PSYCHOPHARMACOLOGY’S DEBT TO EXPERIMENTAL PSYCHOLOGY

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The role of experimental psychology in the development of psychopharmacology has largely been ignored in recent historical accounts. In this article the authors attempt to redress that gap by outlining work in early experimental psychology that contributed significantly to the field. While psychiatrists focused on the therapeutic nature of drugs or their mimicry of psychopathology, experimental psychologists used psychoactive drugs as tools to study individual differences in normal behavior as well as to develop methodologies using behavior to study mechanisms of drug action. Experimental work by Kraepelin, Rivers, and Hollingworth was particularly important in establishing drug-screening protocols still used today. Research on nitrous oxide and on the effects of drug combinations is discussed to illustrate the importance of experimental psychology to psychopharmacology.

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Recent historians of psychopharmacology have tended to characterize the field as an outgrowth of psychiatry and pharmacology and to ignore the substantial role that experimental psychology played in its development (e.g., Healy, 1990, 1996, 1997, 1998, 2002; Lehmann, 1993). Although the use of drugs to mimic or alter the course of mental disorders has been a major pharmacological achievement of the 20th century, the study of drugs and behavior is, and historically, has been broader than that one application. Omitted or only briefly...
mentioned in the last decade’s flurry of histories (e.g., Carlsson, 1990; Healy, 1996, 1997, 1998, 2002) are the research efforts to elucidate the mechanisms and effects of psychoactive drugs on normal behavior, the use of psychoactive drugs to alter states of consciousness (i.e., recreational drug use), individual differences in response to psychoactive drugs, the use of psychoactive drugs as experimental tools to study behavior, and, finally, the use of behavior as a tool to study drug action. Not surprisingly, given the recent developments in molecular biology, as well as in neuroimaging techniques, there is at present more of a focus on the biochemical aspects of psychoactive drugs. This is illustrated by work aimed to design psychiatric drugs for specific neurotransmitter receptors (e.g., Chou, Hall-den, & Farde, 2003). But such work tends to ignore the essential scientific core of the discipline. The study of psychoactive drugs is meaningful not because of explicating the underlying biochemical processes—important as they may be—but because of what the drugs cause or influence the organism to do. Behavior, including, of course, qualitative effects, remains the final court of appeal in interpreting the actions of psychoactive drugs.

To understand better the importance of experimental psychology in the development of psychopharmacology, a brief prehistory of the field is helpful. Use of psychoactive drugs has been documented since the earliest written human records (cf. Porter & Teich, 1995). The benefits of alcohol, opium, and hemp have been variously extolled by ancient Egyptian, Greek, Roman, Babylonian, Chinese, Hindu, and Arabic practitioners (e.g., Holzer & Lembeck, 1983; Kramer & Merlin, 1983; Scarborough, 1995; Westermeyer, 1988). Most such references are concerned with the medicinal properties of the drugs. Even the poet Homer mentions the opium poppy as “quiet[ing] all pains and quarrels” in The Odyssey (Scarborough, 1995, p. 4). Discorides, a Greek physician whose Materia Medica (A.D. 70) was an important pharmaceutical text for centuries, classified drugs according to their functions or what they made the organism do (Scarborough). In support of his classification schemes, he cited both earlier literature and his own clinical observations about the use of drugs, such as opium. The use of drugs as tools to access spiritual forces or to participate in religious rituals has also been well documented (Holmstedt, 1967; Kramer & Merlin, 1983).

By the 17th century, experimentation with psychoactive drugs, such as opium, focused more on elucidating the physiological effects of the drugs rather than the psychological. For example, Charles Alston (1683–1760) published accounts of his experiments with opium comparing routes of administration (Maehle, 1995). Perhaps the most important work to be published on the subject of that period was by John Jones (1645–1709). In Mysteries of Opium Revealed, written in 1701, Jones listed psychological effects of the drugs to dispute the theory of animal spirit action of drugs. The “early self experiments introduced a basic method of psychopharmacology: taking a defined dose of a drug, careful self-observation, and detailed recording of mental and physical symptoms. In the 19th century this method began to be used in a more systematic way” (Maehle, 1995, p. 68). Estes (1979) refers to Jones’ tome as the “Rosetta Stone of ancient opiates” because Jones carefully outlined the various opiate preparations available at that time, together with the appropriate doses (p. 201). This listing allowed informal dose-response relationships to be established for the effects of opium, which were in part behavioral. Thomas de Quincey’s Confessions of an English Opium-eater
in 1821 is a prime example of the romanticized, pseudoscientific, introspective method.

Systematic experimentation with the substances did not appear until the 19th century. A few scholars (e.g., Carlsson, 1990; Healy, 1997; Holmstedt, 1967) mention Moreau de Tours (1804–1884) as the earliest scientist studying a psychoactive drug. He was a Parisian physician, who in 1845 published *Du Haschich et de l’aliénation mentale* about the intoxicating effects of hashish and speculated that naturally occurring psychoactive substances might well explain natural processes in the brain—a clear foreshadowing of modern psychopharmacology. However, his methodology was largely that of self-experimentation and introspection; he carried out some experiments with different doses on his pupils but lacked a method of systematic inquiry which emerged later with experimental psychology. It might be more accurate to propose Moreau as one of the earliest creators of a drug model for mental illness, as is indeed indicated by his monograph title.

However, Siegel and Hirschman (1983) described the earlier studies of A. P. Charvet, another French physician. Siegel and Hirschman regarded his *The Action of Opium and its Principal Constituents on Animal Conduct*, published in 1826, as “the first book on modern experimental psychopharmacology as well as the first book solely devoted to drugs and animal behavior” (p. 323). Charvet documented his comparative study of the effects of opium on a variety of species, ranging from humans to snails. Referring to his method as the “analytical path” (p. 323), he meticulously examined the effects of successive incremental doses on the same dependent variable under somewhat controlled experimental conditions (such as level of food intake).

Indeed, not until the 1890s was there was a serious attempt to apply the new methodologies of psychology that were being formulated in the philosophy departments of German universities to the study of drugs and vice versa. Of interest, James McKeen Cattell, Wundt’s laboratory assistant in Leipzig, did quite a bit of self-experimentation with psychoactive drugs during that time but did not publish any of the results. Like those of James (1882), the experiments were fishing expeditions to compare the relative effects of drugs, such as alcohol, cannabis, opium, and caffeine. After ingesting a drug, he then wrote an account of the effects he observed. Our knowledge of this experimentation comes from his personal journal and his notebooks of the years at Leipzig (Sokal, 1981).

Emil Kraepelin (1856–1926) is commonly known in psychology and psychiatry for developing an early classification scheme for mental illnesses and clinical descriptions of schizophrenia (dementia praecox). Increasingly well known are his contributions to psychopharmacology. He is credited with the first “scientific” treatise proposing that drug action reflected underlying neural mechanisms and, indeed, with the first use of the term *psychopsychology* in 1892 (Healy, 1997; Kraepelin, 1982/1892). While still a student of Wilhelm Wundt in the early 1880s, he studied the effects of “poison on mental reactions” and used tests of the effects of alcohol (Kraepelin, 1897, p. 25). According to Kraepelin’s (1997) *Memoirs*, while working in Wundt’s laboratory he was engaged in studies of the

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1 Lehmann (1993) states that Macht, a pharmacologist at John Hopkins, made the first use of the term *psychopharmacology* in 1920.
effects of various “poisons,” such as alcohol, on mental reactions. In 1883 he “planned to expand tests with drugs, coffee and tea and to measure the mental reactions of psychiatric patients to get a better idea of the mental changes” (p. 28). His initial work, however, was concentrated on examining individual differences in the drug responses of normal subjects. Upon leaving Leipzig to take up a post in Dorpat, he and his assistants continued experiments on the influence of tea and caffeine on mental reactions. Specifically, he established a consistent dependent variable, the number of syllables that could be read in a set period of time, and used that variable to compare the effects of various drugs. Based on his experiments with alcohol, he coined the term *drinker* as a scientific classification, along with a treatise on individual differences of what we would now call tolerance with implications for legal cases involving alcohol (p. 45). By the 1890s, he had broadened the scope of his experiments to examine the effects of alcohol and other drugs on a variety of mental and behavioral tasks. He also was now interested in investigating the relationship of the mechanisms of psychoactive drugs to mental pathologies:

We not only wanted to identify the behavior of the different intellectual processes in mental disease, but also the external and internal influences. As well as comprehension, the capacity to register, memory, association of ideas, all kinds of intellectual tasks, we particularly wanted to define the manifestations of will, the course of simple movements, the energy output, the expressive movements of writing and speech. Finally, it was important to measure the basic qualities of the personality, more exactly, for example, the capacity to practice, fatigue, practice durability, recovery capacity and distractibility. In this way, we hoped to gain insight into the different forms of pathological predisposition. (p. 63)

Kraepelin’s training as an experimental psychologist comes through clearly in the preceding passage. The behaviors mentioned are all typical behaviors of interest in those early years and were suitable for study by the new quantitative methodologies.

But while Kraepelin at least gets credit for his early contributions to psychopharmacology (cf. Healy, 1997, 2002), there was a considerable amount of experimentation going on in psychology by his contemporaries whose work seems to have been neglected. Although James (1892) and Cattell (Sokal, 1981) both wrote about their experiences with nitrous oxide (the former) and various other psychoactive drugs (the latter), it is perhaps not accurate to include their work in this discussion. Both engaged in self-experimentation and after taking a drug would record their qualitative observations. Their experiments were not systematic and did not really incorporate the new methodologies that were becoming so important to experimental psychology from the 1880s onward. Similarly, Freud (1984/1884) published “Über Coca” in 1884, extolling the drug’s virtues, but it contained little experimental work, only his personal clinical observations, anecdotal evidence from colleagues, and informal observations from self-experimentation.

By the early 1900s, the first generation of experimental psychologists began to apply the method of introspection to drug studies both by themselves and by
trained subjects. Although similar in their use of introspection, these researchers differed from Cattell and James in that they typically engaged in systematic, multitrial experiments in which they varied conditions and doses in a controlled manner and utilized a variety of dependent variables thought to reflect psychological functions. The earliest published studies were focused on assessing drug effects in terms of individual differences and also on elucidating the effects on behaviors of particular interest to the field, such as will (Partrige, 1900b), consciousness (Delabarre & Popplestone, 1974; Hoch, 1906; Scripture, 1893), and mental reactions (Partrige, 1900a). Scripture’s (1893) account of his self-experimentation with cannabis is noteworthy, not because of his introspection but because of his suggestions for future research. He proposed that psychomotor and perceptual measures be used before and during trials of drug administration, presumably to analyze further the effects he had experienced under the influence of the drug. His final statement is a refreshingly frank confession: “Owing to disagreeable aftereffects of the drug on my organism, I shall probably be precluded for some time, from carrying out these experiments myself” (p. 234).

Edmund B. Delabarre was another early experimental psychologist who researched the effects of cannabis over a 30-year period beginning in 1893, although he published only one report of his work (Delabarre, 1899). “A Cross Cultural Contribution to the Cannabis Experience” (Delabarre and Popplestone, 1974) is a posthumous account of Delabarre’s experiments with cannabis indica and cannabis sativa and is a striking example of multitrial experimentation, using himself and a few assistants as the participants, on a wide variety of dependent variables. Perhaps the most important result of these studies is Delabarre’s observations about the role of participant expectations as experimental confounds.

The most important work to be published during this time, judging by later citations, was the results of studies in 1906 on alcohol and other psychoactive drugs by Cambridge University psychologist, William Rivers. Trained first as a physician, the anthropologist-cum-psychologist gave a series of lectures to the Royal College of Physicians on his work in the newly founded psychological laboratory. These lectures were published 2 years later in 1908. In his introductory remarks, he noted that the principle guiding his choice of topic was the “desire to show that the science which I teach may be of service to medicine. In accordance with this idea, I shall limit myself to those aspects of the subject which seem to fall within the province of the experimental psychologist. Thus, I shall only deal explicitly with the methods and results of the experimental observations of the living man. . . .” (p. 1). He distinguished his work from previous research by others on lower organisms as purely physiological and stated that in studying humans, there are psychological factors that are “wholly absent in the work of the physiological pharmacologist” (p. 1). Although this point seems obvious to the contemporary reader, it was not so at the time, and Rivers’ discussion is remarkable in that he outlined many of the concepts that were to become a foundation for sound experimental technique. For example, he talked about the necessity of operationalizing dependent variables. In previous work “general fatigue” had been used as a measure, but Rivers pointed out that “muscular fatigue” is a better and

2 Popplestone and McPherson (1974) give a historical account of medical uses and early research on cannabis by early experimental psychologists and others.
more specific measure of drug effects (p. 7). Likewise, he discussed the problem in other research (e.g., Kraepelin’s studies) of measuring a general concept such as “mental fatigue” (p. 8). He discussed various psychological factors that can influence results, such as practice, that make conditions in drug experiments difficult to control. However, he noted that because one can detect individual differences in fatigue, measures of fatigue are ideal for isolating the effects of drugs. He went on to discuss problems that we would recognize today as experimenter bias, demand characteristics (noting that it has “plagued nearly all who have experimented on the action of drugs”), and the lack of placebo controls (p. 18). Rosenzweig (1933) outlined many of these experimental issues almost 30 years later in the now classic article on experimental design and confounding variables. Rivers’ experiments were perhaps the first published in which the drugs and placebos were disguised in a pill form and prepared and administered in such a way that the participants were unaware which one they were ingesting (p. 20). Habit-forming drugs have unique issues regarding tolerance and cravings that further complicate experimentation. The lectures also contained comprehensive literature reviews on previous experimental work primarily from the 1880s and 1890s, but Rivers suggested that much of the work was unreliable because of lack of experimental controls. In his conclusions, he reiterated that “the chief interest of the work which has been recorded in these lectures lies in its bearing on method” (p. 117).

Although Rivers (1908) certainly added a new rigor in experimental method, in a series of studies on caffeine the American psychologist, Harry Hollingworth (1912a; 1912b, 1912d, 1912e, 1912d, 1912e) took drug studies a step further. Rivers’ studies were based on the results of two subjects: himself and a trained assistant. Hollingworth had been hired by the Coca Cola Company to examine the psychological effects of caffeine, a key ingredient in the company’s product, to provide evidence on the safety of the drug in the company’s defense against a lawsuit being prosecuted by the U.S. government. An account of the lawsuit and Hollingworth’s involvement in what was the first use of experimental psychology in a legal proceeding is provided in Benjamin, Rogers, and Rosenbaum (1991). One of the conditions of Hollingworth’s involvement was that he would be able to publish freely the results of his experiments regardless of whether the outcome favored the company’s position or not. Thus, we have a record of his meticulous experiments incorporating suggestions by Rivers (1908), whose work is often cited, but perhaps more importantly, abandoning the introspective, self-experimental approach in favor of averaging the effects on multiple participants during a variety of experimental conditions.

By 1912 one of the leading American psychology journals, Psychological Bulletin, began a series of review articles specific to psychopharmacology that continued on an irregular basis until the 1930s. Hollingworth (1912c) reviewed 14 studies that had been conducted during the past 2 years, including his own five caffeine studies. He especially called attention “to the attempt to develop a rigorous experimental technique and a standardized series of tests for future work in this field” (p. 422). Poffenberger (1914, 1916, 1917, 1919), a colleague and collaborator of Hollingworth at Columbia, took up the next four reviews, covering an average of nine studies per period. There was a shift during this decade toward examining the addictive properties of many psychoactive drugs and/or individual activities.
characteristics, whether psychological or physiological, that might make one more
susceptible to becoming addicted. This focus, of course, reflects the contemporary
social issues of addiction that led to the passage of the Harrison Narcotic Act in
1914 and subsequent related laws. Hollingworth and Poffenberger (1917) estab-
lished psychopharmacology as an area of focus of applied psychology with the
publication of their landmark textbook of the same name. Jacobson (1921) carried
this further in his address to the American Medical Association, pointing out that
although many medical school curricula had incorporated various topics of
experimental psychology, such as attention and memory, drug studies were also
an important contribution. The study of behavior and “the general principles of
experimental psychology, if introduced into medicine, may put observation in the
place of opinion and speculation and may lead to a better understanding of the
human material one deals with” (p. 347).

Meanwhile, experimental attention to hallucinogens (e.g., Hoch, 1906;
Knauer & Maloney, 1913; Klüver, 1926, 1966/1928; Sutherland, 1914) continued
sporadically. Researchers had a particular interest in how the drugs, especially
mescaline, might relate to psychopathology, thus building on the early work of
Kraepelin and Louis Lewin (1850–1929) during the last decades of the 19th
century. Bender (1968) offered a fascinating account of the attempts by employ-
ees of Parke Davis pharmaceutical company in 1887 to obtain samples of
“pellote” (peyote) buttons from the American Southwest after the company
received a letter from a local apothecary describing its use in Native American
religious ceremonies. This interest ultimately led to the identification of mescaline
as the psychoactive agent almost a decade later. James (1905), in his On the
Varieties of Religious Experience, addressed the use of hallucinogenic drugs in
religious ceremonies but only in a descriptive manner. Leuba (1917) also dis-
cussed the relationship between drug intoxication and religious ceremonies. His
work is of especial interest because it is an attempt by an experimental psychol-
ogist to explain drug-induced hallucinations in terms of individual differences and
central nervous system effects. Lewin (1998/1931) summarized his early work on
hallucinogens in his 1931 book, Phantastica. Although Lewin did not consider
himself an experimental psychologist, nor did he publish in those circles, his work
was an important contribution to psychopharmacology. It is interesting that
investigations of the relationship of hallucinogens and mental illness picked up
again in the 1940s with the discovery of the hallucinogenic properties of LSD.
Albert Hofmann (1970) of the Sandoz pharmaceutical firm had first synthesized
LSD first in 1938, but he did not discover its now-famous effects until 1943 and
then it was by accident. In the account of his early work, he gives credit to the
previous research on hallucinogens in the 1890s to 1920s but notes the hiatus of
research until his work in the 1940s.

A quiet period for psychopharmacological research did seem to occur in the
interval between 1920 and 1950. One can speculate that this quietude was due to
a variety of factors. By that time much of the basic research on the specific effects
of psychoactive drugs had already been tackled. In the 1920s much of the research
turned to the problem of drug addiction (e.g., Bishop, 1920; Kolb, 1925). Even
experimental psychologists began to attend to this social issue (e.g., Hollingworth,
1931). Concomitantly, many of the psychoactive drugs had become difficult for
researchers in the United States to obtain since the passage of the Harrison
Narcotic Act in 1914. Subsequent federal laws restricted importation of opium and cocaine and criminalized nonmedical addiction (Courtwright, 2002; Musto, 2002). The methodological issues of operationalizing dependent variables and having experimental control over a variety of conditions were still under discussion by the late 1920s. At the same time, behaviorism was in the ascendancy in experimental psychology. Animal experimentation was thus on the rise, especially for applying the new theories of learning, and, consequently, the new behavioral techniques were used in drug research. Perhaps the very nature of psychoactive drugs, with their effects on states of consciousness—a concept uniquely human that was now relegated to the experimental “back burner” and plagued by more problems concerning experimental controls—discouraged researchers initially from further animal research. Another possibility is that as the respective fields of psychology and pharmacology, as well as other related disciplines, became more developed with distinct professional identities, cross-disciplinary research diminished.

However, another small but detectable trend in the early work done by experimental psychologists was the increasingly systematic use of behavior to elucidate the mechanisms of drug action. The majority of the research had focused on how drugs affect individual differences using various behaviors, ranging from the elementary (e.g., Schilling, 1921) to the more complex (e.g., Hubbard & Johnson, 1916). Better experimental techniques and particularly the spread of Pavlov’s work on the conditioned reflex contributed to this trend. As early as 1909, Igor Zavadskii performed a series of experiments on the effects of alcohol, morphine, cocaine, and caffeine on the conditioned salivary reflexes of dogs in Pavlov’s laboratory (Laties, 1979). It was one of the earliest examples of behavioral pharmacology. Mursell (1925) attempted to distinguish the physiological versus psychological effects of psychoactive drugs by using a sucking reflex. Of interest, he also hoped to prove wrong the current psychoanalytic explanation that “mild drug habits” were vestiges of dysfunctional oral stage development. Miles (1929) advocated using more complex motor behavior patterns (i.e., running mazes), rather than the isolated muscle responses favored by earlier researchers, as one would get a sense of the drug effect on the “whole animal” (p. 451). Skinner did some early work on the effects of various drugs (e.g., caffeine, amphetamine, and phenobarbital) on conditioning and extinction (Heron & Skinner, 1937; Skinner & Heron, 1937). Efforts to understand the growing problem of drug abuse using behavioral techniques were exemplified by the work of Shirley Spragg of the Yale Laboratories of Primate Biology, who used behavioral methods to study morphine addiction in chimpanzees (Spragg, 1940). This government-sponsored research was important in establishing the role of learning in an animal model of a condition that could not ethically be induced and controlled in humans.

Developments in psychopharmacology during the 1950s and 1960s are multitudinous and, frankly, beyond the scope of a single treatise. However, there are a few highlights that can serve as exemplars to help elucidate the influence that experimental psychology has had on the field. Behavioral pharmacology, a subdiscipline that was built upon the earlier work of Skinner, emerged during this time. Notable early contributors include Peter Dews, a pharmacologist who came to Harvard to work with Skinner’s associates, Roger Kelleher and William Morse.
and Joseph Brady, who spearheaded behavioral pharmacology programs at Walter Reed Army Medical Center and Johns Hopkins University (cf. Barrett, Thompson, & Dews, 1990; Brady, 1956). It is interesting that Dews was not trained originally as an experimental psychologist and Brady began his graduate work in clinical psychology but both utilized behavioral techniques that emerged from experimental psychology, especially in developing standardized drug screening methodologies for the pharmaceutical industry (Healy, 1998; Laties, 2003).

The study of individual differences in drug response was also a research area that emerged during the 1950s. Eysenck (1957, 1960) postulated that the personality types of introversion and extraversion reflected cortical arousal or inhibition, respectively, and so individuals with these personality types would respond differently to stimulant and depressant drugs. Subsequent research of this kind was of particular interest for its clinical implications in treating drug addicts as well as using pharmacological therapy for psychological disorders. At the same time, however, increasing concerns about the ethics of human experimentation with psychoactive drugs that were outside therapeutic consideration and mostly now illegal created a less congenial environment for research (Novak, 1997).

Finally, a corpus of research on nitrous oxide conducted during the 1950s and 1960s represents a distinct effort to meld together experimental psychology and pharmacology, returning psychopharmacology to one of its historical roots. The research is of historical interest for two reasons: first, it was a return to human research in which topics that had traditionally been the province of experimental psychology were explored; and second, it exemplified the duality of psychopharmacology in that some of the studies shed light on the behavior in question, whereas others help to explain the mechanism of drug action. Originally, nitrous oxide in these studies was used to classify and/or analyze behavior. The behaviors ranged from cognitive tasks involving reasoning, memory, and motor skills to other activities, such as time perception, size of handwriting, and subjective effects. Specifically, a series of experiments with low doses of the drug were conducted to investigate its effects on cognition (Steinberg, 1954), stress (Russell & Steinberg, 1955; Steinberg, 1955), time perception (Steinberg, 1955), visual perception (Steinberg, Legge, & Summerfield, 1961), abnormal behavior (Steinberg, 1956), learning (Steinberg & Summerfield, 1957), memory (Steinberg & Summerfield, 1959; Summerfield & Steinberg, 1957), incentive (Steinberg, 1959), and motor behavior (Legge, Steinberg, & Summerfield, 1964). Relatively little research on nitrous oxide has been done since then, perhaps because of the comprehensive nature of the original series of experiments (although see Armstrong, Morton, Sinclair, & Tiplady, 1995; Fagan, Paul, Tiplady, & Scott, 1994). The results of studies on cognition and memory (Steinberg, 1954; Steinberg & Summerfield, 1959; Summerfield & Steinberg, 1957) are perhaps the most intriguing in view of contemporary research on neural mechanisms of memory. The Steinberg experiments provide an example of how behavior is used to study drug action. Conversely, the results of the cognition studies also were the foundation for research during the next decade that contributed to the formation of the Atkinson–Shiffrin dual theory of memory (Atkinson & Shiffrin, 1968), thus showing how drugs can be used as tools to elucidate behavior.

So what then are the historical contributions of experimental psychology to the field of psychopharmacology? Certainly contemporary methodologies, both
quantitative and qualitative, have their roots in the discipline. From using trained observers engaging in introspection to the advocacy of double-blind, placebo controls, researchers in the burgeoning decades of experimental psychology sought to bring a more systematic, and thus scientific, method to the study of psychoactive drugs. It was through their work that issues, such as past experience (e.g., Rushton & Steinberg, 1964), experimenter bias, and demand characteristics, were identified, and subsequent solutions were developed. Although there was always an interest in showing a connection between drug-induced pathological symptoms and those observed in naturally occurring disorders, researchers did not limit their inquiries to that topic. Consequently, a large corpus of basic research developed on a wide variety of psychoactive drugs and behaviors. Forty years ago, Klüver (1966) in his preface to a reissue of his 1928 work, *Mescal: The “Divine” Plant and Its Psychological Effects*, lamented that “. . . the exploration of the ‘psycho’ in psychochemistry—that is, the specification and analysis of the psychic functions involved—has not kept pace with advances along chemical lines” (p. ix). He worried that the climate then favoring applied over basic research on psychoactive drugs would result in a limited perspective and thus restrict scientific discovery. The careful attention to methodology led to subsequent developments in psychopharmacology, such as drug combinations (e.g., amphetamine–barbiturate) (Rushton & Steinberg, 1963), which showed that the special effects of combinations, although heavily dose dependent, could surprisingly not be predicted from those of the individual drugs—a state of affairs alien to pharmacological thinking at the time.

Another contribution was the use of animal behavior to study drug action and to show how drug results obtained from more sophisticated animal experiments than had been seen in pharmacology studies could be extrapolated to humans. This approach emphasized the need and the utility for the thorough screening of new drugs. Thus, from psychology and its related discipline, ethology, researchers in psychopharmacology learned the value of complex sophisticated animal experimentation and provided systematic animal models with patterns of behaviors that seemed to be analogous to those observed in humans. Kršiak (1991) pointed to a 1963 Ciba Symposium on Drug Action as a landmark event in drawing attention to the utility of “natural action patterns in the study of behavioral effects of drugs” (p. 439). The influence of ethology is clearly seen in this statement, and there was a call for studying behavior holistically, not only so that effects of different drugs could be discriminated but also because the “evaluation of all identifiable behavioral elements occurring during the test increases the chance of detecting unexpected drug effects” (p. 440). By using these methods, drugs with traditionally “opposite” actions, such as barbiturates or benzodiazepines and amphetamines, were found in combinations to mutually potentiate each other’s actions. The use of drugs in combinations to produce favorable effects has now become widespread not only in psychopharmacology but also in general medicine, including cancer therapy. For example, dose–response ratios have been found to be parallel in rodents and humans (Rushton & Steinberg, 1963). The previously mentioned idea of using drugs as tools to study behavior was another contribution of experimental psychology (cf. Russell, 1960). Finally, by examining reciprocal relationships, the variety of behaviors studied by experimental psychologists did much to illustrate the mode of action of many of these psycho-
active drugs. This is a matter easily overlooked with today’s focus on the biochemical and molecular design of drugs. Whereas developing therapeutic drugs with selective neurochemical targets and minimal side effects is a valuable goal of contemporary psychopharmacology, that goal can be overshadowed if the behavioral or subjective effects of the drugs are not given pride of place.

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