
3. TESTING PSYCHOTHERAPIES AND DRUG THERAPIES: THE CASE OF PSYCHEDELIC DRUGS

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The drug revolution that began 30 years ago has transformed psychiatry, but it has left little imprint on psychotherapeutic procedures themselves. Little attention has been given to the possibility of using drugs directly to enhance the process of psychotherapy — fortifying the therapeutic alliance and facilitating the production of memories, fantasies, and insights. A change may now be coming; for example, a psychiatrist known for his research on the therapeutic alliance has proposed that a “pharmacotherapy of interpersonal processes” might be considered both to study and to improve the alliance [1]. The wait has been long partly because the research involved is complex and hard to perform. The theoretical bases for the two types of therapy are vastly different; these differences are reflected in the way experiments are conducted and the results are evaluated. Reconciliation and unification will not be easy to achieve. One of the best ways to see why that is so is to examine the different significance assigned to placebo effects in drug experiments and psychotherapy studies.

1. INTRODUCTION

Everyone now takes it for granted that the correct psychiatric and medical procedure for determining the effectiveness of drugs is the controlled double-blind trial with random assignment of otherwise matched patients to the experimental drug or a placebo. In medicine the controlled trial is, of course, a standard way to establish causal relationships; it is one form of Mill’s method

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of agreement and difference. The method is now a legal rule as well as a scientific one: the FDA usually does not allow a drug to be marketed for therapeutic purposes unless it has been proved effective in double-blind experiments.

It is in the last twenty years that researchers have become interested in applying this standard to psychotherapy. Psychotherapists are beginning to think that they must obtain scientific credentials in order to get government support and justify insurance payments. They have also been influenced by the success of lithium, phenothiazines, tricyclic antidepressants, and other psychiatric drugs. The experimental literature in the field is already large. But unlike controlled drug experiments, which usually come to straightforward conclusions that produce a fairly quick consensus in the psychiatric community, psychotherapy research is plagued by empirical doubts and conceptual confusions. Even the experts have found it hard to agree on what the results mean. For example:

I believe that it is fair to say that psychotherapy produces modestly or moderately positive results with certain types of cases, but there is tremendous variability among studies, including the types of control group used [2].

All that has been demonstrated in the literature so far is that psychotherapies seem more efficacious than nothing for relatively minor conditions . . . what remains to be shown is that any psychotherapy is more efficacious than simple helping relationships that reduce demoralization [3].

The effects of psychotherapy are equivalent to the effects of a relatively minimal placebo, which is essentially equivalent to knowledge that one is in treatment [4].

As I have attempted to show, research is not likely to adduce precise data on such issues as the "safety and efficacy" of psychotherapeutic modalities or their "cost effectiveness" [5].

The main reason for the lack of consensus is the problem of placebo effects. In testing drugs, it is relatively simple to isolate them, because we have a theory that explains why psychiatric drugs do something that sugar pills do not do: they act directly on the brain, altering the synthesis, release, or breakdown of neurotransmitters by virtue of their chemical structure. This deceptive simplicity has produced some popular but very inadequate definitions of placebo; for example, placebos are said to be inert or non-specific and placebo effects are said to consist of the features that all effective treatments have in common.

To define placebos as non-specific is to confuse effects on neurotransmitters with effects on the disorder or symptom being studied. Each type of drug has a specific effect on neurotransmitters and a sugar pill does not. But a sugar pill acts just as specifically as an aspirin pill when it relieves a headache. Placebos might be regarded as less specific in another sense: they relieve a great many

different symptoms, whereas the neurochemical action of a drug affects only a few. But non-specificity in the sense of wide usefulness cannot be the *definition* of a placebo. If we discovered a single drug that reliably relieved the symptoms of most psychiatric disorders, it would be regarded as a genuine panacea, not a placebo. For similar reasons, the placebo effect cannot be defined as the factors that all useful treatments for a disorder have in common. If we had a theory that explained all those common factors and allowed us to exploit them for the benefit of patients, we would no longer call the factors placebos or part of a placebo response. They would simply be the effects predicted by a true theory of extraordinarily wide applicability.

Distinguishing a placebo by its alleged inertness also means confusing activity with respect to neurotransmitters and activity with respect to the disorder being treated. When a psychiatrist gives a patient a sugar pill and relieves depression, the treatment is certainly active, although the pill itself is neurochemically inert.

The misleading but attractive definitions of placebos as inert, non-specific, or common factors are not even plausible in the case of psychotherapy. Psychotherapy could easily be claimed to be non-specific, inert, or made up only of "common factors." It has no direct effect on the brain and no well-defined neurochemical action. It is supposed to relieve a great many symptoms and conditions rather than a few specific ones. All of the procedures called psychotherapies apparently make use of mechanisms that they have in common with other human relationships and ways of helping. The problem of isolating placebo effects in psychotherapy is so complicated in practice and confusing in theory that some authorities have even recommended abandoning the concept, or at least the word, entirely [6].

The hunt for the elusive placebo in psychotherapy brings to light ambiguities in the term "placebo" as it is used in modern medical and psychiatric research. Its traditional meaning is, very roughly, the "psychological" aspects of treatment — the therapeutic relationship and the attitudes and expectancies of patients and therapists. The second meaning, more formal and technical, has always been implicit in modern drug experiments and has now been fully explicated by the philosopher of science, Adolf Grunbaum [7, 8]. He defines a placebo effect as an improvement in mental or physical health that occurs with no help from the mechanism that is the source of relief predicted by the theory on which the experiment is based. In drug testing the two definitions of placebo more or less coincide, but in psychotherapy research the ambiguity creates serious problems.

Using Grunbaum's definition, a medical treatment is a placebo only in relation to the disorder that is being treated and the theory that purports to explain the effectiveness of the therapy being tested. In other words, what is regarded as a placebo depends on what the experimenter is trying to prove. The therapeutic theory describes certain characteristic constituents of the treatment. Any result of what happens in the therapist's office or clinic is

regarded as a placebo response for the purpose of the experiment if it is incidental from the perspective of the theory. Different theories have different characteristic mechanisms. In controlled experiments testing these theories, various responses not predicted by the theories will occur: the incidental or placebo effects. Since no effect is incidental from the perspective of all possible theories, nothing is everywhere and forever a placebo. We can always construct a theory that explains what first appears as a placebo response and then test that theory in another experiment.

Grunbaum's definition of a placebo is strictly methodological; it is neutral with respect to content. By his account, any therapeutic response that occurs in a control group not receiving the experimental treatment — any incidental or placebo effect — has a mechanism that is indeterminate until further experiments are done. In practice, however, physicians have always had some notions about the kinds of factors that produce most of the incidental responses both in clinical practice and in experiments. These are roughly described by the traditional conception of the placebo as "psychological" elements in treatment — the professional and charismatic authority of the healer, the healer's contagious confidence in the therapeutic procedure, the patient's expectations and suggestibility, the attention devoted to the patient, and so on. Although we understand these influences poorly, we can easily correct for them in a double-blind drug experiment because we have background theories that explain the effects of drugs. In psychotherapy, there is no accepted background theory and therefore no easy way to distinguish specific psychotherapy effects from placebo effects.

Grunbaum's definition of placebo allows for the validation of psychotherapy, because nothing is an incidental mechanism in all possible theories. But separating the characteristic mechanisms of specific psychotherapies from the incidental effects of healing or helping in general seems to require an experimental control treatment that is not a form of psychotherapy but employs, to an equal degree, the "psychological" mechanisms associated with most professional healing and with most other forms of helping as well — expectancies, beliefs, authority, status, social approval, confidence, enthusiasm, emotional warmth, and so on.

Jerome Frank [9] has devised a theory to circumvent this problem. He says that psychotherapy is a healing technique that works by creating an expectation of improvement through inducing the patient to follow certain rules within a relationship with a trusted authority in a place identified as a place of healing. The authority provides a coherent, plausible explanation of why the procedure works; the patient's hope and sense of mastery are mobilized to combat demoralization and accelerate natural recovery. All these things are placebo mechanisms (incidental factors) according to the theories that justify specific types of psychotherapy; they become characteristic mechanisms in Frank's theory.

The theory is pleasantly ecumenical and describes fairly well much of what

goes on in psychotherapy and medicine. If the therapist's enthusiasm and the patient's hopes are aroused and the patient is made to feel secure through symbols of authority, the patient is likely to start feeling better. Even rats run mazes better when the experimenters in charge are confident because they have been led to expect an unusually good performance. There is little doubt that the transactions between psychotherapists and their patients often help the patients, but probably so did the transactions between 18th century doctors and their patients; we now attribute that to a placebo response. A strong application of healing rituals, almost in the pre-modern style, is still a recommended treatment for hypochondriacs, who refuse to talk to psychotherapists at all because they will not admit that their physical symptoms have emotional causes. Hypochondriasis is considered a psychiatric disorder, but many psychiatrists recommend that it be treated by a physician not necessarily trained in psychiatry, who should wear a white jacket, listen sympathetically to the patient's complaints, and offer reassurance along with harmless "medical" comforts, like stethoscope examinations, blood pressure measurements, heating pads, and vitamin pills.

Frank calls psychotherapeutic theories "healing myths." His account of psychotherapy fits very well the traditional conception of a placebo. A sugar pill administered by a sympathetic doctor also mobilizes healing symbols and associations. But even Frank concedes that this sort of charismatic healing without religious faith is hardly subject to experimental test. A control group in an experiment testing this theory would have to avoid using its extremely broadly defined characteristic mechanisms — the healing symbols and rituals, the office or clinic identified as a place of healing, attempts to encourage the patient's hopes and confidence in the therapist. But this would not demonstrate anything of interest.

How can it be shown that psychotherapy is more effective than common-sense helpfulness or charismatic healing? Perhaps the best-known study on the efficacy of psychotherapy is the work of Smith, Glass, and Miller [10]. They performed a meta-analysis, compiling and re-analyzing the results of hundreds of experiments covering more than 25,000 patients with a variety of disorders, who were given many different kinds of psychotherapy. Psychotherapy was defined as follows: the application of techniques derived from established psychological principles by persons qualified through training and experience to understand the principles and apply the techniques to assist patients in modifying behavior, values, and attitudes judged by the therapist to be maladaptive. They say they excluded no form of psychotherapy if the following conditions were fulfilled: clients were identified as having emotional or behavioral problems; they sought or were referred for treatment for the problem; the treatment was psychological or behavioral; the person delivering it was identified as a psychotherapist by virtue of training or professional affiliation. They go on to name some legitimate forms of psychotherapy — cognitive, behavioral, psychodynamic, rational-emotive, and so on.

Smith, Glass, and Miller estimated that the average patient who completes psychotherapy will be better off than similar patients with similar conditions who are not treated. The conclusion was based on elaborate statistical analysis of a vast number of experiments and presumably should be welcome to psychotherapists. Yet it was widely criticized, and the details of their study suggest some reasons why. First, they found that no psychotherapy has been shown to be better than any other psychotherapy for any particular emotional problem or psychiatric condition. It is as if a study concluded that drugs in general are better than pill placebos for a wide range of physical illnesses, but no drug has been shown to be better than any other drug for any particular illness. Almost all that is left is the bald conclusion that psychotherapy works; but this is hardly more useful or revealing than would be a study concluding that medicine works for physical illness. For example, it suggests that one form of psychotherapy cannot be used as control treatment in testing another form of psychotherapy.

They also found that the training and experience of the therapist and the duration of the treatment made no difference. Yet professional training and experience were included in their definition of psychotherapy. An essential feature of psychotherapy therefore seems to be irrelevant in practice.

The placebo control treatment included waiting lists, interview and assessment without further treatment or with periodic phone calls, or counseling and conversation of various kinds. In most of the experiments these apparently lacked credibility; that is, they lacked an equal dose of the features that define the traditional conception of placebo effects. For example, in some of the "counseling" sessions the mock therapist deliberately avoided discussing personal problems. Finally, the experiments were inevitably not double-blind.

The limitations of both Frank's work and the Smith, Glass, and Miller study suggest that there is no scientific test for the efficacy of psychotherapy in general. This is now commonly accepted, and the underlying reason is the lack of a general theory or model of psychotherapy analogous to the (admittedly rudimentary) theory of neurochemical activity that accounts for the characteristic effects of drugs. No explanatory mechanism is common to all psychotherapies, as distinct from all other agencies and procedures used in medicine and psychiatry. Without such a theoretical background, it is impossible to identify effects that are merely incidental and therefore should be regarded as placebo responses. Smith, Glass, and Miller include the application of "established psychological principles" in their definition of psychotherapy, but there are few if any scientifically established psychological principles and probably none that are relevant to psychotherapy.

Certain principles are socially established, in the sense that they are promulgated by various respected psychotherapeutic schools and professional guilds. But these schools and guilds have in some ways the same scientific status as those of 19th century medicine. Their ideas are not only divergent but often incompatible. To take the most obvious example, psychodynamic

theory and behavioral theory apparently contradict each other at almost every point. What could it mean, in experimental terms, to say that both psychodynamic and behavioral therapies are effective as treatments for the same symptoms (psychological problems)? From the perspective of behavior therapy, psychoanalysis and psychoanalytic psychotherapy produce at most a placebo response, and from the psychoanalytic perspective, behavior therapy produces only placebo responses. The mechanisms each therapy regards as characteristic are incidental according to the other. It is not clear that they have any ingredient in common that can be contrasted with a placebo effect in the same way we distinguish the neurochemical action of drugs from the placebo response to the act of prescribing a pill.

Taking recourse to pluralism means evading the issue of incompatible principles. Suppose that in an experiment two drugs are found to be equally good treatments for a physical illness; a well-defined theory is available to account for each drug's presumed activity and the two theories are incompatible. The only proper conclusion would be that this experiment produced only placebo or incidental effects. The improvement could not be shown to result from the supposedly characteristic activity of either drug. The same conclusion is necessary when two psychotherapies with incompatible principles both prove equally effective in treating some psychiatric disorder or symptom.

It has become clear that psychotherapy research requires experiments in which patients are chosen for specific symptoms, standardized training and treatment manuals are used to apply uniformly the theory and technique of specific psychotherapies, therapists are monitored to make sure they observe the rules, and measures of outcome are carefully defined. In what has been properly greeted as the best research so far, the National Institute of Mental Health recently tested cognitive behavioral therapy and interpersonal therapy, two well-defined techniques for treating depression [11, 12]. At three university medical centers, these psychotherapies were compared with an antidepressant drug and with a placebo control consisting of sugar pills and weekly consultations with a psychiatrist. Preliminary results indicated that the drug began to work somewhat sooner, but at the end of 16 weeks the psychotherapies were as effective as the drug and considerably more effective than the placebo (50%-60% versus 29% substantially improved).

This experiment, careful as it is, still leaves many questions open. Cognitive therapy relies on correcting patients' faulty ideas about themselves and the world to improve their mood. Interpersonal therapy concentrates on altering present relationships with other people. It is unclear to what extent the theoretical principles on which these techniques rely are compatible. To the extent that they are not, as we have shown, the experiment would only prove that some common element in the situation, not necessarily an ingredient characteristic of either treatment, had a therapeutic effect. If the theories are compatible, or partially compatible, their characteristic mechanisms may not have

produced the results. In fact, the researchers have emphasized that their main purpose was not to decide whether the psychotherapies were better than a placebo. They were more interested in comparing the psychotherapies against each other, and even in doing so their main purpose was not to decide which of the two was better. Instead, they wanted to find out which patients would do better with each treatment and why (11). Although the evidence is preliminary, they seem to have been largely disappointed. The outcome was about the same in both treatments, and no particular type of patient or symptom seems to have been improved significantly more by one therapy than by the other. Neither treatment was better than the placebo for the less severely depressed patients. The results of psychotherapy also varied greatly depending on the medical center where the treatment took place (which was not true of drug therapy).

In these circumstances it may prove hard to find any characteristic elements of the therapies that were effective. One obvious alternative explanation for the improvement is that the psychotherapy patients had the benefit of enthusiasm and concern from therapists who knew that they were conducting an important experiment. Several months of devoted attention conferred by a respected and authoritative person is a classically powerful placebo. Furthermore, the experiment was, of course, not blind. A double-blind experiment is almost impossible in psychotherapy research, because no one has found a good way to make therapists unaware of whether the treatment they are administering is supposed to be a control. The psychiatrists providing what they knew was meant to be a mere placebo treatment must have found it hard to preserve as much interest and enthusiasm as the ones providing psychotherapy.

The psychiatrists in the control group were also hampered by rules that prevented them from doing anything that overlapped with the psychotherapies tested or with any other forms of psychotherapy. The authors of the manual directing the administration of the control conditions (antidepressant drug and sugar pill) admit that "protocol demands may inhibit the application of the full range of usual and customary therapeutic techniques." They found that in training sessions "a self-consciousness seemed to evolve in some of the therapists resulting in a rigidity that diminished their usual and customary therapeutic responsiveness. Our observations provided us with a number of examples where an inflexible adherence to a rigidly interpreted protocol led to the abandonment of supportive interventions that the pharmacotherapist might ordinarily have made under practice conditions" [13].

Time is also an important element. The cognitive therapy patients had twenty 50-minute sessions, and the interpersonal therapy patients had sixteen to twenty 50-minute sessions. The patients who received either drugs or sugar pills combined with weekly consultations (described by the researchers as "minimal supportive therapy") spent about half as much time with the psychiatrist — one 50-minute session and sixteen to twenty 30-minute sessions.

The appropriate control for time is obvious. A control for the therapist's earnest conviction of effectiveness and devoted attention might be the use of counselors (or even friends) who are convinced that they can help and who talk about personal problems without artificial restrictions, but are not specifically trained in any type of psychotherapy. Smith, Glass, and Miller's conclusion that experience and training make no difference in the outcome of psychotherapy suggests the need for such a control.

A series of experiments of this kind, controlling for various aspects of the treatment, might distinguish the effective characteristic elements, if any exist, of psychotherapies and at the same time separate out characteristic ingredients of the placebo response in the traditional sense. A placebo effect, in the experimental sense elaborated by Grunbaum, is a therapeutic response without an explanation. When indeterminate placebo responses occur, researchers can develop a theory that explains their mechanisms and then devise another experiment to test the theory. Ingredients of what was once seen as a placebo response are employed as a new therapeutic technique, and the new control is some other agent or procedure that is not supposed to have the effects characterized by the new theory as therapeutic. In this way, experimental placebo responses might be analyzed and their constituents successively incorporated into new theories according to which they are no longer incidental effects but characteristic ones.

For example, experiments can test the physiological theory that some or most placebo effects involve the release of endogenous opioids in the body. Experimenters can also try to vary systematically certain characteristics of the patient or the therapist to see if they are associated with improvement. The most important element in any form of psychotherapy may be the way in which the psychotherapist communicates with the patient or the kind of working relationship that develops: the therapeutic alliance. Acknowledging this, some psychotherapists are now interested in process research, which might be seen as an attempt to examine in detail some of the mechanisms of what has been regarded as the placebo response [14]. There is no evidence that trained therapists are better at establishing an effective therapeutic alliance than sympathetic, intelligent lay people [15].

Unfortunately, the explanation and analysis of placebo responses in medicine is not far advanced. In any field, difficulty in determining what conditions do and do not influence the outcome indicates an early stage of science in which theories are inadequate. It is a sign of how little progress has been made in this field that some researchers can still write as though there is a generic placebo effect or as though there are agents or procedures that can serve as placebos in any experiment.

2. THE TESTING OF PSYCHOTHERAPY: FOCUS ON MDMA

In pre-industrial cultures there was an ancient tradition of using drugs to enhance psychotherapeutic healing; and from 1950 to the mid-1960s, there

were 15 years of experimentation with drugs in Europe and the United States — an episode in the history of psychiatry that is now almost forgotten. The drugs used in this research were psychedelic or hallucinogenic substances, both natural and synthetic. It might now be possible to revive this tradition with a synthetic drug that has some of the virtues of the familiar psychedelics without their disadvantages.

Ever since experimentation with psychedelic plants began, users have maintained that the experience could be useful for self-exploration, religious insight, or relief of neurotic and somatic symptoms. The plants have been used for thousands of years in rites conducted by shamans and other professional healers. This religious and therapeutic use of psychedelic plants continues in the Amazon, in southwestern Mexico (where psychedelic mushrooms are used in healing rites), and in the Native American Church services of Indians in the western United States, which make use of the peyote cactus. Psychiatrists have proposed the peyote ritual as an adjunct to the treatment of alcoholism among American Indians [16].

Psychedelics were also used extensively in psychotherapy as experimental drugs, in Europe and the United States for almost two decades. A large number of clinical papers and several dozen books on the subject were published. The drugs were employed for a wide variety of problems, including alcoholism, obsessional neurosis, and sociopathy; they were also used to ease the process of dying [17]. With proper screening, preparation, and supervision, it was possible to minimize the danger of adverse reactions [18].

The literature contains impressive case histories, which can be questioned because they do not allow for spontaneous recovery, the effects of a therapist's special and prolonged devotion, or the therapist's and patient's biases in judging improvement. Most psychedelic drug studies also lacked controls and adequate follow-up. Beginning in the early 1960s, as illicit use of LSD and other psychedelic drugs increased, it became difficult to obtain the drugs legally or get funding for research, and professional interest declined. A generation of physicians and scientists has grown up without the opportunity to pursue human research on these drugs, and the financial and administrative obstacles remain serious. But psychedelic drugs should not be treated as entirely worthless and extraordinarily dangerous. The complexity of their effects may explain the inconsistent therapeutic results and the difficulty in sorting out their best uses.

We now have an opportunity to revive this research. Dozens of psychedelic drugs are known, and some have effects that are different from those of LSD and other familiar substances. In particular, some do not produce the same degree of perceptual change or emotional lability as LSD. MDMA is a relatively mild, short-acting drug. Both users and therapists have said that it heightens the capacity for introspection and intimacy and temporarily frees the user from anxiety and depression. There are no distracting changes in perception, body image, and the sense of self. As compared with the more

familiar psychedelic drugs, it evokes a gentler, subtler, highly controllable experience that invites rather than compels intensification of feelings and self-exploration [19, 20, 21].

Patients in MDMA-assisted therapy report that they become less defensive and more emotionally open, able to get in touch with feelings and thoughts not ordinarily available to them. One patient put it this way: "I found it to be uncanny how easy it was to speak freely... about feelings. I'm generally not very good at that, but the MDMA apparently enabled me to let down the defenses and open up the offenses — but all in a gentle, matter-of-fact sort of way." Many patients find that they feel much closer to the therapist after one such session. If, as many believe, the strength of the therapeutic alliance is the best indicator of a good outcome in therapy, this characteristic of MDMA could be of very general usefulness [22].

But there are serious social and scientific obstacles to therapeutic research on such drugs as LSD and MDMA. The problem goes beyond legal restrictions or social attitudes towards altered states of consciousness and drugs used for non-medical purposes. An even deeper issue is the nature of the scientific validation required.

Probably the most influential controlled experiment in psychedelic drug therapy was the work of Ludwig, Levine, and Stark on alcoholism, which won a prize from the American Psychiatric Association in 1970 [22]. They chose 195 patients in an alcoholism clinic and separated them into four groups. One group received a standard residential milieu therapy. A second group was also given a single dose of LSD, a third group received LSD with psychotherapy, and the fourth group had LSD with psychotherapy and hypnosis. After three, six, nine, and twelve months, the results in all four groups were the same — about 75 percent improved. Some psychedelic drug researchers considered this experiment inadequate, on the grounds that the LSD sessions were not properly prepared and conducted. In some controlled experiments, the group treated with psychedelic drugs was doing better after several months. [24, 25]. (Psychotherapy has never been shown to have more durable effects.) But psychiatrists who used LSD never agreed on standards for preparing and conducting drug sessions, and most controlled experiments, including those performed by advocates of psychedelic drug therapy, were disappointing [26, 27, 28].

Some advocates of the therapeutic use of psychedelic drugs are impatient with this conclusion and with controlled studies in general. They say that psychedelics cannot be evaluated in the same way as ordinary psychiatric drugs with a simple consistent effect. The drug is given to create certain possibilities, not because it reliably relieves any symptoms. Its effects are overwhelmingly dependent on the set, the setting, and the relationship between therapist and patient.

These complaints amount to saying that the use of psychedelic drugs is not a drug treatment but a form of psychotherapy — or at least inseparable from the

psychotherapeutic process it is alleged to promote. It has been observed that most studies on psychedelic drug therapy do not even describe the set, setting, and intentions of the experimenters well enough for replication. They leave out so much that the literature is "rich in the variability of results and premature in its conclusions" [29]. In this respect, it is much like the literature on other forms of psychotherapy. But standards for psychotherapeutic techniques are not the same as standards for drug therapies. Controlled experimental proof of efficacy is not required legally or even demanded for public and professional acceptance. Although the study by Ludwig and his colleagues seemed to show that psychotherapy was no more effective than LSD, alcoholics are still given psychotherapy.

Because no one has yet determined precisely what a placebo is in psychotherapy, controlled research has hardly affected practice in this field. Psychotherapists rarely stop using a technique because of experiments that seem to put its efficacy in doubt. The few exceptions only confirm the difficulty of distinguishing placebo from psychotherapy effects. For example, many professionals gave up psychotherapy with schizophrenic patients after controlled studies showed that drugs and psychotherapy were no better than drugs alone [30, 31]. But psychotherapy of schizophrenics had always been frustrating and unrewarding, perhaps precisely because they have such a poor placebo response (in the traditional sense rather than Grunbaum's technical sense): they are bad at reading feelings, adapting themselves to social situations, developing expectations of their own, and sensing the expectations of others.

Psychiatrists take the results of experimental drug trials much more seriously than they take the results of psychotherapy experiments, and that leaves them much less freedom. Psychedelic drug therapy, as a hybrid between pharmacotherapy and psychotherapy, is in a peculiarly uncomfortable position. Its claims are no easier to establish than those of any other form of psychotherapy, and all the same problems involving placebo effects arise, but the accepted standards, both legal and professional, are the same as those of drug therapy.

In the literature on psychedelic drug therapy, these problems are presented mainly in the form of complaints about the difficulty in conducting a double-blind experiment. In this respect, as in many others, psychedelic drug therapy resembles psychotherapies much more than it resembles standard drug therapies. Unlike psychotherapy researchers, psychedelic drug researchers have felt obliged to try to satisfy the demand for double-blindness. One approved method is to introduce an "active placebo." Since any effective placebo is active, this phrase is misleading. A better term might be "mimicking placebo": a drug that is neurochemically active and mimics certain immediate side effects of the experimental drug but is not thought to have any direct neurochemical effect on the disorder being treated. For example, a proposed antidepressant drug might be too easy to identify because it inhibits salivation, causing dry mouth; the experimenter employs as a placebo another drug that is also known to inhibit salivation but is not believed to have any effects on

depression. This method is hard to apply in practice, since no drug has exactly the same immediate side effects as any other, and the drug used as a mimicking placebo usually has short- and long-term effects of its own that complicate the experiment. In most drug trials, mimicking placebos are not used; experimenters simply take the chance that side effects may be recognized.

Because the immediate effects of psychedelic drugs are often so overwhelmingly obvious, the demand for a mimicking placebo seems both highly justified and almost impossible to fulfill. Experimenters have reported using amphetamine, amphetamine-barbiturate combinations, or a small dose of LSD; they rarely say whether the subjects or therapists recognized the placebo. But concern about the technical issue of double-blind experiments may be misleading here. The deeper problem is that a psychedelic drug, like psychotherapy itself, is given precisely to create a certain experience, not to relieve symptoms unawares, like a standard psychiatric drug. In psychedelic drug therapy as in any other form of psychotherapy, a true mimicking placebo — one that produced the same immediate “experience” as the treatment — would be the same, for all practical purposes, as the treatment itself. Separating immediate effects from the desired therapeutic activity seems impossible, when precisely this immediate conscious response is the basis for treatment. If a double-blind experiment seems impossible in both psychedelic drug therapy and psychotherapy, it also seems undesirable.

Nevertheless, advocates of psychedelic drug therapy must meet the standards of drug therapy rather than those of psychotherapy. Even if double-blind experiments prove impossible, they will have to accept the burden of showing that, say, various forms of psychotherapy for depression along with MDMA give better results than various forms of psychotherapy along with a dextroamphetamine or sugar placebo. In other words, it seems that psychedelic drug therapy must be proved unequivocally superior for at least some patients and some conditions before it will be accepted or even legalized. We have already seen how hard it is to do this for any psychotherapy.

Conceptual and empirical improvements in psychotherapy research may provide some hope. For example, much recent process research finds that good therapeutic results are highly correlated with the early establishment of a solid therapeutic alliance [32]. But this result is subject to the same doubts as the research on outcome in psychotherapy. Can the therapeutic alliance be defined in a way that distinguishes it from other elements of friendship, expectancy, and authority that are part of the traditional placebo response? Is the alliance really a mechanism of improvement, or is it the result of the therapist's and patient's personalities and other conditions that precede therapy? Experimenters may have to find ways of manipulating and improving the alliance systematically, allowing therapeutic ingredients to emerge from the placebo background — the procedure described earlier as turning placebo responses into characteristic mechanisms. If certain drugs proved to enhance or alter the alliance, they might be valuable in such experiments. The phrase

"pharmacotherapy of interpersonal processes" [1] is one that some therapists who have used MDMA could probably adopt as their own.

The placebo problem is associated with another important distinction between drug therapy and psychotherapy. Psychotherapy is accepted despite the lack of scientific proof, partly because it is regarded as something more than a medical procedure designed to bring a patient back to an accepted standard of health. One authority even suggests that the idea of a placebo is inapplicable in psychotherapy because it serves to "subordinate psychotherapy research to scientific and political considerations that are relevant to medical research. This is self-defeating" [6]. The standard or ideal of normal mental health is much vaguer than the standard of physical health. Psychotherapy is often used by people who simply feel dissatisfied with some aspect of their lives and want to improve it. What is regarded as improvement often depends on the patient's own judgment and the judgment of the therapist, rather than a scientific consensus about what is emotionally normal or healthy. (Smith, Glass, and Miller even include the therapist's judgment about what is adaptive in their definition of psychotherapy.) It is not acceptable to use drugs in this way, to enhance rather than to normalize. The history of psychedelic research shows that a mixture of therapeutic claims involving drugs with talk of mysticism, transcendence, and consciousness-expansion is regarded with great suspicion. But psychedelic drugs are not the only ones affected; consider the public outrage about the use of drugs by athletes to improve performance. Here again psychedelic drug therapy will be subject to different standards from those applied to other forms of psychotherapy.

Members of the Native American Church, who use peyote (mescaline) in their rituals, are the only exception to the rule; they have been given the right to use a drug for a kind of enrichment or enhancement in the name of the religious freedom guaranteed by the Constitution. To grant to non-Indians the same right in the name of psychotherapy, we would have to drastically modify our social understandings about appropriate drug use.

3. CONCLUSIONS

This social obstacle to the acceptance of psychedelic drug therapy is closely related to the scientific obstacles. The standards of drug research are different from those of psychotherapy research, and the differences are deeply rooted in our science and society. The social standards for life-enhancement with drugs are also different from those applied to life-enhancement by other means, including psychotherapy. These differences too have deep cultural roots. Therefore any possibility of acceptance for psychedelic clinical research will have to wait on improved scientific standards for psychotherapy research in general.

Psychotherapy survives as a craft with aspirations to the status of science or a way of providing a new experience for people who feel dissatisfied and want

to change their lives. Scientific standards demand more: a series of experiments asking a series of questions to distinguish characteristic from incidental effects, where each new question is suggested by the results of a previous experiment. Progress in this kind of testing will require much more careful and creative thinking about placebo effects, and it is still not clear whether psychotherapy can realize its scientific aspirations. But even without scientific status, most forms of psychotherapy will continue to be socially accepted practices. The dominant cultural and scientific understandings about drugs make social acceptance impossible for psychedelic drug therapy, whether the agent is MDMA or some other drug. Therefore this kind of therapy will probably never become available until psychotherapy succeeds in the difficult task of obtaining scientific credentials of the same quality as those now granted to antidepressant or antipsychotic drugs.

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