and life, or connecting with "non-rational layers of experience, where one's deep suffering lies." Statements like "the plants make you see what you have inside" were common. In one expert's words: "Generally speaking, a plant ceremony is like a large operating room. A very deep kind of energetic surgery is taking place. It is like restructuring, clearing the personal and then also transpersonal weights, inherited problems that one's family lineage may carry and that may create difficulties for the person now."

4.4.3.3. Dietary retreats with teacher plants. Nearly all participants (92%, n = 12) discussed traditional dietary retreats. The expert practitioners reported that this intervention involves spending time (usually 8 days) in an isolated hut in the forest while ingesting teacher plants. The traditional healer visits the patient three times a day to administer the medicines (prepared from teacher plants), attend to his needs, and supply basic food (plain rice and cooked green plantains). Patients are required to follow strict nutritional and behavioral rules during the retreat period; the experts emphasize the omission of salt, sugar, or spices, and restrictions on social contact, sexual activity, exposure to heat or cold, and toiletries. Some of

these restrictions persist for several weeks after the retreat, albeit in an attenuated fashion. One expert described this process as a "technology of use of medicinal plants." They explained that the person needs to be alone in nature and follow these rules so "the plants can work" and will not produce adverse effects. These are also the conditions that enable the plants to teach, say the experts, namely through dreams, visions, or sudden insights. The dietary retreat is described as an intense therapeutic process during which "the strength of the [misused] drug gets liberated from the body." In one case the following description was given: "Childhood problems may come to the surface. One meditates on that and frees oneself from it. The plants activate you, they extract from you, they make you see."

4.4.3.4. Purging rituals with emetic plants. A large majority of participants (85%, *n* = 11) mentioned purging rituals in which emetic plants are administered in a ritual setting. The experts reported that under the guidance of a traditional healer, the prescribed plant extract is ingested along with several liters of water, which are subsequently purged. The experts explained that this is done to detoxify the body and alleviate withdrawal and drug craving. Other effects mentioned included "eliminating memory traces of the drugs from the body," "clearing energetic charges," "establishing a strong contact with one's body," or helping with anxiety. The expert practitioners explained that different purging plants have distinct properties, may act on specific bodily and/or psychological systems, and that effects are multi-layered: "The purging rituals act not only on a physical level, but also emotionally; when they vomit, they vomit not only the toxins, the substances, but also the anger, the rage, and also the spiritual part [...]. The purge is not just a mechanism of cleaning the organism from the drug or the alcohol, but everything gets cleansed at the same time, negative thoughts, emotions, and bad memories, as they say."

4.4.3.5. Further Amazonian modes of treatment. Other Amazonian techniques used for SUD treatment were reported by 85% of experts (*n* = 11), among them plant baths, steam

baths, techniques called "*sopladas*" and "*icaradas*," and the ingestion of tonic plant preparations on a daily basis. Plant baths and saunas are explained to aid the detoxification process and "help balance the person." The *sopladas* and *icaradas* were explained to involve "an intervention in the physical and energetic-spiritual body of the person" and also described as balancing. For example: "An *icaro*, a song the healer had received, is sung, and tobacco or perfume or cinnamon or blessed water, according to what the healer senses, is applied on the body [of the patient] and the person becomes more balanced energetically." The song component of the described intervention is referred to as *icarada*, and is often applied in conjunction with a *soplada*, i.e., blowing tobacco (*mapacho*), cinnamon (*canela del monte*), or medicinal liquids onto the patient's body.

4.4.4. Identification of main SUD treatment method

When asked which of the Amazonian therapeutic methods used at Takiwasi was most efficient for SUD treatment, most expert practitioners expressed that it was not a single method, but the interplay between the different methods and plants that was efficacious. For instance: "it's an integral, it's an ecosystem [...] so I really couldn't say that one is more or less important, I think they're all part of an integral system." We encouraged experts to nonetheless select one or a set of techniques, while allowing for multiple choices per participant. Summing preferential choices per method yielded a score of 5 for purging rituals, 7 for dietary retreats, 5 for healing ceremonies with ayahuasca, and 1 for ceremonies with huachuma (Figure 1). The latter, however, is not currently practiced at the Takiwasi Center and has only rarely been used there in the past.

Figure 1. Identification of Main Amazonian Interventions Used for SUD Treatment

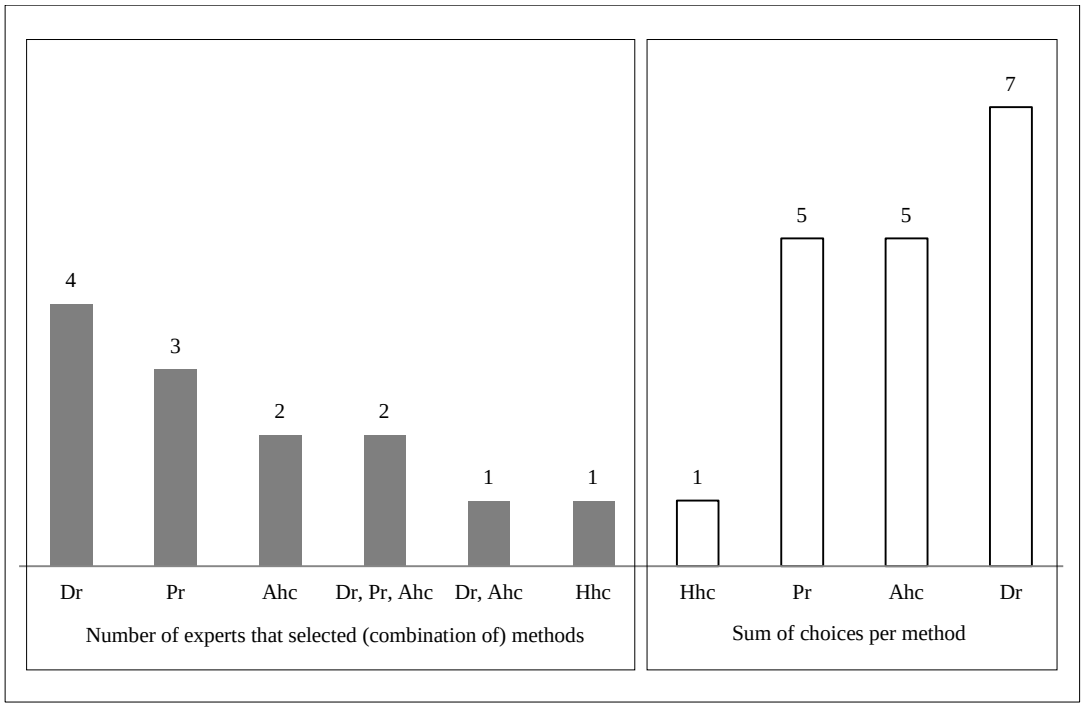

Figure 1. Identification of the main Amazonian interventions used in the context of substance use disorders according to 13 expert practitioners. Grey bars represent the number of experts that selected a given method, alone or in combination; white bars represent the sum of preferential choices per individual method. Ahc = Ayahuasca healing ceremonies; Dr = dietary retreats; Hhc = Huachuma healing ceremonies; Pr = purging rituals.

4.5. Discussion

This study investigated illness concepts and therapies of traditional Amazonian medicine adapted to SUDs. Interviews with 13 expert practitioners revealed a multifaceted understanding of and treatment approach for SUDs. The experts pointed out a large spectrum of relevant aspects on different levels of analysis, including biological, psychosocial, sociocultural, and spiritual-energetic factors. The categories that emerged in the analysis bear resemblance to contemporary scientific concepts of SUDs which use a biopsychosocial explanatory framework. Such models outline how psychosocial factors (e.g., stressful life events), personality features (e.g., sensation-seeking), and contextual factors (e.g., the availability of drugs) interact with physiological predispositions and contribute to

vulnerability to SUDs (Martin-Soelch, 2010, 2013). The expert practitioners discussed substance use as an attempt to regulate affective states, self-esteem, or interpersonal difficulties. This account matches the well-known self-medication hypothesis of SUDs, according to which drug use reflects an endeavor to assuage painful feelings (Khantzian, 1997). Nevertheless, the Amazonian framework of understanding differs from the classical biopsychosocial approach with regard to some observations related to spiritual-energetic concepts. Certainly, the relevance of spirituality noted by the experts is in line with the worldwide spread of spiritually oriented approaches such as Alcoholics/Narcotics Anonymous and related 12-step interventions (Galanter, Dermatis, & Sampson, 2014). Such treatments are exceedingly common today, with evidence of beneficial effects (Kelly & White, 2012), and research investigating the significance of spirituality in these approaches relative to the perspective of traditional healing systems, such as the Amazonian one, would be of interest. Nonetheless, when spiritual-energetic factors refer to non-material forces or subtle energy processes, the Amazonian concepts diverge from the contemporary scientific understanding of SUD. Yet, since a substantial portion of expert accounts emphasized precisely these aspects, future studies should aim to further examine the nature and role of these processes in the Amazonian approach and their significance for treatment.

Regarding Amazonian therapies, the analysis revealed a wide range of methods for SUDs (see Table 4 for a general overview of treatment methods applied in the Takiwasi protocol). The main groups were purging rituals with emetic plants, dietary retreats with teacher plants, and healing ceremonies with teacher plants (for surveys on Peruvian medicinal plants cf. Bussmann & Sharon, 2006; Sanz-Biset et al., 2009). Clearly, the Amazonian therapeutic means differ markedly from Western ones, and call for further scientific study. Indeed, there has been an increase in scientific interest in these methods and specifically in the ayahuasca brew in recent decades (usually a combination of *Banisteriopsis caapi* and admixture plants, such as the dimethyltryptamine-containing *Psychotria viridis*), with a

growing number of studies suggesting beneficial effects for psychosomatic problems, including substance use (Bouso et al., 2012; McKenna, 2004; Santos et al., 2007; Thomas et al., 2013). Interestingly, contrary to what this upsurge of specific interest in ayahuasca would imply, the view that Amazonian treatments need to be applied in conjunction with each other as an integral system prevailed in our sample. A small majority of expert practitioners considered dietary retreats with teacher plants to be especially important for SUD treatment, within the context of an overall view that all the components work together, and purging rituals were also among the top three components identified. However, systematic empirical research examining Amazonian methods other than ayahuasca, such as dietary retreats or purging rituals, is virtually nonexistent at present. An exception is the work of Sanz-Biset and Cañigueral (2011, 2013) on what they termed "strict diets" and "depurative practices" for a wide range of mostly somatic ailments. These ethnopharmacological publications focus mainly on the description of plant specimens, but also include an account of dietary conditions required for some of the examined plants. Behavioral rules, such as certain food restrictions or mandatory social isolation, as mentioned in their work, broadly match the descriptions provided by our sample. Our results further indicate that these dietary conditions are considered necessary for both therapeutic efficiency and safety of the Amazonian plant medicines, as is the adherence to traditional ritual. Another ethnopharmacological study provides an account of Amazonian plant diets not as a therapeutic method, but as a tool for learning the trade of a traditional medical practitioner (Jauregui, Clavo, Jovel, & Pardo-de-Santayana, 2011; for the Amazonian concept of plants that teach medicine see also Luna, 1984). Further research on therapeutic applications of those techniques in the context of psychosomatic problems and specifically SUDs is needed to elucidate the nature of these interventions, the mechanisms involved, and their short- and long-term effects. Since most expert practitioners explained that the efficacy of Amazonian treatments lies in their integral, systemic application, our findings imply that examining the treatment as a whole, rather than

isolating its components, may be the most fruitful approach for study. This is in fact consistent with general methodological recommendations for clinical research on alternative medicines, as practitioners across traditions tend to maintain that the overall effect of their treatment does not necessarily equal the sum of its parts (Fønnebø et al., 2007; Verhoef et al., 2005). Similarly, since our results show that the experts consider the behavioral rules and the ritual component of Amazonian treatments as crucial for both efficiency and safety, these aspects should be included and further examined in future studies. At this stage, more in-depth qualitative research seems most suitable for this purpose.

Table 4

General Overview of Methods Applied in the Takiwasi Treatment Protocol

Main Amazonian methods
Purging rituals with emetic plants
Dietary retreats with teacher plants
Healing ceremonies with teacher plants
Main Western methods
Individual psychotherapy (e.g., Gestalt, Analytic)
Group psychotherapy (e.g., relapse prevention, psychodrama)
Milieu therapy
Occupational therapy
Biomedical health checks

Our strategy of encouraging participants to select a core treatment modality, despite the prevailing view that the treatment consisted of an integral system, unduly deemphasized the holistic nature of the treatment concepts and is thus a limitation of the present study. There are a number of further limitations. As mentioned earlier, our findings cannot be taken

to reflect Amazonian medicine in a historically traditional sense, but represent a contemporary adaptation or hybridization thereof. Medical systems are cultural systems, which are subject to change and adjust dynamically to new contexts and influences (Kleinman, 1978). Arguably, practitioners with less influence from Western society may still exist in remote rainforest areas, but for that very reason are unlikely to have had extensive experience with SUDs. Moreover, this study aimed to identify concepts within the scope of the Takiwasi treatment program. Our informants hence had to be knowledgeable in this specific implementation of traditional Amazonian medicine. However, this requirement at the same time limits the degree to which our findings can be generalized to represent Amazonian conceptions beyond that clinical context. Likewise, some of the participants had received Western health-related training in addition to the traditional Amazonian training, which may partially account for the coherence of their responses with Western concepts. The fact that our participants relied on Spanish terminology such as *curandero/a* to denote their profession also alludes to their embeddedness in a westernized cultural context, since these terms reflect a Hispanic redefinition of originally indigenous concepts and terminologies (e.g., unlike the Amazonian Trio tribe, which uses the term "*pijai*" rather than *curandero/a*[43]). Furthermore, we did not collect in-depth data on participants' characteristics, their cultural affiliation and proximity, their specific teachers, or their motives for working at Takiwasi. This would have facilitated contextualization of results and improved the understanding of these expert practitioners' roles within the cross-cultural medical context. We also did not elaborate on the background history of the Takiwasi Center and its evolution (cf. Mabit & Sieber, 2006), nor did we discuss the center's role as a boundary object (i.e., as an artifact acting at the boundary of different worlds and involved in the coordination between them; Star & Griesemer, 1989; Trompette & Vinck, 2009) in the wider sociocultural context, as this was beyond the scope of this work. Finally, we did not explore the experts' views on treatment success and retention in

the interviews. Future studies should aim to do so and, if possible, compare these parameters to conventional SUD treatments, such as other therapeutic communities.

This was the first study to conduct expert interviews with this focus and thus to provide insight into a largely unexplored but promising approach. In view of the need for improved SUD treatments, alternative approaches such as the Amazonian one clearly warrant scientific attention. Our findings provide conceptual underpinnings for clinical efficacy studies of this treatment, as well as for investigating its transferability to other cultural contexts. Furthermore, understanding cultural convergences and differences with respect to underlying concepts may expand the cross-cultural understanding of SUDs and aid future cooperation between practitioners from biomedical and traditional systems. The Takiwasi approach may serve as a clinical example in this regard, as traditional healers apply their knowledge to a Western problem and join efforts with Western-trained health professionals, who in turn adopt practices from the traditional context. We are confident that this research will aid the development of enhanced SUD treatments that combine efficacious methods from both medical systems.

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5. Empirical Study 2

Who Turns to Amazonian Medicine for Treatment of Substance Use Disorder? Patient Characteristics at the Takiwasi Addiction Treatment Center

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5.1. Abstract

Objective: Substance use disorder (SUD) is currently understood as a chronic illness. Chronic illness management today frequently involves complementary medicines, an approach potentially beneficial also for SUD. Particularly Amazonian medicines, such as ayahuasca, are increasingly discussed in this context. The aim of this multimodal cross-sectional study was to investigate characteristics of people who seek treatment at an accredited healthcare facility that applies Amazonian medicines along with conventional psychotherapy to SUD. **Methods:** We collected clinical and socio-demographic data of consecutive admissions at the Takiwasi Addiction Treatment Center (Peru) using structured questionnaires, interviews, and qualitative motivation letters. Scores of n = 50 male participates were statistically compared to normative values by means of one-sample t-tests; qualitative content analysis was performed on motivation letters (n = 36). **Results:** The sample was culturally heterogeneous, involving patients from the Americas and Europe. Dependence criteria were most frequently met for cannabis, alcohol, cocaine/paste, and usually for multiple substances. Addiction severity in terms of drug use (p <. 001) and psychiatric status (p <. 05) was significantly higher than clinical norms; no significant differences for alcohol and medical status were found. Several well-being indicators were significantly below clinical norms. Motives for treatment initiation are reported. **Conclusions:** Our findings may imply that the Amazonian medicine-based treatment is particularly attractive for highly impaired SUD patients with a history of unsuccessful treatments; the sample's cultural diversity suggests a global interest among SUD patients. These findings are relevant in light of the need for improved SUD therapies and contribute substantially to the emergent research literature on ayahuasca-based SUD treatments.

Keywords: Substance use disorder; addiction treatment; ayahuasca; traditional Amazonian medicine; alternative therapies; patient characteristics

5.2. Background

Substance use disorder (SUD) is now widely considered a chronic illness (Koob & Volkow, 2010; McLellan et al., 2000) due to its persistent nature, tendency for recurrence, as well as accumulated neurobiological evidence showing long-term cerebral adaptations for substance users (Koob & Volkow, 2010; Martin-Soelch, 2013; White et al., 2002). Aside from pharmacological therapies, a wide range of psychosocial treatments exist for SUDs, including cognitive-behavioral interventions (Magill & Ray, 2009), motivational interviewing (Miller, 1996), or twelve-step facilitation (Donovan, Ingalsbe, Benbow, & Daley, 2013), to name a few. Nevertheless, long-term treatment outcomes are often not entirely satisfactory and research remains focused on the optimal approach matched to individual strengths and needs.

Alternative or traditional medicines are an emergent field in the mental health domain and their benefits as adjunct to conventional treatments are increasingly discussed also for SUD (Bill et al., 1993; Khanna & Greeson, 2013; Lu et al., 2009; Min et al., 2007; Posadzki et al., 2016), but clinical research in this context is still scarce. This may relate to procedural obstacles (e.g., regulations/risks of unknown plant substances) making randomized-controlled trials in this context challenging. A practical step for initial stages of such research is to examine existing healthcare facilities that already implement such SUD-treatments (WHO, 2000), which, in addition, can support development of more complex research designs.

The current investigation focuses on such an SUD-treatment that implements Amazonian medicine, a system which has recently become the focus of much scientific interest owing to ayahuasca (Labate & Cavnar, 2014, 2018). The psychoactive ayahuasca brew consisting of *Banisteriopsis caapi* and admixture plants (see Riba et al., 2003 for the pharmacology of ayahuasca) has been used in the Amazon for medicinal and cultural purposes since pre-Colombian times (Luna, 1986; McKenna, 2004). Today, ayahuasca is

increasingly discussed for its potential benefits for mental health, particularly SUD, but also other conditions such as mood or anxiety disorders (Coe & McKenna, 2017; Cruz & Nappo, 2018; Dominguez-Clave et al., 2016; dos Santos et al., 2016; Labate & Cavnar, 2014; Nunes et al., 2016; Osorio Fde et al., 2015; Palhano-Fontes et al., 2018). Observational studies of ayahuasca-based interventions show SUD-improvements (Fernández et al., 2014; Thomas et al., 2013) and large-scale cross-sectional studies point to lower substance use in conjunction with ayahuasca (Barbosa et al., 2018; Lawn et al., 2017). The understanding of therapeutic mechanisms involved (Prickett & Liester, 2014; Soler et al., 2016) and evidence for long-term effectiveness are still evolving, but scientific efforts to this end are rapidly increasing. Concomitantly, the popularization of ayahuasca has led to a growing number of healing centers in Peru that apply ayahuasca in various forms, often alongside an eclectic mix of non-Amazonian therapeutic/spiritual practices (Fotiou, 2016; Ray & Lassiter, 2016). While such centers would, in principle, seem to lend themselves for clinical research, in practice, most of them lack accreditation, defined therapeutic concepts or clinical foci. The Takiwasi Addiction Treatment Center is an exception in this context, being an accredited, SUD-specific treatment facility recognized by the Peruvian Health Ministry. It works along a defined therapeutic protocol that combines Amazonian medicine with psychosocial methods, delivered by trained health professionals from both systems. Due to its 27 years of existence, it has long-standing experience in the application of Amazonian methods to SUD and thus should be examined as a potentially significant reference for forthcoming clinical applications of ayahuasca in Western healthcare. The latter can likely be expected given the rapid entry of ayahuasca into the health and public health arenas, growing evidence for benefits, and increasing demands for policy and regulatory changes (Hamill et al., 2018; Nunes, et al., 2016). Internal statistics of the Takiwasi Center (Giove Nakazawa, 2002) and first scientific assessments (see next section; Berlowitz et al., 2019) suggest promise, but the basic clinical parameters of the treatment and its patients are still not well understood. The current study aims to partially

close this gap by carefully investigating the characteristics of people that seek this SUD treatment. In this manner, our study follows WHO-guidelines (2000) that recommend an initial research focus on patient characteristics when investigating unknown traditional medicines. This focal point is also intended to reveal whether specific subgroups of patients are commonly represented in this treatment, which could be indicative of particular appeal or acceptability of its methods to these groups. Our main research questions were thus (a) who are the people that seek this SUD treatment based on Amazonian medicine, and (b) what motivated their treatment choice? For this purpose, we aimed to investigate socio-demographic and clinical characteristics of patients enrolling in this treatment and compare them to norms (Aim 1). Additionally, since motivation is known to be particularly crucial for treatment engagement and success in SUD (Longshore & Teruya, 2006), we aimed to identify the motives that led patients to initiate treatment at this unconventional facility (Aim 2). We expected to identify the distinctive features of treatment-seekers and reveal predominant motives for choice of this treatment alternative.

5.3. Methods

5.3.1. Study setting and treatment description

This study was approved by the responsible ethics committee (Nr. 88-2013, Fribourg, Switzerland) and was conducted according to the Declaration of Helsinki and international regulatory requirements. The study took place at the Takiwasi Center (Tarapoto, Peru), a healthcare facility founded in 1992 by a French physician supported by the French Ministry of Foreign Affairs (Délégation Générale à la Lutte contre la Drogue et la Toxicomanie) and the European Commission's Directorate-General (DG8). It is the first formally recognized (Peruvian Health Ministry) and accredited health institution applying traditional Amazonian medicine to SUDs worldwide and, as such, has a pioneering character. It offers residential

SUD treatment (18 beds capacity) for males only (due to Peruvian legal restrictions on gender in inpatient treatment), as well as outpatient care for psychosomatic problems for both genders.

The residential treatment follows a defined therapeutic protocol, adaptable to individual clinical needs. Its length may thus vary, but is generally between 3 to 12 months. Admission criteria require the person to be male, speak Spanish, obtain medical clearance to the treatment from the center's medical staff, and manifest treatment motivation in a written letter. The therapy itself combines contemporary Western methods with traditional Amazonian medicine. The latter is an ancient system involving a complex application of Amazonian plants according to traditional techniques (Berlowitz et al., 2017; Bussmann & Sharon, 2006; Luna, 1986). The main types of Amazonian interventions used at the Takiwasi center include healing ceremonies (ceremonially framed ingestion of psychoactive plants like ayahuasca), purging rituals (involving emetic plants), and dietary forest retreats (weeklong; using a variety of medicinal plants) applied at varying time points and frequencies (see also Berlowitz et al., 2017). All of these interventions characteristically involve a ritual component, which is inherent to Amazonian medicine, and which introduces a spiritual dimension to the treatment. In a more traditional Amazonian context, these methods have been used to treat physical, psycho-social, or spiritual/magico-religious ailments for centuries (Dobkin de Rios, 1970a, 1970b; Jovel et al., 1996; Sanz-Biset & Canigueral, 2011, 2013). The Takiwasi model is an adaptation insofar as Amazonian methods are combined with psychotherapy and tailored to the specific demands of SUD patients. Other contemporary applications in the SUD or mental health field tend to involve ayahuasca alone (without other Amazonian plants), but are also typically combined with psychotherapy, akin to the format of other emerging psychedelic-assisted therapies (Argento, Capler, Thomas, Lucas, & Tupper, 2019; Tupper, Wood, Yensen, & Johnson, 2015).

The program is structured into three phases: The first weeks focus on detoxification and especially emetic plants are used in this phase, to lower withdrawal and craving symptoms. Therapeutic efforts in the second phase concentrate on more deep-seated problems relevant to the addiction with a combination of psychotherapy and Amazonian methods. Ayahuasca ceremonies and dietary retreats predominate in this phase, both said to bring to the surface unconscious and emotionally challenging material (incl.trauma), but also spiritual or peak experiences. The concomitant psychotherapeutic work (individual and group sessions) is designed to facilitate the processing of contents that emerged in the plant-based treatments. Finally, the last treatment stage focuses on preparing a patient's return to his life. The overall treatment further involves cohabitation in a therapeutic milieu, completion of daily chores with an occupational therapist (gardening, cooking, etc.), and occasional biomedical health-checks with a physician. It thus deliberately incorporates some of the elements of a conventional therapeutic community (but for instance no practices of 12-step programs). Drug use is not allowed within the residential treatment which aims to achieve abstinence.

5.3.2. Participants

All admitted inpatients between April 2014 and April 2016 were asked to participate in this study and were administered a diagnostic interview. Patients were excluded from the study if they did not meet dependence criteria according to the *Diagnostic and Statistical Manual of Mental Disorders* (DSM–IV–TR; American Psychiatric Association [APA], 2000). From the 63 patient admissions during said time frame, three did not meet dependence criteria, one refused participation (personal reasons), and nine patients entered the study but had incomplete data at the time of analysis. The sample thus consisted of 50 participants. Informed consent was obtained for all participants after they received a complete description of the study.

5.3.3. Measures

Clinical interviews

We used the Spanish version of the Mini International Neuropsychiatric Interview (MINI; Ferrando et al., 1998; Sheehan et al., 1998) to assess psychiatric diagnoses, including affective disorders (major depression, dysthymia, hypo-/mania), anxiety disorders (panic disorder, agoraphobia, social phobia, generalized anxiety disorder, obsessive-compulsive disorder, post-traumatic stress disorder), substance use disorders (dependence, abuse), psychotic disorders (not further specified), eating disorders (anorexia, bulimia), as well as antisocial personality disorder. Severity of addiction was measured by means of the Addiction Severity Index 5 (ASI; McLellan et al., 2006; McLellan et al., 1992), Spanish translation of the 5th edition (Urschel III et al., n.d.). The ASI covers seven areas of functioning relevant to SUDs, namely medical, employment, alcohol use, drug use, legal, familial/social, and psychiatric. We calculated composite scores (range 0–1) as severity indicators for each area, with higher scores indicating higher impairment. We also used selected items from the ASI interview to register socio-demographic characteristics, such as age, education, marital status, etc.

Self-report questionnaires

The Spanish version of the Hospital Anxiety and Depression Scale (HADS; Quintana et al., 2003; Zigmond & Snaith, 1983) was used to assess depression and anxiety symptoms. Responses are scored from 0 to 3 (14 items), with higher numbers indicating higher symptom frequency. An emotional distress score is obtained by summing all items (range 0–42, Cronbach's alpha .87), and scores on the anxiety and depression subscales by summing the corresponding seven items (range 0–21, Cronbach's alpha .82 for anxiety and .81 for depression). We used the Spanish version of the World Health Organization Quality of Life-BREF (WHOQOL-BREF; Lucas-Carrasco, 2012; WHOQOL Group, 1998) to assess quality

of life. The 26 items are rated on a scale from 1 (*very poor*) to 5 (*very good*). Two items are analyzed separately as single-item indicators for overarching quality of life and health (range 1–5). The remainder make up four domains (all ranging 0–100): physical health (Cronbach's alpha .80), psychological health (Cronbach's alpha .84), social relationships (Cronbach's alpha .39 [2]), and environment (Cronbach's alpha .74). The Spanish version of the Craving Experience Questionnaire (CEQ; May et al., 2014) was administered to measure substance craving. This 10-item measure assesses craving frequency on an 11-point visual analogue scale (*0-not at all, 10-constantly*), obtaining averaged scores for total craving (Cronbach's alpha .95) and for intensity, imagery, and intrusiveness subscales. Furthermore, we used the Spanish version of the Spiritual Well-Being Scale (SWBS; Paloutzian et al., 2012) to measure facets of well-being that relate to spirituality or transcendence, which might be relevant for the Takiwasi treatment. This measure comprises 20 items rated from 1 to 6, with higher scores representing higher well-being. The *religious well-being* subscale (10 items, range 10–60, Cronbach's alpha .89) reflects one's sense of satisfaction and connection with God; the *existential well-being* subscale (10 items, range 10–60, Cronbach's alpha .82) is worded neutrally by using terms like "meaning", without alluding to religious concepts. An overall spiritual well-being score is obtained by summing all 20 items (range 20–120, Cronbach's alpha .90). Finally, to assess change motivation, we used the Spanish version of the Readiness to Change Questionnaire based on the stages of change model (Rodríguez-Martos et al., 2000; Rollnick et al., 1992). The RCQ was chosen because of its specific adaptation to patients at the point of starting an intervention. It therefore considers only *pre-contemplation, contemplation* and *action* stages from the stages of change model. Subscale scores are obtained by summing the respective items rated from -2 (*strongly disagree*) to 2 (*strongly agree*), and stage allocation is done on the basis of the highest score per subscale.

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[2] The indicator for this domain may not be reliable, as it consists of only 3 items (WHOQOL Group, 1998).

Qualitative data

For a subset of the sample (n = 36) we collected motivation letters which patients had been required to write as part of the Takiwasi admission procedure. Instructions for writing these letters consisted of the following guiding questions: *What are your motives for the treatment (list at least five)? Why now? Why do you consider Takiwasi to be the appropriate option for you?*

5.3.4. Procedure

Participants were approached within the first week of admission at the Takiwasi Center facilities. Those that agreed to participate and met dependence criteria (MINI; Sheehan, et al., 1998) were administered the aforementioned socio-demographic and clinical battery of measures. Data collection was performed by a trained health professional (first author of this work).

5.3.5. Data analysis

Quantitative analyses were conducted using SPSS version 17.0.1 (SPSS Inc. Released 2008. SPSS Statistics for Windows, Version 17.0. Chicago: SPSS Inc). We calculated mean scores and standard deviations for all scales and used one-sample t-tests to compare the Takiwasi sample scores on the ASI (McLellan et al., 1992), WHOQOL-BREF (WHOQOL Group, 1998), and SWBS (Paloutzian et al., 2012) with normative data (Aim 1). The ASI norms used for comparisons were taken from a large clinical sample entering conventional SUD treatment and general health insurance members (Weisner, McLellan, & Hunkeler, 2000). WHOQOL-BREF scores were compared to a large norming study reporting clinical (psychiatric patients) and general norms from various healthcare settings (Skevington & McCrate, 2011). SWBS scores were compared to norms from a clinical sample of psychiatric patients (Bufford, Paloutzian, & Ellison, 1991). For the ASI and the WHOQOL-BREF, t-test

significance levels were corrected for multiple comparisons since we tested differences with both clinical and general norms (Bonferroni-corrected [BF] level of significance of $p <$. 05/2 = .025, 2-tailed).

Qualitative analysis was performed by computer-assisted (Microsoft Office software) qualitative content analysis (Mayring, 2008) of the textual material (Aim 2). We first determined two main categories on the basis of our research questions and the textual material, namely *motives for treatment initiation* in general and *motives for selecting this particular treatment program*. We then inductively developed a coding system based on the data; meaningful clusters of motives were identified within the two main categories through a stepwise process. Emerging themes were re-checked against the textual material and modified if necessary, until a final set of motivational subcategories ("codes") was established. In order to evaluate the coding system's reliability, 20% of the data set was re-coded by an independent rater (JV) who had been trained in the content analytic method as per Mayring (2008). Between-rater agreement was assessed by means of Cohen's kappa (McHugh, 2012). Discrepancies between the two ratings were resolved through case-by-case discussion and, if necessary, adjustment of codes.

5.4. Results

5.4.1. Socio-demographic and clinical characteristics

Table 5 reports demographic and clinical characteristics of the sample. The mean age was 29 years (*SD* = 7). Most participants had never been married (90%), were living with their parents or relatives (52%), and came from Peru (42%) or other Latin American countries (34%). All participants were diagnosed with DSM–IV–TR substance dependence (APA, 2000) as required by study inclusion criteria. The majority of the sample met dependence criteria for multiple substances (68%). The rest either met dependence criteria for a single

substance (16%), or for a single substance plus abuse criteria for additional substances (16%). Substances predominantly involved cannabis, alcohol, and cocaine/cocaine base paste; also present but less frequent were opiates, tranquilizers, and amphetamines. The most common comorbid psychopathologies were affective disorders (60%), anxiety disorders (44%), and antisocial personality disorder (31%). Past week anxiety and depression symptoms on the HADS (Zigmond & Snaith, 1983) were moderate in the sample, but above the clinical cutoff point of +8 (Bjelland, Dahl, Haug, & Neckelmann, 2002). Average craving frequency on the CEQ (May et al., 2014) was moderate (no clinical cutoff score is available at present).

Table 5
Socio-Demographic and Clinical Characteristics of Participants

	n	*%*	*M*	*SD*
Age in years			29.2	7.2
Years of completed education			13.0	2.6
Gender (male)	50	100		
Marital status:				
- Married	4	8.0		
- Divorced/separated	1	2.0		
- Never married	45	90.0		
Living arrangement:				
- With sexual partner/children	8	16.0		
- With parents/relatives	26	52.0		
- With friends	1	2.0		
- Alone	11	22.0		
- No stable arrangement	4	8.0		
Nationality:				
- Peru	21	42.0		
- Chile	4	8.0		
- Argentina	3	6.0		
- Colombia	5	10.0		
- Mexico	4	8.0		
- Brazil	1	2.0		
- Spain	3	6.0		
- France	4	8.0		
- Belgium	2	4.0		
- Canada	1	2.0		
- USA	2	4.0		

Table 5 (continued)
Socio-Demographic and Clinical Characteristics of Participants

	n	*%*	*M*	*SD*
Context of upbringing:				
- Urban	43	86.0		
- Rural	7	14.0		
Spiritual preference:				
- Christian	22	44.0		
- Buddhist/Vedic	4	8.0		
- Other	2	4.0		
- None	22	44.0		
Diagnoses:[a]				
- Affective disorders	29	60.4		
- Anxiety disorders	21	43.8		
- Psychotic disorders	3	6.3		
- Eating disorders	0	0.0		
- Antisocial personality disorder	15	31.0		
- Substance use disorders	50	100.0		
- Dependent on 2 or more substances	34	68.0		
- Dependent on only 1 substance	8	16.0		
- Dependent on 1 and abuse of further substances	8	16.0		
Substances dependent on:				
- Cannabis	36	72.0		
- Alcohol	26	52.0		
- Cocaine	14	28.0		
- Cocaine base paste	10	20.0		
- Opiates	8	16.0		
- Tranquilizers	8	16.0		
- Stimulants	6	12.0		
CEQ-F[b] (1–10):				
- Total craving			5.2	2.8
- Intensity scale			5.9	2.9
- Imagery scale			4.6	3.1
- Intrusiveness scale			5.3	2.9
HADS[b]:				
- Overall emotional distress (0–42)			19.2	7.6
- Anxiety (0–21)[c]			10.4	4.8
- Depression (0–21)[c]			8.7	4.5

Note. N = 50. MINI = Mini International Neuropsychiatric Interview; CEQ-F = Craving Experience Questionnaire frequency form; HADS = Hospital Anxiety and Depression Scale. [a]Comorbid diagnoses for 2 participants were missing. [b]Higher scores indicate higher symptom frequency. [c]Clinical cutoff at +8 (Bjelland et al., 2002).

5.4.2. Comparisons with normative values

Table 6 presents ASI (McLellan et al., 1992) composite scores for the Takiwasi sample compared against norms from SUD patients entering conventional treatment and general population norms (Weisner et al., 2000). The Takiwasi patients' drug use composite scores were significantly more severe than those of SUD patients entering conservative treatment ($p <. 001$) as well as those of the general population norm ($p <. 001$), at a BF alpha of .025. The psychiatric status of the Takiwasi patients was also significantly more severe than for SUD patients seeking conventional treatment ($p <. 05$) and for general norms ($p <. 001$), at BF alpha of .025. Conversely, the alcohol use of Takiwasi patients was less severe than for conservative SUD treatment-seeking patients, although the difference was not significant ($p = .124$). The Takiwasi alcohol scores were, however, significantly more severe than for the general norm ($p <. 001$, BF alpha of .025). The medical status of the Takiwasi sample did not significantly differ from conventional SUD treatment-seekers ($p = .453$), nor from general norms ($p = .161$). Figure 2(a) summarizes significant differences on the ASI composite scores (no norms are provided for the other ASI problem areas in Weisner et al. [2000]).

Table 6 also shows the sample's quality of life on the WHOQOL-BREF (WHOQOL Group, 1998) in comparison to normative values (Skevington & McCrate, 2011). The Takiwasi patients scored significantly lower than psychiatric patients' norms (Skevington & McCrate, 2011) in the domains of physical health ($p < .05$), social relationships ($p <. 001$), and environment ($p < .01$), at a BF alpha level of .025. We found no significant difference for the psychological domain ($p = .154$). Takiwasi patients scored significantly lower than the general population norms (Skevington & McCrate, 2011) on all four domains ($p <. 001$ for all, BF alpha of .025). Figure 2(b) summarizes the significant differences on the WHOQOL-BREF.

Finally, Table 6 shows the spiritual well-being of Takiwasi patients on the SWBS (Paloutzian et al., 2012) in comparison to normative values (Bufford et al., 1991). Descriptively, the sample's SWBS scores point to moderate levels of life purpose and satisfaction (Paloutzian et al., 2012). However, compared to norms based on psychiatric patients (Bufford et al., 1991), Takiwasi patients had a significantly lower overall spiritual well-being as well as significantly lower religious well-being ($p < .01$ each). No significant difference was found for existential well-being ($p = .188$).

Table 6

Addiction Severity, Quality of Life, and Spiritual Well-Being Compared to Norms

	Takiwasi sample		Clinical norms				General norms			
	M	*SD*	*M*	*SD*	*t*	*p*	*M*	*SD*	*t*	*p*
ASI problem area composite score[f]										
Medical	.30[a]	.32[a]	.27[c]	.37[c]	0.76	.453	.24[c]	.17[c]	1.42	.161
Psychiatric	.44[a]	.20[a]	.37[c]	.24[c]	2.56	*.014	.03[c]	.10[c]	14.34	***.000
Alcohol use	.32[a]	.28[a]	.38[c]	.32[c]	-1.57	.124	.11[c]	.07[c]	5.14	***.000
Drug use	.25[a]	.12[a]	.11[c]	.12[c]	8.01	***.000	.01[c]	.03[c]	13.88	***.000
Legal	.21[a]	.20[a]								
Familial/social	.51[a]	.17[a]								
Employment	.62[a]	.30[a]								
WHOQOL-BREF[f]										
Physical health domain (1–100)	46.71[a]	18.91[a]	54.57[d]	20.62[d]	-2.94	*.005	65.2[d]	22[d]	-6.91	***.000
Psychological domain (1–100)	41.92[a]	19.62[a]	45.93[d]	25.99[d]	-1.45	.154	62.6[d]	18[d]	-7.45	***.000
Social relationships domain (1–100)	41.17[a]	18.16[a]	61.91[d]	20.80[d]	-8.08	***.000	66.5[d]	22[d]	-9.86	***.000
Environment domain (1–100)	52.13[a]	17.28[a]	61.00[d]	17.02[d]	-3.63	**.001	66.8[d]	16[d]	-6.00	***.000
Overall quality of life (1–5)	2.45[a]	1.05[a]					3.5[d]	0.9[d]	-7.10	***.000
SWBS										
Overall spiritual well-being (20–120)	75.11[b]	18.13[b]	83.68[e]	17.91[e]	-2.88	**.007				
Religious well-being (10–60)	38.30[b]	11.40[b]	44.87[e]	10.58[e]	-3.51	**.001				
Existential well-being (10–60)	36.81[b]	9.21[b]	38.84[e]	9.95[e]	-1.34	.188				

Note. ASI = Addiction Severity Index, composite scores range from 0 (no problem) to 1.0 (extremely serious). WHOQOL-BREF = World Health Organization Quality of Life-BREF; SWBS = Spiritual Well-Being Scale. Higher scores indicate higher quality of life/well-being. [a]$N = 50$. [b]$n = 37$. [c]Weisner, McLellan, & Hunkeler (2000); general norms based on $n = 9{,}398$ health insurance members; clinical norms based on $n = 327$ SUD patients entering conventional treatment. [d]Skevington & McCrate (2011); general norms based on $n = 4452$ healthy and sick participants; clinical norms based on $n = 77$–80 treatment seeking patients with various psychiatric conditions. [e]Bufford, Paloutzian, & Ellison (1991); norms based on $n = 182$ psychiatric inpatients and outpatients. [f]Significance at Bonferroni-corrected α of .025.

*$p < .05$, **$p < .01$, ***$p < .001$, two-tailed.

Figure 2. Main Differences in (a) Addiction Severity and (b) Quality of Life;

(c) Allocation of Stages of Change

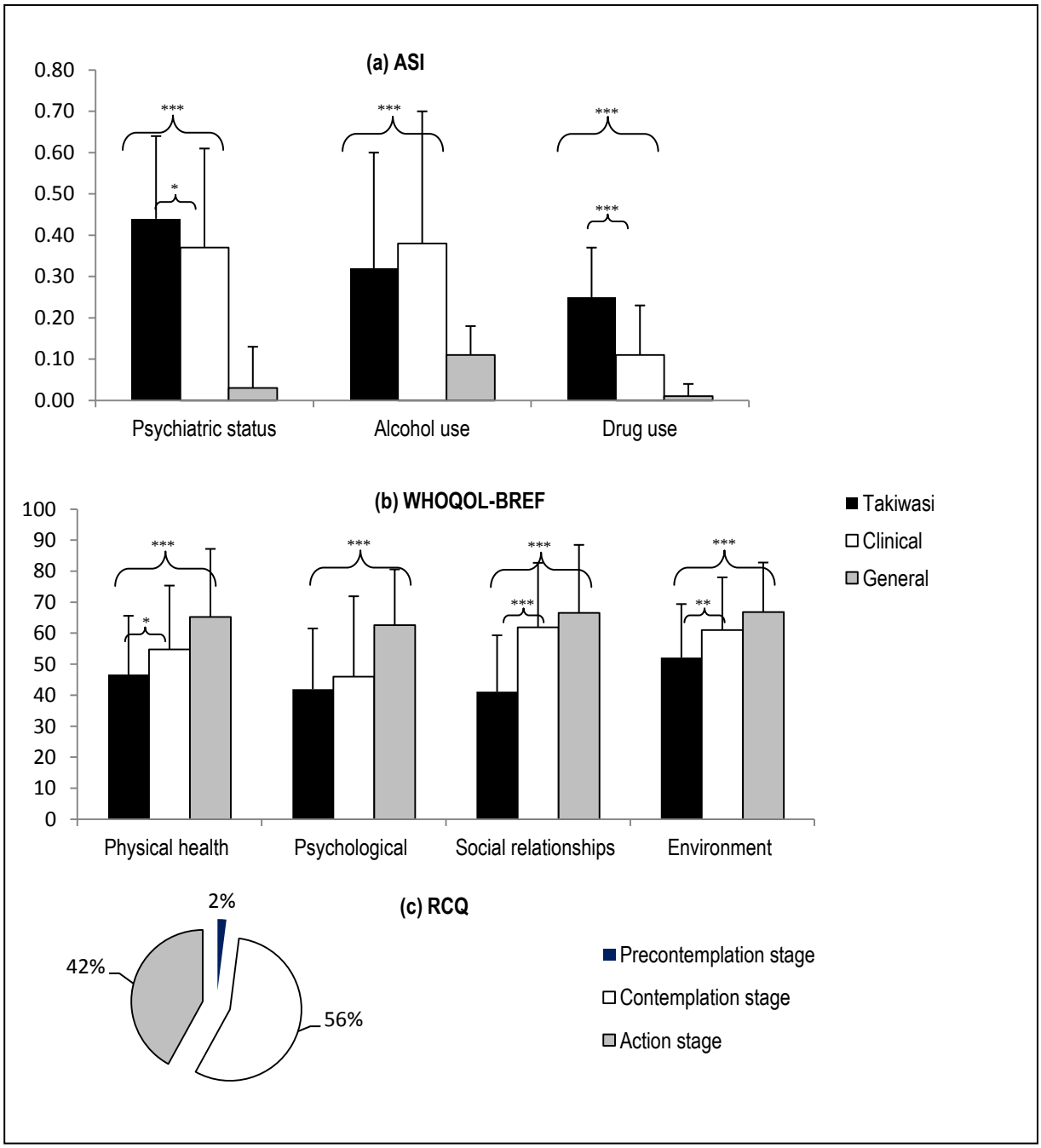

Figure 2. (a) ASI = Addiction Severity Index, composite scores of Takiwasi sample (N = 50) vs. clinical norms (n = 327) and general norms (n = 9,398) (Weisner et al., 2000). (b) WHOQOL-BREF = World Health Organization Quality of Life-BREF, domain scores of Takiwasi sample (N = 50) vs. clinical norms (n = 77–80) and general norms (n = 4,452) (Skevington & McCrate, 2011). Significance at Bonferroni-corrected α of .025. *p < .05, **p < .01, ***p < .001, two-tailed. (c) RCQ = Readiness to Change Questionnaire, allocation of Takiwasi sample (N = 50) to stages of change, at admission time.

5.4.3. Treatment motivation and change readiness

The sample's distribution on the RCQ (Rollnick, et al., 1992) is shown in Figure 2(c). Most participants fell into contemplation and action stages (56% and 42%, respectively). The results of the qualitative analysis regarding treatment motivation are given in Table 7. We found 10 thematic codes for the first, and 7 for the second main category (strong inter-rater reliability in both cases, κ = .82 and κ = .85, respectively). A brief description of codes is provided below via examples.

Main category 1: Motives for treatment initiation

Familial motives were most prominent (64%), which included reasons like "improve relationship with family", "not lose family", or "stop making family suffer". An equal percentage of the sample expressed *self-transformation* as a motive, that is, a wish to change specific behavioral/attitudinal aspects of self, such as "learn to control myself" or "stop being a victim". The next major subcategory concerned *mental health* (56%), including motives such as wanting to "overcome fears and traumas", "heal depression", or "manage emotions and stress". *Spiritual or existential motives* for initiating treatment were reported by 56% of the sample, for instance "feeling spiritually compromised", wanting to "find the purpose of my existence", or to "reconnect with God". Slightly over half of the sample reported reasons related to *striving for life satisfaction* (53%). This category included motives like "attaining happiness", "tranquility", or "to be free". An equal 53% referenced *community relationships and society* as a reason for enrolling in the treatment (e.g., wanting to "repair damages done to others", aspiring for "integration in society" or "contributing to society"). Slightly less than half of the sample directly addressed the desire to *quit drugs and addictions* as a reason for initiating treatment (47%). Examples included wanting to "definitively solve my addiction problem", "quit the drug routine", "learn controlled drinking", or "I don't want to be stuck in cocaine anymore". The achievement of *professional/educational goals* was mentioned by

45% of participants, including wanting to "have a professional life", "to study", or "learn responsibility with work and money". A somewhat smaller portion of the sample reported that their *physical health* played a role in their decision to seek out treatment (39%), expressing a "concern for health", "deteriorating health", or "allergies and health problems". Finally, one third of the sample gave reasons related to finding their *identity* (33%), e.g., seeking self-knowledge and self-understanding, wanting to "gain clarity on interests and values", "know myself" or "know the roots of my problems".

Main category 2: Motives for selecting this program

Reported reasons fell into seven thematic codes. Most frequently, treatment aspects linked to *traditional Amazonian medicine* were referenced as a reason for choice (44% of participants), including interest in or past experiences with specific Amazonian methods, "confidence in the healing potential of plants", "trust in this natural medicine", or "appreciation of ancestral knowledge". The second-most frequent category referred to the *Takiwasi concept* as a whole and its characteristics (42% of the sample), e.g., the "combination of psychotherapy and traditional medicine", "holistic approach", "integral treatment of body, psyche, and spirit", or simply "because it is different". Nearly a third of the sample spoke of *information or recommendation* having led them to choose this treatment program (28%), for instance "I saw a documentary about Takiwasi", or "my cousin got cured at this center". The same percentage of participants reported *unfavorable past experiences with other treatments*, such as "they tried to solve my drug problems with more drugs", "I don't want to take any more colorful pills", or "the other methods evidently didn't work". Having c*onfidence in Takiwasi* as a reason for choosing this treatment was addressed by another 28%, for instance "I am confident that Takiwasi will help me change", or "Takiwasi seems like a serious institution". *Spiritual aspects of the Takiwasi treatment* were pointed to by another 28%, for instance selecting this treatment "because of its health professionals

specialized in spiritual medicine" or "because I feel that only Takiwasi can help with my spiritual illness". Finally, a somewhat smaller portion of the sample explained their choice on the basis of a variety of *personal preferences and interests* (22%), e.g., "I like the rainforest", "because it is not in the city".

Table 7
Motives for Treatment Initiation and for Selection of Alternative Method

	Participants per category, nr. (%)	Mentions per category, nr.
Motives for initiating treatment		
Familial motives	23 (63.9%)	46
Self-transformation	23 (63.9%)	41
Mental health	20 (55.6%)	43
Spiritual and existential motives	20 (55.6%)	27
Striving for life satisfaction	19 (52.8%)	31
Community relationships and society	19 (52.8%)	30
Quit drugs and addictions	17 (47.2%)	24
Professional /educational goals	16 (44.4%)	22
Physical health	14 (38.9%)	18
Finding identity	12 (33.3%)	19
Motives for selecting Takiwasi treatment		
Traditional Amazonian medicine	16 (44.4%)	25
Takiwasi concept	15 (41.7%)	24
Information/recommendation	10 (27.8%)	15
Unfavorable other treatment experiences/opinions	10 (27.8%)	12
Confidence in Takiwasi (staff)	10 (27.8%)	12
Spiritual aspects	10 (27.8%)	11
Personal preferences and interests	8 (22.2%)	9

Note. N = 36. Inter-rater reliability as assessed by Cohen's kappa was strong for both the 10 codes of the first main category (κ = .82) and for the 7 codes of the second main category's (κ = .85).

5.5. Discussion

In this study we investigated the characteristics and motives of patients enrolling in an innovative alternative treatment program combining Amazonian medicine, including ayahuasca, with conventional psychotherapy. Our findings indicate that most Takiwasi patients were young or middle-aged, unmarried males that live with their relatives, mostly in urban areas of Peru. Yet, cultural and geographical backgrounds across the sample were

diverse: Over a third came from other Latin American countries, and about a quarter from Europe or North America. Cultural diversity may, therefore, be considered a distinctive feature of this sample. The large portion of foreigners in the sample may be a result of the international popularization of ayahuasca, but further research is needed in this context. Types of substances used, on the other hand, are in line with global statistics which report alcohol consumption as the most prevalent addictive behavior and cannabis as the most commonly used illicit drug worldwide (Gowing et al., 2015). Our findings are also in line with the observation that cocaine use is more prevalent in the Americas than opiates (Gowing, et al., 2015). Finally, we found a high rate of comorbid anxiety and mood disorders in the Takiwasi sample, which is a common cross-cultural finding for SUD patients in general (Merikangas et al., 1998).

While our results overall suggest that individuals entering the Takiwasi treatment are similar to other SUD patients in terms of substances and comorbidities, clinical severity in terms of drug use and psychiatric status appeared to be above those of other SUD patients entering conventional treatment (Weisner, et al., 2000). A possible explanation for this finding is that the alternative treatment is sought as a last resort strategy after unsuccessful outcomes with other approaches. Indeed, our qualitative results support this notion, as nearly a third of participants viewed unfavorable prior treatment experiences as a reason for initiating treatment at Takiwasi. Another distinctive aspect of the sample was a significantly lower quality of life and spiritual well-being compared with other psychiatric patients (Bufford et al., 1991; Skevington & McCrate, 2011). The Takiwasi treatment thus appears to attract individuals who experience exceptionally low quality of life and spiritual well-being. The latter seems sensible particularly when considering the spiritual dimension inherent in Amazonian medicine and the Takiwasi treatment. Correspondingly, we found patients to explicitly address spirituality or existential motives when asked why they sought treatment at this center. Overall, our data thus suggest that, for the patients that turn to Takiwasi, the

spiritual dimension of the treatment is relevant. Moreover, it is in line with long-standing research showing a relationship between addiction and spirituality (Miller, 1998), recent evidence on its importance to achieving positive outcomes (Schoenthaler et al., 2015), as well as with the widespread popularity of interventions with a spiritual component, such as Alcoholics Anonymous (Kelly, 2016). Interestingly, our comparative SWBS results which indicated low spiritual well-being relative to psychiatric norms held true for the overall scale and for the religious subscale, but not for the existential subscale. This may mean that the lower well-being of patients focuses particularly on those facets of spirituality that relate to institutionalized spirituality/religion involving a God-concept. However, further qualitative data would be necessary for a more accurate interpretation of this finding.

Our results indicate that the most salient reasons for which patients select this program relate to its traditional medicines component and overall treatment model. Motivational factors that were found with regard to the decision of initiating treatment in general are similar to those reported in the literature (McCaul et al., 2006). One study for instance found social influence, self-concept, health, and legal issues as treatment-seeking motives (Downey et al., 2001). Another study identified self-image/self-control, health concerns, interpersonal relationships, legal concerns, social acceptability, and self-efficacy (Chauchard et al., 2013). It is worth noting that direct references to stopping substance use, although present in the data, were not among the most salient motives in our sample. However, it is possible that since this is the defined clinical focus of the Takiwasi treatment, it may have been taken for granted and, therefore, not explicitly stated.

Our study has several limitations. We compared sample scores with normative data rather than a direct comparison group. Furthermore, since more appropriate norms could not be identified, we used norms based on North American and UK populations while our sample was culturally diverse, which limited the cultural adequacy of the comparison. Similarly, even

though the norming sample overall was clinically fit (SUD treatment-seeking men), other systematic differences (e.g., variables related to health insurance ownership) could have impacted our results. Future studies should ideally include a matched sample from a conventional facility in a similar cultural context for comparison. A quantitative importance rating of the motivational factors here reported would be valuable in this context, as would a qualitative examination of how the motives expressed prior to treatment initiation evolve over time and if they are considered adequately met by the treatment.

Findings from this study have important implications. Our results demonstrate that the Amazonian medicine-based therapy attracts a diverse clientele not limited to regional/national residents. This in turn implies an extant interest in such therapies among international SUD patients and highlights the importance of further investigation of the acceptability and applicability of Amazonian methods to different cultural profiles, as well as of the general flux of treatment seekers (medical tourists) to the Amazon and ensuing implications for local patients (are they at a disadvantage due to lesser financial means or rather supported by the increase of self-paying foreigners via subsidization?). Future research should also empirically test if the Takiwasi and similar approaches are especially suited to the needs of SUD patients with high clinical severity. Challenges for such studies will involve internationally varying jurisdictions on plant substances such as ayahuasca, the particular context required for certain Amazonian interventions (e.g., retreats in the forest, ceremonial settings), and the need for trained Amazonian practitioners that can safely administer the treatments. These challenges equally apply for the future implementation of modalities like Takiwasi's, which are based on plants that on an international level lack regulation or may be prohibited. Furthermore, it remains to be seen if these practices can be brought to scale to serve more patients, or if a broader application of ritual and cultural-specific practices could alter the manner in which they are perceived by patients or dilute effects. Findings from the aforementioned naturalistic study (Berlowitz, et al., 2019) provide preliminary outcome results, and a more extensive

prospective follow-up study is currently underway at the Takiwasi Center. A future step may involve a controlled intervention study *in situ* using a patient sample from a selected country/culture for this purpose. Research is also needed on the effectiveness of the treatment for particular sub-groups of patients. This emerging research program may, in the long-term, open new treatment avenues for SUD, which, in view of the high relapse rates and general gap in service provision in this context is imperative (Brandon et al., 2007; United Nations Office on Drugs and Crime, 2016).

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6. Empirical Study 3

Short-Term Treatment Effects of a Substance Use Disorder Therapy Involving Traditional Amazonian Medicine

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6.1. Abstract

Chronic illness management today commonly involves alternative medicines. Substance use disorder (SUD), as a chronic psychosomatic illness, might benefit from a similar approach. The accredited Takiwasi Center offers such an SUD treatment program involving Amazonian medicine combined with psychotherapy. The current study assessed this integrative program's short-term therapeutic effects. We measured baseline data from 53 dependence-diagnosed males admitted to treatment (T1) and repeated clinical outcome variables at treatment completion (T2). Paired samples t-tests were used to assess changes between T1 and T2 (n = 36). Nearly all participants (age M = 30.86, SD = 8.17) were dependent on multiple substances, most prominently cannabis, alcohol, and cocaine-related drugs. A significant decrease (T1 to T2) was found for addiction severity outcomes drug use (p <. 001), alcohol use (p <. 001), psychiatric status (p <. 001), and social/familial relationships (p <. 001). Emotional distress also diminished significantly (p <. 001), as did substance craving (p <. 001). Quality of life increased significantly from T1 to T2 (p <. 001). Our results provide first indications for significantly improved SUD symptoms after the Amazonian medicine-based treatment. These findings are preliminary given the design, but strongly encourage further investigation of this therapy, which in the long-term may open new therapeutic avenues for SUDs.

Keywords Substance use disorder; Amazonian medicine; addiction treatment; ayahuasca; drug abuse; alternative medicine

6.2. Background

Substance use disorder (SUD) is a large-scale public health problem that continues to affect global modern society. It is associated with extensive costs and adverse consequences, including health impairments, accidents, and early death (Gowing et al., 2015). Today SUD is increasingly understood as a chronic illness, due to the disorder's persistent nature, characteristic tendency for relapse, and on the basis of neurobiological evidence showing long-term cerebral adaptations associated with regular drug use (Brandon et al., 2007; Koob & Le Moal, 2008). Nonetheless, existing treatments for SUD are frequently delivered as if for an acute condition (McLellan et al., 2000; White et al., 2002). It has been suggested, therefore, that SUD therapy could benefit from more alignment with state-of-the-art health-care models that are being employed in somatic medicine for chronic illnesses (McLellan et al., 2000). Present day chronic illness management is often integrative and may, for example, involve referral protocols for patients to access therapies other than biomedical, such as acupuncture, osteopathy, or homeopathy (for instance in the case of chronic musculoskeletal pain; Jong et al., 2016). Thus, chronic care today increasingly combines conventional treatments with alternative or traditional medicines (Molassiotis et al., 2005; Templeman & Robinson, 2011; World Health Organization, 2013), a model that could be beneficial also for SUD. The Takiwasi Addiction Treatment Center (Peru) offers an SUD treatment protocol that parallels this somatic chronic care framework, combining methods from traditional Amazonian medicine and modern psychotherapy.

Amazonian medicine is an ancient indigenous healing system making use of medicinal plants from the Amazon rainforest, according to sophisticated application methods and ritual techniques (Berlowitz et al., 2017; Bussmann & Sharon, 2006; Luna, 1986; Sanz-Biset et al., 2009). Among Amazonian medicinal plants, *Banisteriopsis caapi*, the ayahuasca vine, has become well-known in the modern west, and is increasingly discussed for its potentials for

assisting the treatment of psychosomatic problems, such as SUD (Bouso & Riba, 2014; Fabregas et al., 2010; Labate & Cavnar, 2014; McKenna, 2004; Riba et al., 2003; Thomas et al., 2013). Nonetheless, Amazonian medicine offers numerous other plants aside from ayahuasca (Sanz-Biset et al., 2009; Shepard, 1998), some of which are being applied at the Takiwasi Center to target symptoms of SUD, such as withdrawal or craving, as part of the addiction treatment program (Berlowitz et al., 2017). Internally generated data from the center suggests favorable results (Giove Nakazawa, 2002), but clinical parameters and outcomes have not yet been scientifically established. Consequently, the goal of the current study was to empirically assess the short-term therapeutic effects of this innovational treatment program.

At an early stage of therapeutics evaluation it is necessary to ask whether an intervention has any benefit at all, rather than testing incremental utilities using comparisons (Donovan et al., 2012). We therefore explored the short-term effects of the Takiwasi treatment by means of a naturalistic design, with a particular focus on (a) addiction severity, (b) substance craving, (c) depressive and anxiety symptoms, and (d) quality of life. Outcome indicators were chosen with reference to international recommendations for the evaluation of addiction treatment effects (Tiffany, Friedman, Greenfield, Hasin, & Jackson, 2012). We hypothesized a reduction in clinical symptoms (a-c) and an increase in quality of life (d) after treatment completion.

6.3. Methods

6.3.1. Participants

Study inclusion criteria consisted of substance dependence diagnosis as per *Diagnostic and Statistical Manual of Mental Disorders* (DSM–IV–TR; American Psychiatric Association [APA] 2000) based on the Mini International Neuropsychiatric Interview (MINI; Sheehan et al., 1998), and of the fulfillment of admission criteria to the Takiwasi inpatient treatment (i.e.,

medical clearance from the center's medical team, Spanish language skills, written motivational statement). Since this research was designed before the DSM-5 release (American Psychiatric Association, 2013), we used the prior version of the DSM for the purpose of this study. Data collection was initiated in April 2014 and pre-treatment assessment (T1) was discontinued in June 2016. Post-treatment (T2) data collection carried on until January 2017. From the 68 patient admissions during this time frame, 2 preferred not to participate (personal reasons), 3 did not meet dependence criteria, and 10 entered the study but had incomplete baseline data and were therefore excluded (see Figure 3). The sample at T1 consisted of 53 participants. Since 17 participants dropped out of treatment, the final sample with post-treatment measures at T2 consisted of 36 participants. The study was conducted according to international regulatory requirements and the Declaration of Helsinki and had been approved by the responsible ethics committee (University of Fribourg, Switzerland).

6.3.2. Study setting

The study was conducted at the facilities of the Takiwasi Addiction Treatment Center in Tarapoto, San Martín Province, Peru. This health-care center offers inpatient treatment (maximum of 18 beds capacity) for individuals with addictive problem. The program is limited to males, due to a Peruvian legal restriction of gender-specificity in this type of residential therapy. In addition, outpatient services are available to both genders, and provide assistance for a broad range of mental health problems. The Takiwasi Center has a pioneering character as the world's first accredited, governmentally recognized health institution (Peruvian Health Ministry) applying traditional Amazonian medicine to SUD. It was founded in 1992 by a French medical doctor after a mission with Doctors Without Borders for a primary health-care project (unrelated to addictions) in the Peruvian Andes. Due to the spread

Figure 3. Flow Chart of Participants During Recruitment and Assessment

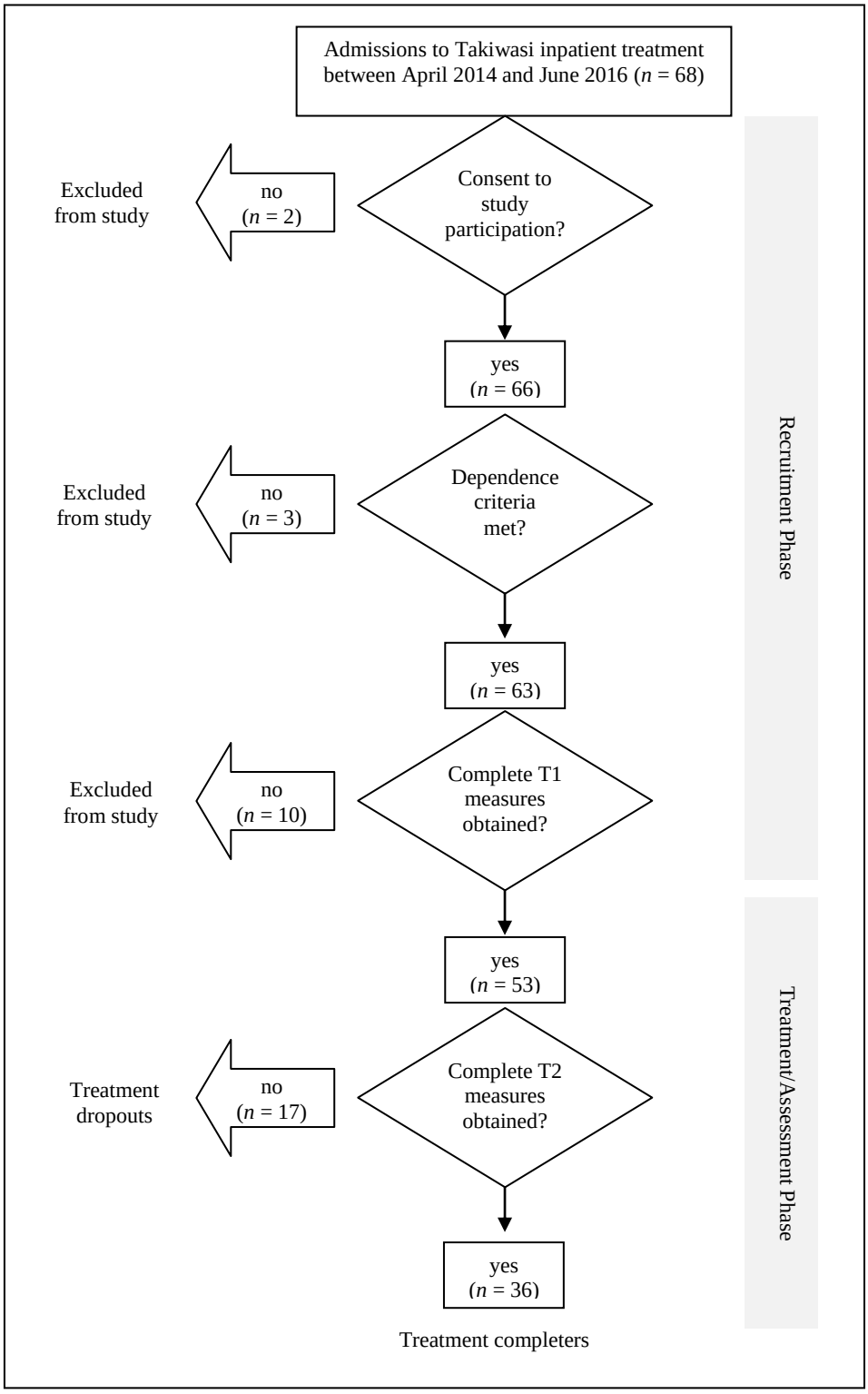

Figure 3. Flow chart illustrating rate of consent to participation, study exclusion/ inclusion, and treatment dropout throughout recruitment and assessment.

of cocaine production sites in the Amazon during the 1980s, there had been a substantial rise in incidence of cocaine and cocaine base paste dependence in the Peruvian San Martín Province (Giove Nakazawa, 2002; Sanz-Biset et al., 2009). The Takiwasi Center was created to provide assistance to this situation by making use of local medical resources and Western knowledge about SUD. Today, owing to extensive governmental efforts that supported the cultivation of alternative produce, such as coffee or corn, cocaine production in this area has virtually ceased. The necessity for addiction treatment in the region however remains. The work of the center has become known throughout Peru and beyond its borders, such that it now receives requests by treatment-seekers from around the globe. The clinical staff of the Takiwasi Center is composed of health professionals from both traditional Amazonian and Western medical systems, i.e., specialized traditional healers as well as Western-trained psychologists and physicians, who are operating within a plurimedical and intercultural framework.

6.3.3. SUD treatment protocol

The SUD inpatient treatment at the Takiwasi Center typically lasts between 3-12 months, with duration varying according to individual needs. The therapeutic protocol includes both traditional Amazonian treatments and Western psychotherapeutic methods and involves three stages: 1) an initial phase (2-4 weeks) focusing on detoxification; 2) a stage where the therapeutic work deepens and key issues, which often underlie the addictive problem, tend to be addressed; and 3) a final stage in which the person's return to a professional and social life is gradually prepared. All three stages involve the application of both traditional Amazonian and Western therapeutic methods.

Main methods from traditional Amazonian medicine applied at Takiwasi

Amazonian methods for SUD treatment applied at the Takiwasi Center can be grouped into three broad categories, all making use of local medicinal plants in a ritualized context (Berlowitz et al., 2017). First, *purging rituals* use plants with emetic effects that are thought to detoxify the organism, alleviate withdrawal symptoms, and craving. This technique is applied several times a week in the initial detoxification period, and with a lesser frequency throughout the entire treatment. Second, *dietary forest retreats* are weeklong retreats where patients stay socially secluded in forest huts and are administered medicinal plants by a curandero/a (traditional healer), while adhering to strict nutritional and other behavioral rules. This intervention aims to facilitate emotional processing and self-understanding, as well as to detoxify the client. Dietary forest retreats are prescribed about once every three months, with several weeks of "post-diet" during which certain restrictions still need to be kept. Third, *healing ceremonies* are introduced after an initial detoxification period and are then administered twice a month on average. They involve a ceremonially framed group setting guided by a curandero/a, who administers specific plant medicines, among them also preparations based on the aforementioned ayahuasca plant. These interventions intend to increase awareness of self, of one's relationship to the world, as well as to cleanse the client from toxins. Plant ceremonies and retreats may involve peak experiences, and are believed to help reconcile unresolved emotional trauma, as well as facilitate an increased sense of connection with life, purpose, or meaning.

Main Western therapeutic methods applied at Takiwasi

Besides the Amazonian treatments, all patients have weekly psychotherapy sessions with trained psychotherapists, participate in group therapy on a daily basis (e.g., relapse prevention, psychodrama) and occasionally undergo biomedical health checks. They live

together in a therapeutic community and perform daily chores guided by an occupational therapist.

Both Amazonian and conventional therapeutic methods are applied simultaneously, however the specific therapy plan of a given patient is adapted to that person's clinical necessities.

6.3.4. Measures

Psychiatric diagnoses were assigned using the *MINI* (Ferrando et al., 1998; Sheehan et al., 1998). The *Hospital Anxiety and Depression Scale* (HADS; Quintana et al., 2003; Zigmond & Snaith, 1983) was used to assess emotional distress (range 0-42; Cronbach's alpha .85), consisting of two subscales measuring depression and anxiety (range 0-21; clinical cutoff +8; Bjelland et al., 2002). We measured severity of dependence symptoms with the *Addiction Severity Index 5* (ASI; McLellan et al., 1992), assessing areas of functioning through medical, employment, alcohol use, drug use, legal, familial/social, and psychiatric composite scores (range 0–1; clinical cutoff scores are available for alcohol use [.17] and drug use [.16]; Rikoon, Cacciola, Carise, Alterman, & McLellan, 2006). We used the ASI also for assessing socio-demographic characteristics of participants. The *Craving Experience Questionnaire* frequency form was employed to measure substance craving (CEQ; May et al., 2014). This 10-item questionnaire assesses craving frequency on an 11-point visual analogue scale, obtaining averaged scores for total craving (range 0–10; Cronbach's alpha .94) and three subscales (intensity, imagery, and intrusiveness of craving). Finally, to assess quality of life we used the *World Health Organization Quality of Life-BREF* (WHOQOL-BREF; Lucas-Carrasco, 2012; WHOQOL Group, 1998). Its 26 items are answered on a scale from 1 (*very poor*) to 5 (*very good*). Two items are combined to provide an indicator for overall quality of life and health (range 1–5). Four domain scores (range 0–100) are computed out of the

remaining 24 items, concerning physical health (7 items; Cronbach's alpha .78), psychological health (6 items; Cronbach's alpha .80), social relationships (3 items; Cronbach's alpha .40[3]), and environment (6 items; Cronbach's alpha .72), with higher scores representing higher quality of life. Change motivation was assessed using the *Readiness to Change Questionnaire* (RCQ; Rodríguez-Martos et al., 2000; Rollnick et al., 1992), with items rated on a scale from -2 (*strongly disagree*) to +2 (*strongly agree*). Motivational stage was assigned on the basis of the highest score among the RCQ stages (pre-contemplation, contemplation, and action).

6.3.5. Procedure

Participants were approached within the first week of admission and informed about the study. Those that agreed to participate wrote an informed consent and completed the battery of socio-demographic and clinical measures for the baseline assessment (T1). The tests related to the main outcome measures (i.e., ASI, HADS, CEQ, WHOQOL-BREF) were re-administered upon treatment completion (T2) within one week (i.e., plus/minus 4 days) of the final treatment day. The average test-retest interval was 215.6 days (*SD* = 84.7). We have measured post-treatment outcomes in the short-term (i.e., in the immediacy of treatment completion), but since the average treatment duration and test-retest interval were extended, the T2 assessment may be argued to reflect medium-term effects with regard to T1.

6.3.6. Data analysis

Statistical analyses were conducted using SPSS 17.0.1 (Statistics for Windows, released 2008, Chicago: SPSS Inc). We performed chi-square and Fisher's exact tests to determine if there were systematic differences among dropouts and treatment completers in the distribution of key categorical variables (i.e., substance type, single vs. poly-substance

[3] Due to the small item number in this domain's scale, the indicator for internal consistency may not be reliable (WHOQOL Group, 1998)

use, comorbid psychiatric diagnoses, nationality, context of upbringing, marital status, change readiness).

Paired-samples t-tests were used to evaluate differences on the outcome variables between T1 and T2. We tested for the normality of distributions of the pre-post difference scores using the Kolmogorov-Smirnov test. Normally distributed variables included the ASI composite scores' medical status, $D(36) = .10$, $p = .20$; alcohol use, $D(36)=.14$, $p=.06$; drug use, $D(36) = .08$, $p = .20$; familial/social relationships, $D(36) = .08$, $p = .20$; psychiatric status, $D(36) = .10$, $p = .20$; the HADS' overall emotional distress, $D(36) = .20$, $p = .20$; and the WHOQOL-BREF overall quality of life, $D(36) = .13$, $p = .16$. Only for overall substance craving (CEQ), difference scores were significantly non-normal, $D(36) = .15$, $p < .05$. We therefore used the Wilcoxon Signed Rank test for this outcome variable. Significance levels were corrected for multiple comparisons (Bonferroni-corrected [BF] level of significance of $p < .05/8 = .00625$, 2-tailed) since we tested differences on 8 distinct scales. In case of significant differences on the t-test, Cohen's *d* was calculated as an effect size measure; *r* was used in the instance of the non-parametric Wilcoxon test.

6.4. Results

6.4.1. Sample characteristics

Table 8 displays sociodemographics and clinical features at baseline (T1) for the total initial sample ($n = 53$), for participants who completed the treatment ($n = 36$), and for those that dropped out ($n = 17$). The mean age of treatment completers was 30.86 years ($SD = 8.17$) with an average of 13.07 years of education ($SD = 2.96$). Most completers had never been married (86.1%) and were living with their parents or other relatives (47.2%). Almost 40% of the completers were from Peru. An equal percentage came from other Latin American countries and about 20% came from Europe or North America. A large majority of

completers grew up in an urban rather than a rural context (91.7%). Types of substances, for which dependence was diagnosed, involved cannabis (72.2%), alcohol (63.9%), cocaine or cocaine base paste (61.1%), opiates (13.9%), amphetamines and related stimulants (11.1%), and tranquilizers (11.1%). The SUDs of about 80% of the completers involved several DSM–IV (APA, 2000) diagnoses of dependence and/or abuse simultaneously; only 16.7% used exclusively one substance. Comorbid diagnoses of affective disorders were prevalent among completers (58.3%), as were anxiety disorders (36.1%) and antisocial personality disorder (27.8%). RCQ scores (assessed at T1) placed most completers in the contemplation stage (61.1%) and the rest in the action stage. None were placed in the pre-contemplation stage.

6.4.2. Treatment completion and dropout

About one-third of the initial sample abandoned treatment prematurely (32.08%). The participants who completed the treatment stayed at the center for an average of 217.2 days (SD = 85.0). Significance tests for categorical differences between dropouts and completers are displayed in Table 8. Nationality was the only variable that was significantly associated with whether or not treatment was completed ($p < .05$); standardized residuals of the chi-square test indicated the significant difference to reflect an overrepresentation of North American participants amongst dropouts ($se_i = 2.1$).

6.4.3. Treatment effects

Table 9 shows means and standard deviations of the outcome variables and paired-samples t-tests for each outcome variable's main scale. Significant differences on the ASI were found at a BF corrected alpha of .00625 for average drug use ($p < .001$, $d = 1.59$), alcohol use ($p < .001$, $d = 1.21$), psychiatric status ($p < .001$, $d = .91$), as well as social/familial relationships ($p < .001$, $d = 1.44$), all of them being significantly lower after treatment than before. The medical status composite score also decreased from T1 to T2, but

the difference was not significant (p = .317). There was a significant increase in overall quality of life on the WHOQOL-BREF from T1 to T2 (p < .001, d = .98). Average emotional distress on the HADS diminished significantly from T1 to T2 (p < .001, d = .97), as did overall substance craving on the CEQ (p < .001, r = .60). Figure 4 displays the significant pre-/post-treatment differences found for addiction severity (Figure 4a) and for substance craving, emotional distress, and quality of life (Figure 4b) on the paired samples t-tests.

Table 8

Demographics and Clinical Features of Treatment Completers, Dropouts, and Total Initial Sample at baseline (T1), and Chi-Square Analyses Comparing Completers vs. Dropouts

	Total initial sample	Completers	Dropouts	Chi-square analysis	
	N = 53	*N* = 36	*N* = 17	$\chi 2$(df)	p^b
Age in years, *M (SD)*	30.05 (7.74)	30.86 (8.17)	28.34 (6.66)		
School education in years, *M (SD)*	12.86 (2.97)	13.07 (2.96)	12.41 (3.04)		
Male sex %	100	100	100		
Living arrangement %					
with sexual partner/children	18.9	16.7	23.5		
with parents/relatives	47.1	47.2	47.1		
with friends	3.8	5.5	0		
alone	22.7	25	17.6		
no stable arrangement	7.5	5.6	11.8		
Marital status %					
married	7.5	11.1	0	2.27(2)	.361
divorced/separated	3.8	2.8	5.9		
never married	88.7	86.1	94.1		
Nationality %					
Peruvian	43.4	38.9	52.9	9.50(3)	.027
Latin American (except Peru)	34	38.9	23.5		
European	17	22.2	5.9		
North American	5.6	0	17.7		
Context of upbringing %					
urban	84.9	91.7	70.6	4.00(1)	.094
rural	15.1	8.3	29.4		
[a]MINI diagnoses %					
substance use disorders	100	100	100		
affective disorders	62.7	58.3	73.3	1.02(1)	.360
anxiety disorders	43.1	36.1	60	2.46(1)	.135
psychotic disorders	5.9	5.6	6.7	.02(1)	1.00
antisocial pers. disorder	35.3	27.8	53.5	3.03(1)	.112

Table 8 (continued)

Demographics and Clinical Features of Treatment Completers, Dropouts, and Total Initial Sample at baseline (T1), and Chi-Square Analyses Comparing Completers vs. Dropouts

	Total initial sample	Completers	Dropouts	Chi-square analysis	
	N = 53	*N* = 36	*N* = 17	*χ2*(df)	*p*[b]
Dependence diagnosed for %					
2 or more substances	71.7	69.4	76.5	.30(2)	1.00
1 substance + abuse of others	13.2	13.9	11.8		
1 substance only	15.1	16.7	11.8		
Substances dependent on %					
cannabis	71.7	72.2	70.6	0.02(1)	1.00
alcohol	54.7	63.9	35.3	3.81(1)	.077
cocaine	30.2	38.9	11.8		
cocaine base paste	24.5	22.2	29.4		
opiates	15.1	13.9	17.6	0.13(1)	.700
amphetamines/related stimulants	11.3	11.1	11.8	0.01(1)	1.00
hallucinogens	1.9	0	5.9	2.16(1)	.321
tranquilizers	15.1	11.1	23.5	1.39(1)	.252
Dominant RCQ stage %					
precontemplation	1.9	0	5.8	2.71(2)	.268
contemplation	56.6	61.1	47,1		
action	41.5	38.9	47,1		

Note. MINI = Mini International Neuropsychiatric Interview; RCQ = Readiness to Change Questionnaire.

[a] Comorbid diagnoses for 2 participants were missing. [b] p-values for Fisher's exact test.

Table 9

Dependent-Samples t-Tests with Means and Standard Deviations of Outcome Variables

	Pre-Treatment		Post-Treatment		95% CI of mean difference		*t*(df)	*p*
	M	*SD*	*M*	*SD*	Lower	Upper		
ASI composite scores								
Severity of medical status	.26	.27	.21	.21	-.05	.14	1.02(35)	.317
Severity of alcohol use	.38	.28	.06	.10	.22	.40	7.28(35)	p < .0001
Severity of drug use	.26	.12	.06	.06	.16	.24	9.52(35)	p < .0001
Severity of family/social relationships	.49	.19	.26	.15	.17	.28	8.64(35)	p < .0001
Severity of psychiatric status	.44	.21	.21	.17	.14	.31	5.46(35)	p < .0001
CEQ								
Total score (overall craving)	4.73	2.65	1.36	1.38			[a]5.10	p < .0001
Intensity	5.46	2.93	0.99	1.09				
Imagery	4.13	2.96	1.47	1.34				
Intrusion	4.79	2.89	1.60	2.06				
HADS								
Total score (emotional distress)	18.69	7.08	10.56	6.42	5.31	10.97	5.83(35)	p < .0001
Anxiety scale	10.25	4.03	6.67	3.99				
Depression scale	8.44	4.05	3.89	3.39				
WHOQOL								
Overall quality of life	2.58	1.07	3.78	0.93	-1.61	-0.78	-5.87(35)	p < .0001
Physical health domain	47.42	19.35	70.93	18.29				
Psychological domain	43.17	18.21	66.78	16.98				
Social relationships domain	40.05	17.23	56.25	19.76				
Environment domain	52.00	17.25	59.81	13.53				

Note. ASI = Addiction Severity Index; CEQ = Craving Experience Questionnaire; HADS = Hospital Anxiety and Depression Scale; WHOQOL-BREF = World Health Organization Quality of Life-BREF. Higher scores indicate more extreme responses in the direction of the assessed construct for all scales. [a]z-score from the Wilcoxon Signed Rank test. *p < .05, **p < .01, ***p < .001, two-tailed, significance at Bonferroni-corrected α of .00625.

Figure 4. Significant Pre-/Post-Treatment Differences

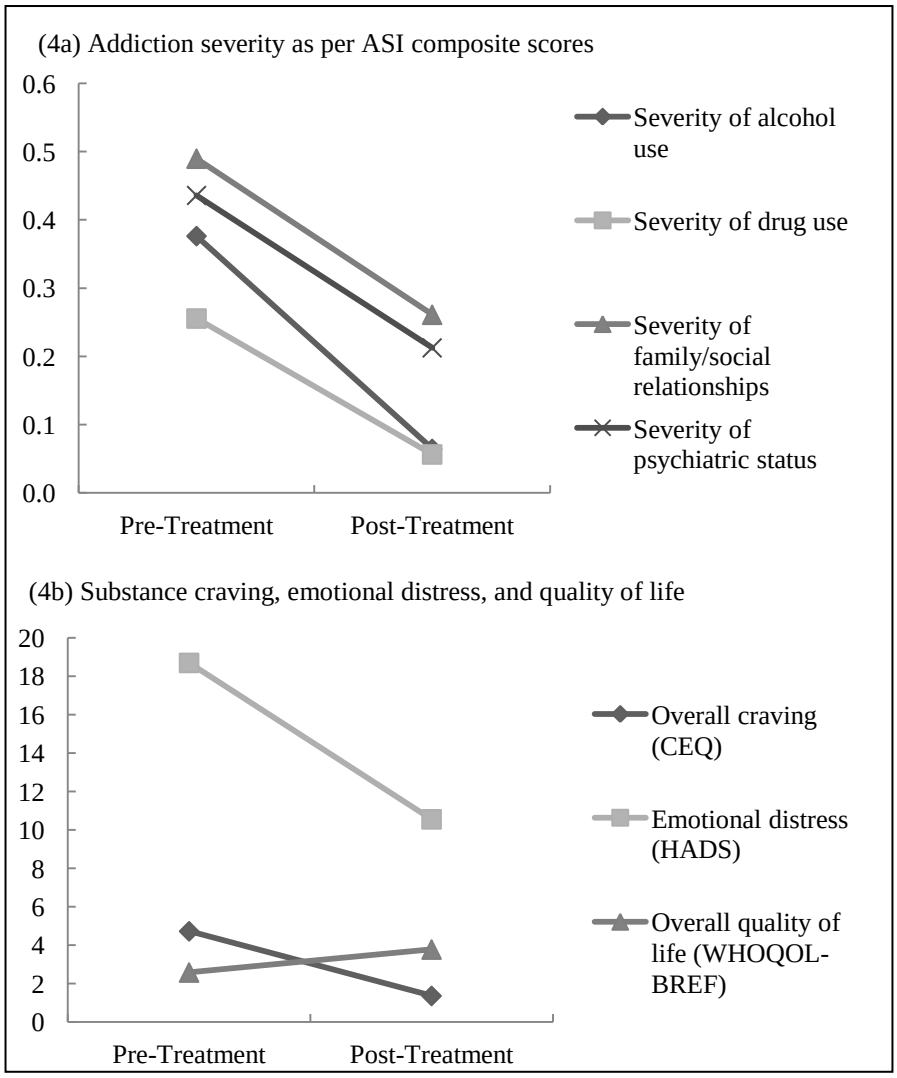

Figure 4. Significant results of the paired-samples t-tests on the outcome variables. 4(a) displays significant differences on the Addiction Severity Index (ASI) composite scores. ASI scores may range from 0 (no problem) to 1.0 (extremely serious). 4(b) shows significant differences on the Craving Experience Questionnaire (CEQ) in overall craving frequency (from 0 = no craving at all, to 10 = constantly craving the substance), on overall emotional distress (from 0 = none to 24 = severe) of the Hospital Anxiety and Depression Scale (HADS), and on overall quality of life of the World Health Organization Quality of Life-BREF (WHOQOL-BREF) scale (from 1 = very poor, to 5 = very good quality of life). ***$p <$ .001 (two-tailed) for all effects, significance at Bonferroni-corrected α of .00625.

6.5. Discussion

This naturalistic study investigated short-term therapeutic effects of an alternative SUD treatment which applies a therapeutic protocol combining traditional Amazonian medicine and contemporary psychotherapy. We found significant improvements after treatment for nearly all outcomes, including the severity of addiction symptoms (drug use, alcohol use, psychiatric status, social/familial relationships), substance craving, emotional distress (anxiety and depressive symptoms), as well as overall quality of life, with large effect sizes. An exception was the somatic medical status of the addiction severity index, which did not significantly change in response to treatment.

Overall, and in accordance with our hypotheses, these results suggest that the long-term, integrative treatment delivered at this center was associated with beneficial changes in key symptoms of substance dependence. Our results reflect short-term outcomes in relation to the end of the treatment, but medium-term effects with regard to T1 measurement. Our findings are in line with observations by the WHO and others suggesting indigenous medicines to be promising for SUD treatment (Bill et al., 1993; Lu et al., 2009) and with studies reporting positive effects of ayahuasca for SUD (cf. Labate & Cavnar, 2014; Nunes et al., 2016). Several large-scale cross-sectional surveys report associations between reduced substance use and ayahuasca applied in varying contexts (Barbosa et al., 2018; Lawn et al., 2017). A small pilot study on patients attending biweekly ayahuasca sessions over 3-9 months in Brazil observed amelioration of psychological factors related to drug dependence (Fernández et al., 2014). Similarly, an observational study reported improvements of problematic substance use indicators in a Canadian aboriginal sample after a brief retreat involving ayahuasca (Thomas et al., 2013). Other studies explore applications in the context of specific SUDs, for instance crack cocaine dependence (Cruz & Nappo, 2018). The Takiwasi treatment, however, consists of a complex blend of methods from traditional

Amazonian medicine not limited to ayahuasca, as well as methods from psychotherapy. The associations found in this study may hence not be specifically related to one plant, but should be interpreted in light of the intricacies of the overall treatment.

The sample's high prevalence of comorbid affective and anxiety disorders as well as antisocial personality disorder replicates large-scale cross-national findings of SUD patients' most common comorbid psychiatric disorders in general (Merikangas et al., 1998). As our findings demonstrate, in addition to improved SUD-specific symptoms such as urge for consumption, the Takiwasi treatment was also associated with improvements in anxiety and affective states. One potential mechanism within the overall treatment explaining these changes could be the ceremonial usage of ayahuasca. Several studies report antidepressant effects in this context, including a first randomized placebo-controlled trial with clinically depressed patients (Osorio Fde et al., 2015; Palhano-Fontes et al., 2018; Sanches et al., 2016). Studies also report anxiolytic effects of ayahuasca, but evidence is less conclusive (Coe & McKenna, 2017; dos Santos, Osório, Crippa, & Hallak, 2016; Santos et al., 2007). Further, a recent study found improvement of emotion dysregulation in a sample with borderline personality traits (Domínguez-Clavé et al., 2018). However, mechanisms other than ayahuasca, such as the Amazonian plants and techniques applied in the scope of dietary retreats and purging rituals, may also support the beneficial changes we found. Indeed, indications from ethnobotanical studies point to other Amazonian plant medicines with relevance for psychological well-being (Sanz-Biset & Canigueral, 2011, 2013; Shepard, 1998). Further, there are early indications for peak experiences, such as the ones that may arise in Amerindian plant ceremonies, to be associated with lasting structural changes, including shifts in personality traits (MacLean, Johnson, & Griffiths, 2011). Such changes could be reflected also on a neurobiological level, which could be especially relevant in relation to the aforementioned long-term cerebral adaptations typically observed in SUD patients' brains (Koob & Volkow, 2010). Indeed, current neuropharmacological research

describes evidence for certain alkaloids of the ayahuasca brew to play a role in neuroregeneration (Frecska, Bokor, & Winkelman, 2016) and hypothesize ayahuasca to facilitate neural architectural changes in the cerebral reward system (Prickett & Liester, 2014). Given the complexity and integrative nature of this treatment, individual contributions of the various therapeutic constituents may not be mapped on the basis of our study. Carefully designed randomized placebo-controlled studies could provide complementary information about therapeutic effects of specific methods within this multifaceted integrative treatment.

The lack of significant change we found in the medical composite scores may suggest that the Takiwasi treatment impacts specific psychosocial and consumption-related factors, but does not significantly improve the general somatic health of patients. A large-scale study that compared ASI scores of a general health insurance membership sample (N = 9,398) with a clinical sample of insurers with SUD (N = 327) reports that, while differences for the other ASI areas were striking, the medical composite scores showed similarity, with the clinical sample's score being only slightly higher (Weisner et al., 2000). That this measure did not differentiate markedly between clinical and general population in a large-scale between-subject design may imply that the medical base rate of SUD patients may be relatively high on a population level and/or that a more elaborate instrument with increased sensitivity would be required to understand the nature of differences in this context.

The finding that there were no individuals in the pre-contemplation stage may be attributed to the Takiwasi admission procedure. Since the Takiwasi treatment demands patients' engagement over a lengthy period of time, it may not be suited for individuals with very low change readiness, which, in turn, may have implications for the transferability of this approach to other settings (where clients in the pre-contemplative stage may not be filtered out).

Dropout in our sample was at a similar level as the generally reported average rate for psychosocial SUD interventions found in a meta-analytic review (35.4%; Dutra et al., 2008). Participants who dropped out of treatment did not significantly differ from completers in any of the tested clinical and socio-demographic measures with the exception that North Americans abandoned treatment more frequently than expected, which may imply a lesser cultural fit of this treatment for people from these geographical regions. However, while it is plausible that specific cultural aspects may have played a role in the increased dropout among North Americans, the number of such participants in the overall sample was small (n = 3). This finding could therefore also reflect a sample bias and should be interpreted with caution. A possible reason for why the increased dropout was observed for North American, but not for European participants, might relate to a higher degree of familiarity of Europeans with the micro-cultural climate at this center, which is influenced by its European founder and the Hispanic context of Peru. Future studies should aim to further explore the patients' cultural profiles in relation to the cultural characteristics of this treatment program and its staff.

This study has a number of limitations. Treatment outcomes were assessed in a naturalistic setting without a comparison group, and outcomes were available only for treatment completers. This design does not allow causal interpretation and limits generalisability. We measured outcomes only in the short-term, and sample size was relatively small. The lack of outcome assessment upon participants' return presents a limitation in that the Takiwasi treatment entailed a prolonged period away from a context likely to have been critical in the perpetuation of the pathological substance use. Furthermore, participants were heterogeneous with several comorbidities, however, this is generally representative of substance dependent individuals in residential treatment settings (Chen et al., 2011; Merikangas et al., 1998; Weisner et al., 2000).

In sum, our findings are preliminary, but indicate multiple positive outcomes and suggest the need for further investigation of this treatment approach. Future studies may build on our findings and extend them to the long-term. Whilst the naturalistic research design inevitably had costs, it also had the advantage of capturing synergistic effects arising from the interplay between the various treatment methods, which is considered especially relevant for traditional medical systems (Fønnebø et al., 2007). The loss of synergistic effects is indeed one of the main reasons why, for traditional medicines research, comprehensive paradigms (i.e., whole systems research) are generally preferred to designs that study the various components individually and isolated from the rest of the medical system (Verhoef et al., 2005; World Health Organization, 2000). This is to our knowledge the first study empirically assessing the therapeutic effects of this accredited Amazonian medicine-based addiction treatment program, generating novel findings in a field where improved therapeutic means are considered a need on a global level. Our results may aid the development of enhanced SUD therapies combining western treatments with traditional medicines and, in the long-term, open new treatment avenues.

Acknowledgements

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7. General discussion

The primary goal of this work was to investigate therapeutic potentials of traditional Amazonian medicine for SUD as applied at an integrative addiction treatment center in Peru. For this purpose, three empirical studies were conducted using a multimodal, cross-disciplinary framework. Taken together, our results point to a promising alternative treatment approach to SUD that deserves further scientific attention. Findings from this study contribute to the increasing body of literature on novel SUD treatments and to the emergent field of research on traditional Amazonian medicine, so far mainly focusing on the usage of ayahuasca. In what follows, the main results of each empirical study will be summarized and subsequently discussed. The limitations of the current work will then be outlined, followed by an outlook, and, finally, some concluding remarks.

7.1. Summary of findings

7.1.1. Main results of Study 1 – Conceptions and practices of an integrative treatment for substance use disorders involving Amazonian medicine: Traditional healers' perspectives

This study aimed to investigate illness and treatment concepts from traditional Amazonian medicine adapted to SUD, to identify the main Amazonian method for SUD treatment, and to relate findings with Western scientific concepts. Interviews with 13 expert practitioners of Amazonian medicine revealed a multilayered understanding and treatment approach of SUD. Factors relating to disease etiology that were mentioned included biological, psychosocial, sociocultural, and spiritual-energetic aspects, a list that, with the exception of the last factor, bears resemblance to current academic scientific views postulating a biopsychosocial framework (Küfner & Metzner, 2011; Lindenmeyer, 2011; Martin-Soelch, 2010, 2013). With reference to Amazonian therapies, the analysis revealed a

range of methods for SUDs, which may be broadly grouped into (1) purging rituals with emetic plants, (2) dietary retreats with teacher plants, and (3) healing ceremonies with teacher plants. The Amazonian therapeutic means differ markedly from conventional psychiatric ones and call for further scientific study. The experts emphasized the integral nature of Amazonian medicine, which made it difficult to point out a mainly important method for SUD. The efficacy of Amazonian medicine was explained to lie in the combined, complexly interwoven usage of medicinal plants and ritual techniques.

7.1.2. Main results of Study 2 – Who turns to Amazonian medicine for treatment of substance use disorder? Patient characteristics at the Takiwasi Addiction Treatment Center

The goal of this study was to investigate sociodemographic and clinical features of treatment-seeking individuals admitted to the Takiwasi addiction therapy. Results showed that most Takiwasi patients were young or middle-aged, unmarried males living with their relatives in urban regions. Almost half of participants were Peruvian, over a third came from other Latin American countries, and about a quarter from Europe or North America. In line with current global statistics on substance use (Gowing et al., 2015), cannabis and alcohol were the most prevalently used substances. Anxiety and mood disorders were common comorbid psychopathologies, as is characteristic of other SUD patients (Merikangas et al., 1998). Addiction severity in the Takiwasi sample was elevated compared to norms from SUD patients entering conventional treatment (Weisner et al., 2000) on several indicators, and quality of life and spiritual well-being were significantly lower compared with other treatment-seeking psychiatric patients (Bufford et al., 1991; Skevington & McCrate, 2012). The motives for which individuals decided to initiate treatment included familial motives, self-transformation, mental health, spiritual and existential motives, striving for life satisfaction, community relationships and society, quitting drugs and addictions, professional

and educational goals, physical health, and finding one's identity. Motivational factors with regard to why this particular treatment was selected related to its traditional medicine component, the Takiwasi concept overall, information or recommendation by others, unfavorable prior treatment experiences, confidence in Takiwasi, spiritual aspects, and personal preferences and interests.

7.1.3. Main results of Study 3 – Short-term treatment effects of a substance use disorder therapy involving traditional Amazonian medicine

The aim of this study was to explore short-term treatment effects of the overall Takiwasi therapy, consisting of a combined SUD treatment protocol involving conventional and alternative therapies. Of the initial sample (n = 53), about one-third abandoned treatment prematurely, a rate comparable to conventional psychosocial SUD therapies. For treatment completers (n = 36) we found significant improvements of addiction severity from baseline assessment (T1) to treatment completion (T2) on the ASI composite scores of drug use, alcohol use, social/familial relationships, and psychiatric status. Overall substance craving decreased significantly from T1 to T2, as did overall emotional distress (i.e., anxiety and depression symptoms combined), and quality of life increased significantly from T1 to T2. Taken together, the results point to a substantial improvement of key symptomatic features of SUD after completing the treatment.

7.2. Discussion of findings

The empirical studies conducted in the scope of this work were designed to address three main research questions, namely: *(1) How is SUD understood in traditional Amazonian medicine and what are the methods for its treatment; (2) Who are the treatment-seeking individuals that select this alternative SUD therapy based on traditional Amazonian medicine; and (3) What are the short-term therapeutic effects of the integrative SUD*

treatment. Since the empirical studies could identify relevant concepts underlying the treatment and indeed found a reduction of symptoms in response to the treatment, findings from this investigation support the central research hypothesis stated at the outset of this work.

Study 1 addressed the first research question on a conceptual level. The Amazonian understanding regarding SUD etiology was somewhat overlapping with conventional scientific views, but Amazonian treatment concepts were unlike Western ones. Of particular interest in this context was the finding underscoring the integral application of Amazonian methods. This is in line with the observation that holism is a distinctive feature of traditional medicines across systems (WHO, 2000) and parallels accounts of practitioners from different traditional medicines, who explain that dissecting their treatments into components will cause essential aspects to be lost (WHO, 2003; Fønnebø et al., 2007). This may have important implications for research, specifically relevant also for ongoing ayahuasca research, which often examines the effects of this medicine apart from the rest of the Amazonian medical system. Based on our results, rather than studying ayahuasca in isolation, such studies should be conducted within an overall traditional Amazonian medical framework. This also matches general methodological strategies for traditional medicines research, which advise against disassembling and/or focusing on purported active ingredients, but rather allow the system to function as it is practiced in clinical reality (Verhoef et al., 2005). This also entails the involvement of competent traditional medical practitioners as part of both the intervention and the study, practitioners who can diagnose and prescribe the range of Amazonian treatments (not only ayahuasca) in a personalized manner, according to what they consider the indicated treatment per clinical case.

Somewhat relatedly, results from Study 1 also highlight the significance of the ritual component and rules and restrictions of Amazonian treatments. The experts describe these

aspects to be pivotal for both safety and efficacy of treatment in the context of all the types of interventions they described. This suggests research to focus on these ritual processes and rules, but also suggests to include them as part of the intervention when investigating Amazonian medicines (including ayahuasca), in order to avoid underestimating effects, at best, and causing harm to participants, at worst. Our results based on the experts' reports thus suggest that prematurely discarding the ritual component of Amazonian treatments, which is intrinsic to this medicinal system, runs the risk of throwing out the baby with the bath water. Indeed, research has long warned against the "rationalization" or "biomedicalization" of traditional medicines, a process likely to occur as the local traditions become more globalized (Janes, 1999; Pedersen & Baruffati, 1985). It has been stated that such a process is prone to reduce health-related wisdom of great antiquity into "narrow herbal traditions and a loss of those elements of diagnosis and therapy which may be the most valuable and effective" (Janes, 1999, p. 1803). Our findings are also in line with the observation made by the WHO (2000) that successful treatments in traditional medicines are often the result of herbal medicines and "traditional procedure-based therapies" acting synergistically, and not of the herbs alone. If in the case of Amazonian medicine, not only effectiveness, but also patients safety is at stake, establishing an understanding of these aspects should be a priority for future research, given also the rapidly increasing popularity of ayahuasca worldwide.

Studies 2 and 3 then explored a different angle, namely the perspective of patients undergoing the treatment themselves, in order to respond to the second and third research questions aimed to understand who the patients are that seek out this therapy and what its short-term outcomes are. Standing out amongst findings from Study 2 were particularly the treatment-seekers' relatively higher levels of impairment in terms of drug and alcohol use, psychiatric status, as well as their relatively lower quality of life and spiritual well-being compared to norms from other psychiatric patients. This could mean that this kind of treatment program is particularly attractive for more severely, and perhaps also more

chronically impacted addiction patients. It is also possible that such individuals turn to this type of alternative treatment as a last resort strategy after failed prior treatments. And indeed, nearly a third of Study 2 participants reported having had unfavorable previous treatment experiences as one of their main motivations for treatment initiation at Takiwasi. Another noteworthy finding was the saliency of traditional medicine as a reason for selecting this particular treatment, suggesting an existing interest or perhaps demand for traditional medicine-based therapies among SUD treatment-seekers. Taken together, these findings suggest future research to further examine SUD treatments based on traditional medicines such as the Amazonian approach, and to test if such treatments are indeed specifically suited to the needs of highly impaired SUD patients or if more severely impaired SUD patients respond particularly well to this kind of treatment.

The results from Study 3 then provided a first indication as to the short-term therapeutic effects of this treatment. We found highly significant post-treatment improvements for several key symptoms of SUDs, which is strongly suggestive of short-term benefits of the Takiwasi treatment. Yet, due to the naturalistic design and lack of control, these results are preliminary and need to be confirmed in further studies. Examining effects in a naturalistic setting was an important and necessary evaluative step for early stage research, and had the advantage of introducing only minimal distortion to the intervention (less than for instance trials that require blinding or randomization), thus assures a high representativeness of the clinical practice examined (Walach, Falkenberg, Fonnebo, Lewith, & Jonas, 2006). In the same way, additional studies are needed with regard to the increased dropout rate found for North American patients, and it remains to be seen if it is the case also in a larger sample with a more substantial portion of North American participants. The role of cultural parameters should be addressed by future research especially in view of potential application of Amazonian treatments in other cultural contexts, and. Overall, the findings from Study 3 present strong arguments in favor of further scientific investigation of this treatment.

Finally, the question of the significance of spirituality emerged as a relevant topic across studies. The patients, on the one hand, mentioned spiritual problems and spiritual seeking as reasons motivating them to enroll in the Takiwasi treatment. Moreover, their self-reported spiritual well-being was found to be low compared to other psychiatric patients (Bufford et al., 1991). At the same time, the experts described spiritual aspects to play a crucial role in the etiology and treatment of SUD from the Amazonian perspective. Overall, our data thus suggest that (a) there is a spiritual dimension to the Takiwasi treatment, and (b) spirituality is relevant for the types of patients that choose to get treated at Takiwasi. The latter is particularly interesting also given that we found Takiwasi patients to be of fairly heterogeneous cultural backgrounds, a feature that undoubtedly accounts for distinctive world views and experiences of the treatment. In consideration of this heterogeneity, it would be useful to obtain qualitative data on patients' subjective treatment experiences, such that we could compare specifically how the treatment's spiritual aspects are conceived of and responded to by patients from different cultural backgrounds. Taken together, our findings with regard to the relevance of spirituality are consistent with the worldwide popularity of the spiritually oriented Alcoholics Anonymous or twelve-step facilitation treatments (Kelly, 2016), and in line with research literature showing a relationship between addiction and spirituality (Miller, 1998). On the basis of this link, some authors have proposed to expand the biopsychosocial model of addiction to a biopsychosocio-*spiritual* one (Leukefeld & Leukefeld, 1999). Our findings are also congruent with sociocultural etiology models that explain SUDs in terms of alienation from and loss of connection with society (Elliott et al., 1982). A hypothetical link has been proposed between the international rise in substance use over the last centuries, and an observed disorientation in a rapidly changing, increasingly globalized, and highly complex modern society, which has developed in parallel to a disintegration of more traditional societies and cultures (Heggenhougen, 1984). Should there indeed be a link, then promise may be expected from therapies that assist individuals to

reconnect with their surrounding social and natural world, and which facilitate spiritual contemplation (i.e., a questioning with regard to the transcendent or transpersonal; Miller, 1998), such as the one examined in this work.

7.3. Limitations

Beyond the specific limitations per study that have been outlined in the respective chapters, a number of general limitations are notable from the current work.

First, the main limitation of this investigation was arguably the naturalistic, single-group design in the two studies that were based on patient samples. This design limited our ability to control confounding variables (such as comorbid psychopathology or treatment motivation) or to discern spontaneous recovery from specific treatment effects. It thus allowed only preliminary conclusions that need confirmation from further studies. The chosen design also did not enable us to distinguish relative contributions of the different medicines or methods applied in the Takiwasi treatment. However, this is an inevitable cost of investigating a healthcare system (so called *whole systems research* in traditional medicine research; Verhoef et al., 2005) and conversely has the advantage of capturing also synergistic effects of the interplay of constituents, which are particularly relevant for alternative medicines. The design we used is also in line with the proposition of the WHO (2000) to use a *black-box* paradigm for early stage clinical research of traditional medicines, that is, a design that studies a "treatment package" in terms of its effects, without necessarily studying the contents of the package.

A second limitation of this work consisted in the lack of follow-up measures in Study 3, which assessed effects only at the time of treatment completion, and thus did not allow conclusions as to the mid- and long-term benefit of the therapy. This will be a crucial next step for assessing the treatment's general therapeutic potential, and future studies should

assess the evolution of treatment responses over time by repeating the outcome measurement at medium and long-term intervals post treatment.

Third, the relatively small number of participants across studies limited our capacity to perform analyses that required splitting participants into subgroups. This would have been valuable given the heterogeneity of the samples, particularly in view of the diversity regarding cultural background, which characterized both the patients and the practitioners samples. Moreover, in case of Study 3, the loss of participants due to treatment drop-out further reduced the sample size for post-treatment measures. This however is a common phenomenon in clinical studies and the rate of dropout was comparable to the one reported in a meta-analytic review for similar studies with SUD patients (Dutra et al., 2008).

Fourth, since the Takiwasi patients decided to enroll in the treatment on the basis of self-selection, we cannot rule out the possibility of a selection bias in the samples, which may have influenced both Study 2 and Study 3 results.

Fifth, the patients samples were based on males only, which limited the generalisability of our results to the general population of SUD patients and we do not know if this treatment would show similar effects for female SUD patients. There were other specificities in the patients samples that may have compromised generalisability, such as the aforementioned cultural heterogeneity and comorbidities.

Sixth, we unwillingly introduced a methodological bias to Study 1 by encouraging participants to select a main treatment method despite their prevailing view that all methods were equally important, stressing that Amazonian medicine was an integral system whose efficaciousness requires the balanced use of all its methods.

Finally, the practitioners that were the informants of the qualitative study were subjected to a significant degree of Western influence due to personal background, the cross-

cultural context of the Takiwasi Center, and the more general phenomenon of hybridization of Amazonian medicine. We therefore stress again as a caveat that the results reported in the current work correspond to Amazonian medicine in an adapted form specifically aligned to SUD treatment at the Takiwasi Center, and may not be generalized to represent traditional Amazonian medicine in a broader sense.

7.4. Outlook

Departing from the findings of the present work, we identify two parallel lines of research which ought to be followed in order to further elucidate traditional Amazonian medicine-based treatments for SUD such as the one delivered at the Takiwasi Center.

Most critical at this stage is arguably to conduct further basic qualitative research, working towards a more comprehensive and in-depth conceptual understanding regarding the Amazonian treatment approach. This is in line with general recommendations from methodological research in complementary or traditional medicines, which consider a thorough philosophical understanding of the medical paradigm in question to be essential and prerequisite for randomized controlled trials (Carter, 2003; Verhoef et al., 2005; WHO, 2000). In our context, future research should involve in-depth interviews with qualified traditional healers, focusing on each of the Amazonian interventions identified in the current investigation, as well as their systemic, interrelated application. This entails a careful description of each therapeutic technique (plant as well as ritual component), clinical indications, counter-indications, necessary rules and restrictions for safety and efficacy, common effects and desired outcomes, adverse effects and risks, as well as hypothesized mechanisms of action. Although valuable ethnobotanical taxonomies of plant medicines from Peru have been complied (e.g., Bussmann & Sharon, 2006, 2009; Jauregui et al., 2011; Sanz-Biset et al., 2009; Sanz-Biset & Canigueral, 2011, 2013), we also need studies that describe

the therapeutic methodology around the plants applied for mental health, using a clinical psychological perspective and a focus on procedural, functional, and systemic aspects of clinical application. In addition, a narrative research approach documenting individual cases from both practitioner and patient perspectives could significantly enhance the emerging scientific understanding of Amazonian treatment methods.

A second line of research should continue to examine treatment effects quantitatively. Since the current findings underscored the importance of an integrated paradigm, we would advise future studies to begin by further examining the Takiwasi treatment or other such therapies as a whole and avoid studying elemental treatment components in isolation at present, and this is precisely what general research methodologies for alternative medicines recommend as well (Fønnebø et al., 2007):

> [...] many CAM [complementary and alternative medicine] therapists hold that CAM treatments cannot be split up into parts that can be investigated separately. They argue that the total effect adds up to more than the sum of its parts [....] If CAM is to be evaluated comprehensively, one needs to extend the research focus to all aspects of the treatment approach. To study only the specific effect of needling in acupuncture isolated from other interventions initiated by the acupuncturist, or the effect of a single, isolated homeopathic remedy separated from other aspects of homeopathic practice, is to neglect other potentially important components of these interventions. (p. 3)

Caution is therefore warranted for the one-to-one transfer of analytic research designs from the conventional health sciences, as they may not necessarily be in line with the functioning of the medical system under study and potentially mask existing effects (Carter, 2003). Ideally, qualitative data generated in the proposed first line of research may feed into

the definition of adequate study parameters, methodologies, and designs for this second line of research. The results of this quantitative line of research in turn may sensibly inform and triangulate the former (Walach et al., 2006). Some researchers even advise that before efficacy of traditional medicines be assessed, epistemological data on the efficacy concept itself should be collected, in order to understand from the perspective of a practitioner (that is, from within the medical system) in which cases a treatment is considered successful, thereby avoiding ethnocentric biases in the operationalization of this concept (Waldram, 2000).

Carefully designed outcome studies should aim to examine therapeutic effects of the Takiwasi approach and other Amazonian treatments after short-, mid-, and long-term follow-up intervals and expand the test battery used in the current work with relevant measures. Furthermore, future studies of the Takiwasi treatment should aim to include control conditions; a waitlist group could be the most feasible next step for this purpose. However, the design ought to be checked against and adapted to specific methodology guidelines for traditional medicines research (Walach et al., 2006; World Health Organization, 2000) and, if appropriate, further comparison groups (like matched subjects undergoing conventional treatment or well-designed placebo-controlled studies) be added further along. To include experienced traditional healers as part of the research team and already in the conceptual phase (WHO,2000) seems an exceptionally sensible strategy, also for determining which study designs are suitable at what stage.

Furthermore, future studies should endeavor to address specific questions that emerged from the current work and test corresponding hypotheses. Using larger sample sizes and longer time frames, such studies should test if this kind of treatment is indeed particularly well-suited for more severely impaired SUD patients and should clarify the role of patients' nationality and cultural background for treatment retention and success. The latter is critical as well for the assessment of the transferability of these methods to other cultural contexts.

Similarly, further research is needed in order to know if the effects we found are replicable in mixed gender samples.

Finally, on the basis of our finding, we would propose as a transversal topic for both lines of research to further examine how spiritual aspects or "spiritual-energetic" factors are understood in the Amazonian medical framework and the role these aspects play in Amazonian medicine in general and for SUD treatment in particular.

7.5. Conclusions

Given the characteristic long-term treatment responses and high relapse rates of SUDs on the one hand (Brandon et al., 2007; Brownell et al., 1986; O'Brien & McLellan, 1996), and the identified necessity for broadened care provision models which account for the chronic nature of SUDs on the other hand (McLellan et al., 2000; O'Brien & McLellan, 1996; White et al., 2002), developing and studying novel SUD therapies such as the one examined in this work is essential and is a highly topical field (Kiluk & Carroll, 2013; Lu et al., 2009; Witkiewitz & Bowen, 2010). The current work offers a substantial contribution to this field by reporting first empirical data on treatment effects and concepts of a compelling alternative SUD therapy based on Amazonian medicine.

The relevance of this work is further given with reference to the worldwide SUD treatment gap (UNODC, 2016): due to insufficient access and low affordability, SUD therapies are markedly underprovided on a global scale. Yet, rich resources from traditional medicines are readily available (Ong, Bodeker, Grundy, Burford, & Shein, 2005), generally low in cost, and, in large parts of the world, this is the kind of treatment that most of the population can and does access (Bill et al., 1993; Bodeker, 2001). Traditional medicine-based SUD treatments may therefore hold a tremendous potential for reducing the worldwide gap in

addiction treatment, provided research findings such as the ones reported here continue to confirm their benefit for recovery.

In their traditional medicines strategy report for the forthcoming years, the WHO (2013) maintained that "the predicted increase in the global burden of chronic diseases [...] is the most urgent reason for developing and strengthening collaboration between conventional and traditional/complementary sectors" (p. 40). As a chronically relapsing disease (Koob & Volkow, 2010), SUD clearly falls into this category and may be expected to similarly benefit from an integrative treatment strategy. The collaborative practice of the Takiwasi Center is a rare case already implementing this call for medical integration from the WHO: Health professionals from both sectors have been collaborating at this center for 25 years aiming to combine efficacious methods from different medical systems into one overall treatment. Although the present work did not focus on the Takiwasi Center's collaborative aspects specifically, it recognized this setting as an exceptional opportunity for clinical scientific research, which is one of the strengths of the current work. The implementation of a multimodal and cross-disciplinary clinical research framework specifically adapted to this setting represents a further strength of this investigation. An additional advantage of this work lies in its simultaneously addressing highly relevant basic and applied research questions. Traditional medicines are not simply a new or unfamiliar collection of treatments that need to be tested for their efficacy, but involve fundamentally different ways of thinking about health, illness, and treatment (Fønnebø et al., 2007; Kleinman, 1978; WHO, 2000). Medical systems like the Amazonian one include sophisticated epistemologies of body, mind, and their relationship to family, community, and the natural world (Janes, 1999). Scientific research of such medicines may thus lead to a cross-culturally more valid, and ultimately, scientifically more accurate understanding of these fundamental concepts and processes. Findings from the current work add a valuable contribution to this type of cross-cultural, basic health research, while at the same time offering first indications as to the clinical applicability of these

concepts. The present work may in the long-term help open new treatment avenues for health problems that concern contemporary society on a global level, such as SUD.

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