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Constructing drug effects: A history of set and setting

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Abstract

Set and setting is a term which refers to the psychological, social, and cultural parameters which shape the response to psychedelic drugs. The concept is considered fundamental to psychedelic research and has also been used to describe nonpharmacological factors which shape the effects of other agents such as alcohol, heroin, amphetamines, or cocaine. This paper reviews the history and evolution of the concept of set and setting from the 19th-century Parisian Club des Hashischins, through to 1950s psychotomimetic research on nondrug determinants of psychopharmacology, the use of extra-drug techniques by psychedelic therapists of the 1950s, and the invention of the concept of set and setting by Leary. Later developments and expansions on the concept of set and setting are discussed, and the term of collective set and setting is suggested as a theoretical tool to describe the social forces which shape individual set and setting situations. The concept of set and setting, it is argued, is crucial not only for psychedelic research but also for advancing drug research and developing more effective drug policy.

Keywords

drug policy, hallucinogens, non-drug factors, psychedelics, psychopharmacology, set and setting

Introduction

To what extent are the effects of psychoactive drugs fixed and predictable, and to what extent are they a construction produced by society and culture? The question of "nondrug parameters of psychopharmacology," as it was sometimes called in the 1960s (Feldman, 1963), has been debated extensively over the past century, yet it has still not been answered in full. We know about the significant role played by the placebo effect (Brown, 2012; Moerman, 2002), and we know that the effects of drugs can vary significantly between users across societies, cultures, and subcultures (Wallace, 1959), yet we are still lacking a solid working theory as to how and why that happens.

In a world which is growing increasingly skeptical of a long and failed war on drugs, and which is seeking alternatives in decriminalization, legalization, and a host of other approaches to drug reform (Boggs, 2015; Golub et al., 2015; Hari, 2015), the question of extra-pharmacological variables is becoming increasingly urgent. Studying the ways in which drug effects are shaped by social and cultural parameters is essential to developing effective strategies for harm reduction, and a more effective drug policy which would reduce drug harms and allow the emergence of more beneficial patterns of drug use.

A key concept in the field of drug research that offers a testable, applicable, and a potentially fruitful approach to studying the role of extra-pharmacological parameters on drug effects is the concept of *set and setting*, which emerged within the field of 1960s psychedelic[1] drug research and has since become accepted both within the drug research community as well as in extra-academic discourse.

The set and setting hypothesis basically holds that the effects of psychedelic drugs are dependent first and foremost upon set (personality, preparation, expectation, and intention of the person having the experience) and setting (the physical, social, and cultural environment in which the experience takes place)

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(Hartogsohn, 2015). While the concept of set and setting was born out of psychedelic research, and though it seems to be of special applicability in that domain, it has also been proven useful for researchers who have studied the effects of various stimulants, depressants, and antipsychotics such as alcohol, heroin, methylphenidate (Ritalin), methamphetamine, cocaine, and crack cocaine (Cohen, 1990; Ditman et al., 1969; Dwyer and Moore, 2013; Hart, 2013; Zinberg, 1984). In actuality, current research suggests that nonpharmacological effects are responsible for a major part, if not a majority, of therapeutic benefits in a variety of accepted drug treatments (Brown, 2012; Kirsch and Sapirstein, 1998; Moerman, 2002).

Issues of set and setting play an important role in both popular and scholarly accounts of mid-20th-century psychedelic research, part of an extended discussion which has been going on since the 1960s about why experimental results varied so wildly at the time (Dyck, 2008; Lattin, 2011; Lee and Shlain, 1992). Indeed, Langlitz's *Neuropsychedelia*, the most comprehensive investigation of the current wave of psychedelic research, points to the fact that set and setting continues to complicate and shape investigations in the field even today (Langlitz, 2012). In a time when psychedelic research is being resumed and performed in an increasing variety of set and setting conditions such as psychotherapy research (Griffiths et al., 2006), psychotomimetic research (Vollenweider et al., 1998), and MRI research (Carhart-Harris et al., 2011), the issue merits further consideration and thorough integration into the discussion. This paper wishes to contribute to the discourse on the ways in which set and setting shaped hallucinogenic research in the past, and the ways in which they continue to do so today.

Set and setting, it is important to note, is critical not only to experimental results obtained in labs but also to the ways drug experiences play out in the field. Indeed, if one lends an ear to what drug users themselves have to say, the ubiquity of issues of set and setting within their discourse points to the matter being much more than a mere academic pursuit. Drug users are often surprisingly occupied with considerations of set and setting and credit such conditions both for negative as well as safe and positive drug experiences (McElrath and McEvoy, 2002; Shewan et al., 2000). Thus, studying set and setting and educating citizens about their importance seems essential to the success of any drug education program working both within the framework supplied by current drug policies as well as in a potential post-prohibition age.

Yet despite its popularity and applicability, the concept of set and setting has never been integrated into the study of psychopharmacology. Integrating variables of set and setting into clinical drug research would entail great complications for a pharmaceutical industry bent on randomized controlled trials (RCTs) and with limited patience for injecting fuzzy social and cultural elements into its considerations. This is lamentable because a better understanding of set and setting can often serve to reduce drug harm and increase potential drug benefit more efficiently than seeking new molecules or banning drugs altogether. In a pharmaceutical culture set on developing magic bullets and eliminating extra-drug parameters from drug research, set and setting serves as a reminder that extra-drug parameters cannot be eliminated from actual drug use, and point the way toward a more comprehensive conceptualization of drug effects.

Partly, this neglect might be due to the fact that the discourse on set and setting has remained largely underdeveloped over the years. The abandonment of the mid-20th clinical psychedelic research has, as a side effect, led to the marginalization of the concept of *set and setting*. The literature on drugs effects still lacks an account of the history and evolution of the concept of set and setting. Such an account would be valuable not just as a matter of historical curiosity, but because by tracing the genealogy of set and setting we can better understand it: how it evolved, how to make sense of it, and how it can be relevant for a variety of clinical and extra-clinical situations. Indeed, in a period when psychedelic research is reemerging and governments worldwide are considering drug policy reforms, such an account would seem timely and essential.

In this paper, I wish to present a preliminary history of the concept of set and setting and its evolution, as well as suggest some ways in which a better understanding of set and setting can prove useful to advancing current research as well as to reducing drug harms and fostering safer patterns of drug use.[2]

The origins of set and setting

The coining of the concept of set and setting is commonly credited to Timothy Leary, the controversial Harvard psychologist who played a crucial role in introducing psychedelics into the cultural discourse of 1960s America. According to Horowitz et al. (1988: 103) the term has first been published in a paper presented at the annual meeting of the American Psychological Association on 9 September 1961 (Leary, 1961).

Leary and his group would publish a number of formulations of the set and setting hypothesis during the 1960s decade (Leary et al., 1963, 1964; Metzner and Leary, 1967). While some of these early formulations differ in their emphases, together they make the claim that the set and setting is the most important determinant of the contents of psychedelic experiences. Set is understood as anything related to the internal state of

a person, including personality, preparation for the experience, intention, as well as "mood, expectations, fears, wishes" (Metzner and Leary, 1967: 5). Setting is understood as anything related to the environment in which the experience takes place, including the physical environment, the emotional/social environment, and finally the cultural environment—the ideas and beliefs which are prevalent in the society regarding drug effects and the world in general.

Although the term set and setting emerged in the 1960s, its roots go further back. The history of drug use provides us with constant reminders to the fact that drug effects were not always divorced from their social and cultural context. In fact, considerations of extra-drug variables have been an integral part of the use of psychotropics since the prehistory of medicine. Shamanic healing rituals are fundamentally a performance in which various elements are carefully brought together to enhance the purported healing process induced by a psychoactive (Beyer, 2010: Chapter 3; Helman, 2001: Chapter 1). Shamans apply elaborate schemes to amplify and control drug effects. They do this by manipulating set and setting through the use of icaros (ritual songs), whistles, smoke blowing, and sucking, as well as host of other indigenous techniques familiar to anthropologists and scholars of religion (Beyer, 2010; Dobkin de Rios, 1975; 1984). Such extra-drug manipulations are considered an essential part of the tribal healer's craft and testify to the level of his expertise and competence.

When Hashish, the first psychedelic to be reintroduced into Western society after an hiatus of over a thousand of years, was discovered by Parisian society, the principles of set and setting were quick to remerge. The arrival of this novel psychoactive, one might recall, attracted a number of the notable luminaries of 19th-century French literature. Figures such as Charles Baudelaire, Victor Hugo, Honoré de Balzac, and Alexander Dumas were all members of the Parisian Club des Hashischins, a bohemian club dedicated to pharmacologically assisted consciousness exploration (Abel, 1980: Chapter 8). The basic principles of set and setting can already be found in the writings of these 19th-century European drug explorers.

Psychiatrist Jean Joseph Moreau, an early champion of psychopharmacological self-experimentation and "the first psychiatrist with an interest in psychopharmacology" (Holmstad, 1973: XIX), was the one who supplied the drug to the curious literary club. In his writings, Moreau noted some of the principles which govern the effects of hashish, already foreshadowing many ideas which would later become part of the set and setting hypothesis. For example, he noted that identical doses of the drug can produce fundamentally different results and observed that the use of hashish requires the utmost care in the selection of surroundings since the user must "ward off anything that might turn their madness into depression or might arouse anything other than tender affectionate feelings" (Moreau, 1973: 5). The effects of Hashish, Moreau explained, were highly suggestible and malleable to external cues which include "everything that strikes his [the user's] eyes and his ears. A word, a gesture, a look, a sound or the slightest noise, by demanding his attention, will confer a special character on his illusions" (Moreau, 1973/1845: 79).

Moreau was not the only one to pay attention to the suggestible aspects of the hashish experience. Poet Charles Baudelaire also noted that the effect of hashish "varies widely, in line with the temperaments and nervous susceptibility of different individuals" and "even in a single individual" (Baudelaire, 1998: Locations 209–210). On some occasions, Baudelaire asserted, hashish will produce great immoderate elation, while at other times it will induce sleep. In order to ensure a positive reaction, he suggested that the user clears his schedules so that he should not be encumbered by obligations of any type. "Any grief, anxiety, or thoughts of duty that may call on your will and attention at certain moments will cut like a deathknell right through your intoxication, and poison all your pleasure" (Baudelaire, 1998: Locations 266–267). Nevertheless, the poet assured that the outcome of the experience would in all probability be positive if basic preconditions are observed, "if you find yourself in the right environment, such as a picturesque landscape or an apartment that has been decorated artistically, and if you can also hope for a little music" (Baudelaire, 1998: Locations 267–269).

A substantial part of what would later be considered integral to set and setting was already present in the writings of these 19th-century writers, specifically, the reference to elements such as preparation, state of mind, physical setting, and the use of music. Yet, for a good part of a century, the insights of these hashish eating French bohemians would generally be lost to drug researchers for all practical terms. When such insights did occur, they were usually limited to the extra-medical circles of anthropologists and drug enthusiasts. One such occasion was the late 1800s occult revival, which gave rise to some renewed literary-mystical experimentation with hashish, and led English occultist Aleister Crowley to write *The Psychology of Hashish* (2001/1907), which revisited some of Baudelaire's ideas about hashish and the dependency of its effects on personality, mood, and intention. Crowley was so fascinated by the idea that specific aspects of the varied effects of hashish could be isolated and produced using specific techniques, that he even prided himself on having "discovered the theory

and perfected the practice of the instrument'' which purportedly allowed him to choose at will out of the varied effects of hashish: from fantastic visions to sexual excitement and spiritual exaltation (Bennett et al., 1995: 253). Another example can be found in James Mooney's ethnographic report of the mescal ceremony (1896) which attributed the differences in the reactions of Indian and western imbibers of mescal to the influence of their respective cultures, and pointed out to the fact that much of the psychological effect was a product of ceremonial elements such as prayer, song, rattle, and the use of fire.

Medical investigations into extra-drug variables did take place during the first half of the 20th century. However, these tended to be more limited in their frame of reference and concentrate exclusively on the role of constitution and personality.One prominent example is Lewin's (1998/1924) ''toxic equation'' concept which addressed the ''greater or lesser sensibility of the body or its organs to the effects of various chemical substances'' (Lewin, 1998/1924: 8), leading to different reactions to the same substance and dose by different individuals. Lewin's *Nebenwirkungen* (1899) mentioned a number of parameters which might alter an individual's response to a drug, such as distinct biological constitutions, race, and climate. Still, Lewin's account left out such elements as preparation, expectation, intention, or social environment. Similarly, German mescaline researchers such as Walter Jaensch (1920), Alfred Storch (1922), and Kurt Beringer (1927) took interest in the dependency of mescaline effects on personality. In Beringer's case, this investigation was even driven by the hope to use mescaline reactions as a diagnostic tool for personality disorders, yet the attempt was eventually abandoned, for while Beringer did note a distinct variance in reactions to the drug, he was unable to draw any final conclusions on the relationship between personality and drug effects. And though Beringer casually mentions the shaping of the mescaline experience by the experimental conditions, and even the inevitable differences between the reaction to the drug upon first and second exposure, he too did not dedicate much attention to parameters other than constitution and personality. Similarly, 1930s and 1940s German research into Pervitin led to the realization that the drug's effects varied widely between patients and patient groups, but did not lead to conclusive inferences on how and why such differences emerged other than pointing to the possibility that different disease groups were marked by different biological constitutions leading to the differences in response, and labeling the question ''a multi-factor problem with a long list of unknowns'' (Flügel, 1941: 1288; Snelders and Pieters, 2011).

It is hardly surprising that the larger, more encompassing vision of the role extra-drug variables escaped those in the medical profession during those years. The idea of set and setting, after all, appears to run contrary to a basic principle of pharmacology, that drugs exert basically conform effects on their users (DeGrandpre, 2006). It would seem nonsensical to claim that a drug experience could differ fundamentally depending on the place in which the drug is taken or the people present. Yet this is exactly what the set and setting hypothesis asserts.

Though discarded and lost for almost a century, the insights of the members of the club des hashischins regarding the importance of extra-drug parameters would resurge in a crucial historical moment. In 1960, when Timothy Leary was just starting his research on psilocybin, he received a visit from English Author and psychedelic advocate Aldous Huxley, who presented him with an excerpt by Théophile Gautier, one of the original members of the club de Hashischins. The excerpt, taken from one of Gautier's essays on the hashish experience, stresses, similarly to Moreau and Baudelaire, the necessity of preparation and a ''tranquil frame of mind and body,'' predicting ''ineffable pleasure'' to those follow his advice but ''terror'' and ''suffering'' to those who disregard it (Leary, 1983: 42).

The ideas of the 19th-century Parisian club would prove influential for mid-20th-century hallucinogenic drug research in another crucial way, by popularizing the psychotomimetic hypothesis of hallucinogenic drug effects. Following his investigations on hashish, Moreau would publish *Hashish and Mental Illness* (1845). There he surmised that the effects of hashish mimic the symptoms of mental illness and suggested that it could be used to enable investigators to temporarily imitate the symptoms of mental illness and observe the roots of insanity. Distinguishing eight different mental phenomena common to both the hashish eater and the mentally ill, Moreau declared that ''there is not a single, elementary manifestation of mental illness that cannot be found in the mental changes caused by hashish'' (Moreau, 1973: 18) and suggested the drug as an invaluable tool which will revolutionize the study of mental illness. Moreau's ideas did not enjoy the reception he had hoped for. However, the idea that hallucinogenic agents—now LSD—could function as tools for the temporary induction of psychosis, returned to psychiatry a century later with the rise of a psychotomimetic Lysergic acid diethylamide (LSD) research.

Psychotomimetic investigations of extra-drug parameters

LSD research of the 1950s was dominated by the idea that the drug could be used to induce and study mental illness. By labeling LSD a psychotomimetic and

expecting a certain outcome from experiments, psychiatrists instigated the very responses they expected to find. Presupposing that patients become mentally ill under the effects of LSD, they were creating expectancies which fostered negative experiences and aggravated adverse effects. Other factors of set and setting were also liable to unleash a variety of adverse reactions. Many of the subjects who participated in research were hospitalized psychiatric patients who had little choice about partaking in experiments. Preparation for sessions was poor, often consisting of the casual suggestion that the patient will experience a few hours of madness following the ingestion of the drug, not a soothing notion, to say the least. The possibility of positive experiences or therapeutic benefits was not mentioned, and there was no therapeutic intention involved. Setting was equally bleak. Experiments habitually took place in the formal environment of hospital rooms lit by fluorescent lights. There was often no possibility to recline or get the rest which can be direly needed in some stages of hallucinogenic drug reaction, and patients were often subjected to endless batteries of psychological and physical tests. The social setting was composed of hospital psychiatrists who studied patients impersonally. After the experience, users were left without any peers with whom to share their experiences and without any framework with which to make sense of it. It is no wonder then, that experiences were overwhelmingly negative (Hartogsohn, 2015: Chapter 4). Psychotomimetic psychiatrists described hallucinogens as "essentially anxiety producing agents" (Hoch, 1957: 442) and insisted that no one who takes LSD wants to repeat the experience ever again (Abramson, 1960: 58).

And yet, as the 1950s progressed a growing number of publications were describing the LSD experience in radically different terms. Instead of the distorted perceptions and thought retardation described by psychotomimeticists, psychotherapeutically oriented LSD researchers were describing "cognitive enhancement" and "consciousness expansion." Rather than a drug whose effects mimic insanity, these researchers considered LSD a drug which could bring about "a new sanity" (Janiger, 1959: 258). By contrast to those who participated in psychotomimetic LSD research, participants in psychotherapeutically oriented LSD research asked to repeat the experience time and again (Abramson, 1960). The striking differences in the description of the effects of LSD can readily be explained by the striking differences in the set and setting which existed between the two schools of research. In psychotherapeutic, research subjects were often students and professionals who volunteered for the study. They often received a thorough preparation to the experience, expected positive and even life-transforming experiences, and arrived with therapeutic intention. The setting for such research was also considerably more benign: experiments often took place in comfortably furnished rooms, with sofas and pillows, and subjects were allowed to recline and listen to music with headphones. The social setting was supportive and often included friends with whom participants could later share their experiences, as well as a framework for the integration of the experience. Little wonder, considering the theory of set and setting, that such experiences turned out to have dramatically different outcomes than those instigated by psychotomimetic researchers. Yet by the end of the 1950s the great incongruency in results between the two main camps of hallucinogenic drug research was responsible for many misunderstandings and much argument. (e.g. Abramson, 1960).

As new reports about the therapeutic uses of LSD were arriving, psychotomimetic drug researchers were starting to look closer at possible extra-drug parameters which seemed to control the effects of the drugs. Might their results be shaped by the experimental environment were taking place?

Mid-20th-century literature on the topic of extra-pharmacological determinants of drug action includes papers by some of the era's leading psychotomimetic researchers. Louis Lasagna (1963) established a relation between personality and the response to hallucinogenic drugs, whereas Paul Feldman (1963) noted the essential role of the physician in determining the success of drug therapy. Dimascio and Rinkel (1963) considered a variety of parameters which might influence LSD effects and analyzed reactions to the drug according to two basic personality types: the athletic and the esthetic type. Dimascio and Klerman (1960) distinguished five variables which determine response to LSD including the subject, the research team, the physical environment, the social setting, and the relationship between subject and researcher. Max Rinkel, one of the earliest proponents of the psychotomimetic hypothesis, even served as a chairman for a symposium on "Specific and Non-specific Factors in Psychopharmacology," which was held as part of the of the Third World Congress of Psychiatry in 1961 and was later published as a book containing a number of essential contributions on the subject (Rinkel, 1963).

The most comprehensive research on the topic of extra-drug effects was conducted by Robert Hyde, a colleague of Rinkel in the Boston Psychopathic Hospital (Hyde, 1960). Hyde, who wanted to find out how the interaction with staff members might shape the LSD experience, studied the effects of the social milieu and study design over a period of three years, modulating the research setting year after year in an attempt to isolate the role of social and psychological factors. In the first year, conditions of stress and support, and

rigidity of design varied. In the second year, subjects were required to perform highly structured tasks and were treated impersonally as ''objects of study'' (Hyde, 1960: 302). The third year of the experiment allowed patients greater relaxation, more rapport, and human contact. The outcome showed a clear relationship between setting design and the results obtained: average symptom severity oscillated between 3.4 in the first year, 4.0 in the second, and 2.8 in the third. Hyde concluded that impersonal treatment and the necessity of performing structured tasks lead to intensified symptom severity, whereas support and freedom lessened it (Hyde, 1960).

Further experimentation showed that results also varied widely depending on whether subjects spent the time of their experience in a familiar environment or in strange and hostile situations in the ward. Subjects who had the experience in a group tended to show less ''sensory distortions'' and fewer ''thinking and speech disturbances'' than those who had a solitary experience (Hyde, 1960: 302). Tests and examination such as polygraph testing or being exhibited to a group of students for teaching purposes resulted in an intensification of negative symptoms in 88% of the patients, whereas an amelioration of symptoms was noted in 85% of the patients who were with members of a peer group, were not expected to produce anything, and were not questioned except in an casual, friendly fashion. In addition, a variety of personal data seemed to be of significance: younger subjects seemed to react ''more severely'' than older ones; single subjects ''more severely'' than married ones; and educated subjects ''less severely'' than those with a lower level of education. Members of the research group who were allowed to experiment with LSD in an environment to their choosing displayed the least incidence of schizophrenic-like reactions.

Elucidating these findings, Hyde concluded that a rigidity of research design characterized by unconcern for the subject as a person, impersonal, negative or investigative attitudes of others, and nonacceptance led to intensified negative response, whereas peer support, familiarity with surroundings, flexible research design, acceptance, and opportunity for expression led to significantly more favorable reactions. He ordered the dimensions of LSD response on a few basic dimensions which included ''rigidity-flexibility of goals; familiarity-unfamiliarity of environment; attitudes of acceptance-nonacceptance of the subject's behavior and feelings; and presence or absence of others with a common culture'' (Hyde, 1960: 306).

Psychotomimetic literature on extra-drug research stressed the importance of new elements which were absent from the reports of previous investigators, while disregarding some of the elements which were present in previous accounts. Specifically, the components of social setting, social interaction and the degree of freedom from tasks and examinations now received attention in studies on solitary versus group ingestion, different demographic groups, and the relationship between subject and researcher. By contrast, elements such as physical surrounding and preparation were now absent from the picture.

While the 1950s literature on the topic of extra-pharmacological determinants of drug action came primarily from psychotomimetic authors, it is interesting to note that these authors did not take the subject to its final conclusion and avoided reconsidering the universal validity of earlier research results with LSD in light of the evidence. The realization that many of the results of hallucinogenic research reflected external conditions more than some fixed effects of the drugs themselves would emerge only later, within psychotherapeutically oriented literature on hallucinogens.

Psychotherapeutic and socioanthropological investigations of nondrug variables

As psychotomimetic researchers began considering the possible import of nondrug parameters in shaping drug effects, pioneers within the nascent psychedelic therapy community of the 1950s were exploring the ways in which such nondrug variables could be used constructively in order to navigate and control the effects of hallucinogenic agents, to which they referred as psychedelics. One of these early pioneers who could probably be credited for being the first to attempt the creation of a therapeutic environment for the optimization of LSD effects was Alfred Matthew Hubbard, a colorful figure widely known as the ''Johnny Appleseed of LSD.'' A high level Office of Strategic Services officer, Hubbard was introduced to LSD in 1951 by British psychiatrist Ronald Sandison. Soon he was arranging LSD sessions to treat alcoholism, incorporating music and religious iconography into his sessions in an effort to optimize results (Dyck, 2008: 68). Reputed to introduce more than 6000 people to LSD, including key figures from various domains, Hubbard would soon come to play a crucial role in disseminating the idea that one could improve LSD's therapeutic results by manipulating the environment.He convinced LSD therapy pioneers Humphry Osmond and Abram Hoffer of the potential benefits of integrating new elements of setting into their LSD therapy for alcoholics and was also influential in bringing the principles of set and setting to the attention of psychiatrist Oscar Janiger who performed the most extensive research on LSD creativity, and to Myron Stolaroff another LSD pioneer who performed research on LSD and technical inventiveness

(Fahey, 1991; Markoff, 2005). An early textbook of psychedelic psychotherapy *The Handbook of the Therapeutic Use of LSD,* which was published in 1959, confessed "the debt which the authors owe to the work of A.M. Hubbard" (Blewett and Chwelos, 1959: 3) and credits Hubbard for being the one from whose work the methods presented in the book grew out (Blewett and Chwellos, 1959: 17).

By the end of the 1950s, the idea that extra-drug parameters are crucial to determining the effects of hallucinogenic (or "psychedelic") drugs was becoming increasingly accepted by researchers and was receiving growing recognition as a fundamental concept of psychedelic therapy. The first written report on the ways in which set and setting can be incorporated into psychedelic therapy appeared in the writing of psychologist Betty Eisner. After participating as a subject in an LSD experiment in 1955 and having her initially positive experience marred by endless batteries of tests and insensitive treatment by the research team, Eisner became acutely aware of the importance of creating better conditions which will enable subjects to receive the full benefits which LSD psychotherapy seemed to promise (Eisner, 2002). In 1957, she was charged by psychiatrist Sidney Cohen with the task of studying the techniques for creating the optimal conditions for integrative psychedelic experiences (Novak, 1997). Over the next couple of years, Eisner would become a prolific and original investigator on the role of set and setting in shaping and determining the outcome of psychedelic experiences, experimenting with a variety of variables and methods aimed at carefully adjusting the LSD experience to make subjects' experiences as comfortable, evocative, and integrative as possible. Eisner's designs were informed by the ideas of Hubbard and Osmond, with whom she stayed in close contact, and who were concurrently investigating the effects of external stimuli on psychedelic experiences, yet she was the first to write about the various facets of therapeutic LSD session design, the use of musical selections, and ways to organize space. In her 1958 paper "Psychotherapy with lysergic acid diethylamide" Eisner discusses principles in the selection of LSD patients for therapy, the preparation process, as well as the use of music, photographs, mirrors, and postsession activities in the hospital's art clinic. A year later, a paper by researchers from Osmond's Saskatchewan team would reprise and expound on the theme, providing a second scholarly account on the use of extra-drug parameters to control psychedelic drug experiences (Chwelos et al., 1959). Such early papers on psychedelic therapy focused their attention on the constructive use of various nondrug factors rather than on empirical and theoretical efforts of the kind made by psychotomimetic investigators. The elements of set and setting were now almost fully represented with questions of personality, preparation, expectation, intention, physical, and social setting already becoming part of the clinical picture. And yet one crucial element was still missing, the link with a greater scheme of things, the question of how hallucinogenic drug experiences interacted with the greater culture in which they were embedded.

This essential contribution to the discussion was made by Canadian anthropologist Anthony F.C. Wallace who drew attention to the role of cultural beliefs and values in shaping the effects of hallucinogens (Wallace, 1959). Wallace's "Cultural Determinants of Response to Hallucinatory Experience" focused on the phenomenon of hallucinations, noting the great discrepancy in the perception of hallucinations between western psychiatry and indigenous societies. In western psychiatry, hallucinations are considered a prime indicator of mental illness and their occurrence often leads to intervention by medical or law enforcement agencies. Not only are such negative value judgments absent in primitive societies, but, as Wallace noted, in such societies hallucinations are often cherished and regarded as potentially valuable for the individual and the culture. This difference in the perception and interpretation of hallucinogenic drug experiences, he suggested, was responsible for differences between how these manifest themselves in various societies. When Wallace contrasted the effects of mescaline given to white subjects in clinical trials with the effects of mescaline ingested in the ritual setting of Indian ceremonies using peyote (a cactus whose main psychoactive agent is mescaline), the incongruities were striking.

While white users of mescaline exhibited extreme mood swings, alternating between depression, anxiety, and euphoria, their native American counterparts manifested a relative stability of mood, characterized by enthusiasm and religious awe. Whereas white mescaline users often forsake their social inhibitions, exhibiting sexual and/or aggressive behavior, participants in peyote ceremonies kept up their proper behavior. While white subjects displayed a host of psychiatric disorders such as suspiciousness bordering on paranoia, as well as "unwelcome feelings of loss of contact with reality, depersonalization, meaningless, 'split-personality' etc." (Wallace, 1959: 63) Indian peyotists displayed no such phenomena. Finally, while white subjects showed no therapeutic benefits or behavioral changes following their peyote experience, their Native American counterparts reported feelings of deep connection with a more meaningful, higher order of existence, which was supportive to their integration in the community.

To Wallace, these differences seemed to be the result of the different cultural framings of hallucinations.

He suggested that cultural response to hallucinogens could be defined by a number of parameters such as *communication* (is the content received during an hallucination construed as a meaningful message or mental gibberish?), *mechanism of control* (is the hallucinator able to control his experience?), *induction* (does the hallucinator seek to induce or repeat the experience?), *concealment* (must the hallucinator conceal his experience from others?), *punishment* (must the hallucinator fear punishment because of his hallucination?), *therapy* (is the hallucination part of a therapy?), *role assignment* (does the experience qualify the individual for a social role?), and *behavior guidance* (can the content of the experience be used as guidance by the individual or his social group?) (Wallace, 1959).

Hallucinogenic drug users, noted Wallace, incorporate the views and perceptions which their surrounding society holds on the topic of hallucinations. This situation, he proposed, held grave implications for western users of hallucinogens, often needlessly aggravating the anxiety and misery of the hallucinating person. The results of clinical research with hallucinogens, Wallace suggested, should be considered cautiously, since the content of hallucinations is influenced by the cultural context in which an hallucination takes place and it was disturbingly probable that clinical research subjects are "influenced by the negative attitude toward any distortion of normal sensory and cognitive perception" (Wallace, 1959: 63).

Another 1950s investigator who contributed to the discussion on the social aspect of extra-drug variables was sociologist Howard Becker. Becker's classic paper "Becoming a marihuana user" (1953) examined the learning process by which a novice marihuana smoker comes to interpret its effects through the prism provided by his peer group, learning to recognize marihuana-induced sensations as pleasant and desirable. In later publications, Becker (1963, 1967) warned that society's notions of deviance and its pathologization of drug experiences carry devastating consequences for drug users by shaping their experiences negatively. He pointed to the potential importance of drug cultures in mitigating drug harms by providing a framework which supports the production and dissemination of knowledge and skills contributing to informed use of psychoactives. Using this logic, he predicted that the number of LSD psychoses will diminish in conjunction with the development of an LSD culture, as has earlier been the case with marihuana psychoses.

The term set and setting emerges

By the end of the 1950s, the idea that extra-pharmacological factors play a detrimental role in shaping the effects of hallucinogens was becoming well established in the field of hallucinogenic drug research. A 1958 World Health Organization report on *Ataractic and Hallucinogenic Drugs in Psychiatry* noted the striking dependence of psychedelic effects "on the precise constellation of environmental factors" (WHO, 1958: 35). In the 1959 second Macy Conference on LSD, chairman Frank Freemont-Smith exclaimed in response to the many contradictory reports on the effects of LSD:

> Our whole concept of pharmacology is built, perhaps, on an obsolete idea: that there is a response, an appropriate response to a given stimulus. We know that the response to a stimulus is as much dependent upon the situation as it is upon the nature of the stimulus. . . . The same drug, in the same dosage, can cause a diametrically opposite physiological response if the experimental conditions are different. It is essential to remember that in drug therapy of any kind there is a multidimensional, multi causal frame of reference. (Abramson, 1960: 31)

Timothy Leary's concept of set and setting was thus not original in suggesting that psychological and social factors play a crucial role in the formation of hallucinogenic drug experience. Rather, it turned a growing sentiment into a simple slogan and made explicit the crucial importance of the set and the setting in which a drug experience takes place. When Leary examined the effects of psilocybin in his paper "Reactions to Psilocybin," he did not attempt to portray the reactions to psilocybin per se, but rather how these manifested in a specific set and setting, taking into account that such reactions might vary widely and is set and setting specific (Leary et al., 1963). Leary also suggested that set and setting should be calculated when reporting the results of psychedelic studies by documenting subject and researcher expectations beforehand, an idea that would later reappear in contemporary hallucinogenic research (Johnson et al., 2008).

Leary's most comprehensive account of set and setting can be found in *The Psychedelic Experience: A Manual Based on the Tibetan Book of the Dead* (1964). A classic of 1960s psychedelic literature, the book offered the first elaborate and popular account of the principles of set and setting, disseminating the concept into American youth culture. Leary, Metzner, and Alpert discussed basic elements of set and setting such as use of music, lighting, the availability of food, as well as the arrangement of the space. They also considered a variety of additional aspects of set and setting such as the difference between immediate set and long-term set; different types of expectations such as medical, religious, or intellectual expectations; and the difference between nights sessions versus day sessions, or indoor sessions versus outdoor sessions. Readers were advised to allocate at least three days for the experience and its

integration, and to prepare themselves for a psychedelic session by practicing meditation, reading appropriate books, and engaging in thorough introspection and self-examination.

Leary's work with psychedelics during the 1960s could be viewed as an ambitious exploration of the many ways in which psychedelics might interact with different set and setting conditions. Revealingly, in Leary's report on his meeting with beat-generation icon Neal Cassidy, he tells Cassidy that he is interested in measuring the effects of psilocybin "under a variety of set and settings to chart the range of reactions" (Leary, 1983: 52). Indeed, no other investigator experimented with psychedelics under such a variety of set and setting conditions such as Leary. During the 1960s, Leary and his collaborators gave psilocybin to artists, musicians, writers, psychologists, spiritual gurus, intellectuals, divinity students, ministers, and even prisoners, with sessions performed in churches, prisons, meditation rooms, faculty living rooms, and bohemian pads.

Leary would continue to consider the issue of set and setting well into to the second part of the 1960s, a time when he was working well outside the realms of academic discourse. His most ambitious work on the subject, a paper titled "On Programming the Psychedelic Experience" (Metzner and Leary, 1967), set up highly pretentious goals for the science of set and setting, by suggesting that psychedelic experiences can be programmed beforehand through the use of specific cues and techniques such as Tibetan yantras, mantras, incense, and specific yogic postures. Set and setting, it was suggested, could turn into an almost exact science that would enable psychedelic voyagers to actively program their experiences according to their wishes, like viewers programming their TV.

Such hopes would not come to pass and the study of set and setting would be almost entirely abandoned shortly thereafter, with the breakdown of the psychedelic movement, yet the impact of Leary's concept of set and setting was long and profound. Leary's popularization of the concept of set and setting probably had some mitigating effect on the 1960s psychedelic movement he helped unleash. As simple and limited as it was, such common user advice such as "use only at a good time, in a good place, with good people" served to prevent untoward effects and raise the probability of a positive experience (Zinberg, 1984). The awareness to set and setting remains Leary's most valuable contribution and legacy for generations of researchers and drug users since.

Post-1960s developments in the theory of set and setting

The story of mid-20th-century hallucinogenic drug research provides ample examples for the centrality of set and setting in shaping drug effects. It is not only the great discrepancy in the results reported by psychotomimetic and psychotherapeutic researchers which attracts attention. In actuality, no less than nine distinct types of uses existed for LSD at the time, including the use of the drug for religious/spiritual purposes, creative purposes, scientific invention, political activism, military combat, and special operations (Hartogsohn, 2015). Using such highly divergent types of set and setting conditions, researchers ended up describing the effects of LSD in an assortment of ways. Small wonder that researchers have since likened the story of mid-20th-century LSD research to the story of the blind men and elephant, in which each of the blind men fumbled a different part of an elephant's body, later giving highly divergent descriptions of what an elephant is (Cohen, 1964; Fadiman, 2011).

Yet by the 1970s, following the abandonment of psychedelic drug research and the classification of psychedelics as Schedule I drugs, the concept of set and setting would all but disappear from the literature. In the 1980s, the concept would reemerge in Norman Zinberg's *Drug, Set and Setting*: *The Basis for Controlled Intoxicant Use* (1984), the most extensive research up to date on the role of set and setting in shaping drug effects outside the laboratory. In it, Zinberg sought to integrate the ideas of set and setting into a theory of harm reduction which examined not only psychedelic use but also drugs such as alcohol, cocaine, and heroin, a contribution to which I will return further on.

An additional dimension was added to set and setting by Betty Eisner, who drew attention to the role of pre- and postexperience setting on the outcome of a psychedelic experience. Eisner's "Set, setting and matrix" (1997) reported some of her observations on the subject of set and setting following years of experience as an LSD therapist. Eisner proposed adding the concept of matrix to the scheme of things in order to refer to the pre- and postsession environment to which a patient returns after his psychedelic experience. Matrix included the patient's family and living situation, the environment in which they live during therapy and to which they return after successful therapy. A successful matrix, according to Eisner, is a continuous process which supports the integration of the experience so that "the setting becomes one in which patients can change and mature" (Eisner, 1997: 215). Matrix is thus an environment in which a psychedelic experience can be adequately framed and worked through, and in which individuals are allowed to transform themselves in safe, nonjudgmental, supportive surroundings which enable the transcendence of past barriers and sustain new venues for growth.

While sociocultural aspects of set and setting featured prominently in sociological and anthropological

accounts of drug action (Becker, 1967; Dobkin de Rios, 1984; Wallace, 1959) such elements have been largely left out of the accounts of therapists and medical practitioners who concentrated their efforts on the immediate factors shaping drug effects in concrete circumstances. One attempt to bridge the gap between the individualistic and collectivist accounts of the principles of set and setting can be found in the concept of *collective set and setting,* an attempted synthesis of Leary's theory of set and setting and Wallace's cultural determinants to hallucinatory experience, which points to the links between the two and proposes that all the aspects of the set and setting of individual psychedelic experiences are determined by a broader collective level of set and setting.

Individual (immediate) set and setting conditions never exist in a vacuum. They are shaped by external social and cultural forces. Thus, an individual's personality is shaped by the society and culture in which they grow up and live, as does the preparation they will have before entering a psychedelic experience, or the expectations and intentions they will bring to such an experience. Similarly, physical setting will invariably depend on the kind of culture in which the experience takes place (e.g. different topographies, a preference to outdoor or indoor sessions, styles of architecture and design). So will, naturally, the social setting, composed by other members of the society, and of course a person's belief system. We thus find that individual set and setting is always nestled within a greater collective set and setting, which is shaped by the society and culture in which a person lives and develops.

The concept of collective set and setting bears resemblance to John Law's concept of *hinterland*. Law's hinterland concept is used to refer to assemblages of "preexisting social and material realities" (Law, 2004: 13) composed of already established practices, skills, instruments, and actors which lead to the emergence of certain kinds of realities but not others. Dwyer and Moore (2013) employ the hinterland concept to point to the way in which, through use of "mutually constituting activities" which include epidemiological research methods, drug policy, media reporting, and Western Metaphysical assumptions about reality, "particular epistemological and ontological understandings of methamphetamine are privileged and other ways of knowing are silenced" (Dwyer and Moore, 2013: 209). Similarly, collective set and setting can be conceived as the composite sum of factors such as values, beliefs, media coverage, drug laws, social trends, and cultural discourse elements which determine what types of individual set and setting conditions are probable to emerge in a given society and what types are improbable, unachievable, perhaps even unthinkable.

The concept of collective set and setting helps make sense of the markedly divergent types of responses LSD elicited in the 1950s and 1960s American society, when it was used by a growing number of groups and in a wide variety of individual set and setting conditions. Robert Forte notes that back in the 1950s extensive LSD research was already happening in Harvard, however nothing resulted "in terms of social movement, controversy, or visionary breakthroughs," whereas a few years later, with the arrival of Timothy Leary "there's an uproar and a movement beginning to take form" (Forte, 1999: 228). As I showed elsewhere (Hartogsohn, 2015), what happened in the Harvard psilocybin project of the early 1960s did not take place a decade earlier, arguably because the cultural set and setting of the early 1950s would never have permitted it. In an era governed by the communist scare and a conservative mentality, LSD was in the hands of the CIA, and the young generation who would take LSD and turn it into a countercultural symbol was not yet in sight, as well as the whole cultural and spiritual climate which would sustain such a movement. The changes that occurred in the collective set and setting as the 1950s gave way to the 1960s, ushering in a sexual revolution, a fourth great spiritual awakening and a plethora of radical youth movements were responsible for allowing LSD to become all it has become during that decade (Lytle, 2006; McLoughlin, 1978). Thus, when former Grateful Dead lyricist John Perry Barlow writes that it is as if the American nation went through a shared trip in the 1960s, more than mere metaphor is involved. LSD and other psychedelics are deeply cultural drugs that interact intimately with the collective set and setting conditions of the society into which they are injected. Their effects vary from one culture to another and from one historical period to the next. Appropriate to their designation as mind-manifesting agents (psyche-mind, delos-manifesting), these molecules reflect not only the mind states of their users, but the mind states of entire societies and cultures by acting in a variety of different ways depending on the time and the place.

Set and setting and other drugs

But what about other drugs? To what degree are their effects governed by the principles of set and setting, and might these principles help control their effects?

Psychedelics are habitually noted for being the substance family whose effects are most susceptible to changes in set and setting conditions (Langlitz, 2012: 240). Becker (1967) went as far as distinguishing between drugs whose effects are radically malleable such as marihuana and LSD, and those whose *interpretative flexibility* (Pinch and Bijker, 1984) appears more limited due to their more predictable effects such as the opiates.

It is no coincidence that the ideas of set and setting surfaced twice in relation to the emergence of the use of hallucinogenic agents. First, when hashish was introduced to Parisian society in the mid-19th century, and then, a second time, when LSD and other psychedelics were introduced to American society a century later. No other group of drugs appears to be as plastic and responsive to conditions of set and setting as the psychedelics—mind-manifesting drugs whose very name points to their character as nonspecific reflectors of extra-drug conditions.

Nevertheless, the role of set and setting has not been absent from accounts on the extra-pharmacological construction of other, nonpsychedelic, drugs. Already in 1959, Wallace observed that cultural determinants are at play not only in the case of hallucinogenic drugs but also in shaping the effects of tranquilizers, sedatives, and stimulants (Wallace, 1959). Could the concept of set and setting also be used in the study of other types of drugs? The answer seems to be, not to the same degree, but definitely yes. Indeed, over the past decades, several scholars have used the concept of set and setting to examine how extra-drug parameters shape the effects of nonpsychedelic drugs.

The first and most obvious example can be found in the work of psychiatrist Norman Zinberg. Zinberg's *Drug, Set and Setting* (1984) examined the habits of drug users and the phenomenon of controlled drug use, users' tendency to follow certain rules and principles in their substance use. The reason for adding the "drug" component in the title of his book is precisely because Zinberg expands the concept of set and setting beyond the psychedelic realm. Thus, a drug experience was now shaped by three factors—the specific palette of psychoactive experience offered by a certain substance, and then, on top of that, set and setting conditions which can modulate the drug's experience in profound ways.

Bringing the concept of set and setting into the issue of heroin use, Zinberg observed the ways in which the setting created by the military service in the Vietnam war, characterized by boredom and sense of purposelessness, contributed to the soaring use of heroin within the American army (35% of enlisted men in Vietnam used heroin). Government plans to stop heroin use through treatment failed, showing some 90% recidivism rate. Nevertheless, that it was a certain type of setting which encouraged the use of the drug can be shown by the fact that when heroin using ex-soldiers returned to the US, 88% of these ex-troopers stopped using the drug spontaneously, a fact which bluntly contradicts prevalent views about heroin addiction such as "once an addict, always an addict" (Robins et al., 2010). The element that changed and allowed these users to stop using was not some mysterious physiological transformation which occurred upon their return to US soil, but rather the setting to which they got back. Once users returned to a different environment devoid of the external stimuli that drive habit, the users abandoned their habit (Robins et al., 1974, 1975).

Another drug whose effects have been known to be profoundly shaped by society and culture is alcohol. MacAndrew and Edgerton's seminal *Drunken Comportment* (1969) demonstrated that social and cultural parameters play a determinant role in shaping alcohol effects by documenting the ways in which the effects of alcohol vary across societies, as well as within societies over time, and depending on the context in which it is consumed. As Heath, a widely cited expert on the subject writes:

> Numerous experiments conducted under strictly controlled conditions (double-blind, with placebos) on a wide range of subjects and in different cultures have demonstrated that both mood and actions are affected far more by what people think they have drunk than by what they have actually drunk ... people who expect drinking to result in violence become aggressive; those who expect it to make them feel sexy become amorous; those who view it as disinhibiting are demonstrative. (Heath, 1998)

Cohen (1990) uses set and setting to examine the habits of Dutch cocaine users, differentiating various kinds of motivations, situations, and rules which govern the use of the drug and shape its effects, while Dwyer and Moore (2013) employ it to argue for the importance of social factors in shaping methamphetamine effects in recreational users. Additionally, the concept of set and setting was recently used by neuroscientist Carl Hart (2013) to discuss the ways in which the effects of cocaine and crack-cocaine differ between high earning executives and homeless people, with the later displaying high degrees of paranoia. Hart also refers to Bruce Alexander's famous rat park experiment, which challenged the results of previous experiments indicating that given free access to morphine rats will quickly become addicted and use the drug compulsively. Alexander hypothesized that a crucial part of the reason why rats become so easily addicted to morphine in lab experiments is that laboratory conditions—a solitary existence in a closed cage—deprive the animals of the kinds of environmental stimuli that characterize a normal rat's life, turning drugs into an attractive route of escape. He thus constructed an enriched environment with alternative reinforcers such as social contact, mating opportunities, exercise toys, and dark refuges to nest in, creating a more engaging habitat for the animals. The results

were remarkable. Solitary rats drank up to 19 times more morphine solution than the rats living in rat park. Even when Alexander sweetened the morphine solution to make it especially appealing to the animals, the rats in rat park still tended to prefer plain water and drank much less of it than the rats in solitary cages (Alexander et al., 1978; Alexander, 2001; Hadaway et al., 1979). Similar findings have since been made in studies on the addictive properties of cocaine and amphetamines on rats in enriched-stimuli environment (Chauvet et al., 2012; Stairs et al., 2006; Whitaker et al., 2013). A change of setting can thus drastically alter drug using habits, as Robins found out in her studies on heroin users veterans going back from Vietnam. The rat park story therefore functions, for Hart, as an allegory, in which the rat cage symbolizes the slums and ghettos in which much of modern drug abuse takes place. It demonstrates how restrictive, impoverished environments lacking alternative reinforcers play a great role in contributing to patterns of drug abuse, a contention which is becoming increasingly documented in research (Galea et al., 2005).

If the concept of set and setting is useful in the study of other drugs, might it not also prove helpful to explaining human experience in general. Indeed, personality, expectations, and intentions govern a variety of everyday experiences from a visit to the amusement park to a meeting with friends, even when no psychoactives are involved. A 1976 study sought to gauge the ''impact of set and setting on religious experience in nature'' (Rosegrant, 1976) and Ralph Metzner, one of the original articulators of the set and setting hypothesis writes: ''The 'set and setting' hypothesis . . . really applies to any state of consciousness – hypnosis, meditation, dreams, or what we call the ordinary, waking state of consensus reality'' (Metzner, 2011: 18).

Trying to fit the whole range of human experiences into the set and setting scheme might prove counterproductive for our purposes. By becoming overly inclusive, the concept might lose its usefulness in explaining and controlling drug-altered states of consciousness, whether invoked by psychedelics or by other agents. In the next section, I will conclude and briefly show how the concept of set and setting can prove useful and sit well with current trends in drug research and drug policy.

Integrating set and setting into medicine and culture

With the recent resurgence of psychedelic research, the concept of set and setting has once again become relevant. Current research into the therapeutic potential of psychedelics shows a fundamental awareness to issues and principles of set and setting, while working within the current dominant model of controlled trials which is often understood as demanding the neutrality of experimental conditions in order to isolate drug effects (Griffiths et al., 2006; Johnson et al., 2008). Thus, to some extent, the dependence of psychedelic research on set and setting still defines it as an odd bird in a medical industry where efficacy is validated in RCTs which seek to neutralize or at least control for any extra-pharmacological variables.

This dilemma is not a new issue for psychedelic therapy. It is interesting to note that the rise of RCTs in the 1950s was a major challenge for psychedelic therapy at the time. Double blind experiments with psychedelics are notoriously difficult to perform (e.g. Leary, 1995: Chapter 15), and the effects of psychedelics are not very amicable to pursuing standardized ''objective'' settings, whatever that would mean. Attempts to achieve objective or even neutral set and setting are problematic by definition because set and setting is a complex notion defined by many imprecise variables. A ''neutral'' setting might be conceived as negative or positive by different persons, so that ensuring a neutral/objective set and setting is almost impossible. Back in the 1950s, the Canadian Addiction Research Foundation (ARF) challenged the results of LSD treatment for alcoholism by Saskatchewan psychiatrists Osmond and Hoffer, claiming that the researchers failed to effectively remove the effects of environmental parameters from their design. Yet the whole notion of trying to create an ''objective'' study was highly contentious. When ARF scientists tried to re-create the results reported by Osmond and Hoffer in an objective setting, they ended up instructing observers not to interact with patients and reached lower improvement rates, supposedly disproving Osmond and Hoffer's results, even though a number of other researchers which employed positive set and setting conditions confirmed the Saskatchewan results (Dyck, 2008). In this case, the attempt to create an objective set and setting ended up creating less than optimal set and setting conditions which did not serve to truthfully assess the drug's potential.

The emphasis on standardizing extra-drug variables might not be the most effective way to learn about some drugs and their utility. As Tooley and Pratt wrote already in 1964:

> the quixotic attempt to eliminate the effects of participant-observation in the name of a misplaced pseudo-objectivity is fruitless, not so much because it is impossible but because it is unproductive. . . . the question becomes not how to eliminate bias (unaccounted-for influence) of participant observation, but how optimally to account for and exploit the effects of the participant observation transaction in terms of the purposes of the research. (Qtd in Doblin (1991: 6))

The role of culture in medicine needs to be acknowledged again. Wallace lamented the lack of cultural controls in 1950s hallucinogen research and called for integrating those into research (Wallace, 1959). Hyde went in that direction when he analyzed how various social variables influenced the effects of LSD on subjects, and Metzner et al. studied how expectation and mood shape psilocybin reactions (Hyde, 1960; Metzner et al., 1966). Nevertheless, such efforts were largely abandoned. Today, we need a research program which focuses on questions of set and setting and controls for a variety of factors which shape set and setting, studying them much in the same way in which some investigators working in the placebo field control and measure various factors which shape placebo response (Finniss et al., 2010). Research papers on psychedelics and other psychoactives should ideally incorporate a detailed description of the set and setting conditions in which research took place, including reference to such parameters as subject selection, researcher expectations, subject expectation, preparation, and physical setting. Only in this way can the results of hallucinogenic drug experiments be compared, and a more accurate understanding of how the various aspects of set and setting function and interact in research settings be arrived at.

As psychedelic drug research reenters the picture, it is important to avoid excessive reliance on a biomedical model which disregards extra-drug factors. Contemporary psychedelic research shows awareness of the importance of incorporating non-drug factors into modern study designs, by attempting to create a supportive set and setting while adhering to the double-blind structure of RCTs (Griffiths et al., 2006). Yet the existence of a wide variety of set and setting conditions in contemporary research—a prominent example would be neuroimaging studies, which provide a less than perfect setting for the ingestion of psychedelics—is still capable of confounding results (Slater, 2014). Furthermore, it has recently been suggested that the expansion of clinical psychedelic investigations into the phase III stage might pose considerable challenges, due to variations in set and setting (Langlitz, 2015). It is important to note that there is not one ''correct'' type of setting, and other ''incorrect'' types of setting, but rather, that factors of set and setting need to be transparent and taken into consideration when investigating psychedelic drug effects. Either way, the lessons of the psychotomimetic/psychotherapeutic divide in the perception of LSD appear to be no less relevant today.

Over the last decades, principles of set and setting have been employed both as drug policy measures as well as by local and community initiatives in order to reduce the drug harms. Prominent examples include the case of Dutch coffee shops, as well as chill out rooms and free availability of water in clubs where MDMA is commonly used (Goulding et al., 2009; Monshouwer et al., 2011). Recent years have also seen a further increase of awareness to issues of set and setting within the drug culture. This can be recognized in the growing prevalence of psychedelic harm reduction services in international events such as *The Boom Festival* and *Burning Man* (Carvalho et al., 2014, Ruane, 2015) as well as in the growing presence of printed and online ''psychedelic manuals'' which offer guidelines for creating favorable set and setting conditions (e.g. Fadiman, 2011; Kilham, 2014). Research into the social aspects of set and setting might examine the effect which such measures have on drug harms. Furthermore, as suggested by Becker (1967), sociopharmacological research needs to look at the ways set and settings play out in the field by comparing the effects of drugs in different user groups with diverging sets and setting conditions, and by providing meaningful examples of how specific set and setting elements shape drug user experiences.

Studying the ways nondrug factors shape the effects of drugs both inside the lab as well as outside it can significantly contribute to our understanding of the ways drugs act in the real world and allow us to make strides by focusing not only on the science of psychopharmacology, but also on the art of using psychopharmacological agents, thereby optimizing their patterns of use. In addition, social harms of drugs can often be prevented or minimized by integrating set and setting into discussions on drug policy. Back in the late 1960s, the percentage of bad LSD trips rose sharply. Then, in 1979, Sociologist Richard Bunce hypothesized that this was caused because of the negative collective set and setting conditions which arose in the late 1960s, referring to the many dire messages that were later invalidated (Dishotsky et al., 1971; Halpern and Pope, 2003), yet proliferated at the time and warned users that LSD destroys the brain, damages the chromosomes, and causes flashbacks. These, after all, were days when marihuana users were getting 30-year sentences for sharing a joint with an undercover agent. In this climate of paranoia, LSD experiences took a turn for the worst and the percentage of bad LSD trips rose sharply. Nevertheless, by the mid-1970s, when the political controversy and moral panic surrounding LSD have abated, the occurrence rate of bad trips sank by a dramatic 45%, a fact which Bunce credits to changes in the cultural climate which led to a corresponding improvement in set and setting conditions, and led to a reduced number of negative experiences (Bunce, 1979).

Stories like this demonstrate the profound impact which social policy can have on set and setting conditions and thereby on the levels of harms drug users

suffer (Dwyer and Moore, 2013; Race, 2011). They point to the fundamental responsibility which the state carries for the welfare of drug using populations, because of its role in shaping collective set and setting conditions.

Creating positive set and setting conditions for drug experiences is one of the first actions which can be undertaken to reduce drug harms. It needs to be understood that drug users are helped not by deterrence and scare tactics but by creating an open environment of information, trust, and support. Instead of pointing a finger at drug users, research and state would do better to produce information which can be valuable for those that decide to use drugs despite government prevention efforts.

Learning to create positive set and setting conditions is an urgently needed skill in a drug suffused world—both for individuals, as well as for society as a whole. In some countries, medical marihuana patients receive training. They learn how to consume the drug and get guidance on the various aspects of its effects from trained guides. Such initiatives show that educating the public on set and setting is not impractical or inconceivable in any way. Why should objective information about drugs and the ways to control their effects not be part of the basic education of every citizen? The science of how to use drug responsibly and effectively should be made accessible by educating the public on the principles of set and setting, a shared body of knowledge on the do's and don'ts of responsible and effective drug use in a world where drug harms cannot be nullified but can doubtlessly be minimized.

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Notes

1. The question of terminology, when referring to agents such as LSD, psilocybin, mescaline, or DMT, is a tricky one. These agents have been referred to as psychotomimetics, hallucinogens, psychedelics, and entheogens among other names, often depending on the theoretical or political leanings of writers (Hartogsohn, 2015). For the purposes of this paper, I will use the terms hallucinogens, psychedelics, and psychotomimetics interchangeably, often depending on the context in which these drugs are discussed and without going into the potential implications of these terms.
2. My history of set and setting focuses on hallucinogens for historical as well as practical reasons. Not only did the concept of set and setting arise within the discourse on hallucinogens, but they have repeatedly been singled out as the drugs most susceptible to conditions of set and setting (Langlitz, 2012: 240). This does not mean that set and setting is irrelevant to other drug families. As I show in this paper, set and setting is highly relevant to many types of drugs.

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