JOURNAL OF THE EXPERIMENTAL ANALYSIS OF BEHAVIOR 1991, 56, 415-423 NUMBER 2 (SEPTEMBER)

BEHAVIORAL PHARMACOLOGY IN CONTINENTAL EUROPE: A PERSONAL ACCOUNT OF ITS ORIGIN AND DEVELOPMENT

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LOCATING THE FIRST OPERANT CHAMBER ON THE CONTINENT

The present paper does not offer a systematic historical account of the birth and growth of behavioral pharmacology in Europe. Desirable as it is, such an ambitious project would take us far beyond the limits, both in time and in space, of this special issue of the *Journal of the Experimental Analysis of Behavior*. I hope it will be carried out some day by the young European Behavioral Pharmacology Society. What follows may provide useful pieces of information. It is restricted to my own personal history and the history of the Laboratory of Experimental Psychology in Liège, and includes, of course, aspects of the international network that developed from individual encounters and joint scientific ventures. It will be no surprise that privileged interactions have been developing with geographically close territories and with areas sharing the same language (i.e., French). I shall leave out the United Kingdom, except to allude to some personal links, because behavioral pharmacology there had an early and indeed quite intensive development, probably due, at least in part, to direct linguistic access to American science.

I am indebted to a number of colleagues and friends for providing me with information on the early applications of behavior analysis to pharmacology on the European continent. I am especially grateful to Giorgio Bignami, R. Dantzer, Theo Meert, and Jef Slangen. I am of course fully responsible for errors or distortions in the use of the material they have provided. To keep the present paper within reasonable space limits, only selected references from our as well as from other laboratories have been included. This necessarily implies a selection, which means many omissions. The reader will easily complete his information by searching in the name index of textbooks for now classical contributions.

The present paper was prepared while the author was benefiting from a sabbatical grant from the *Fonds National de La Recherche Scientifique* of Belgium and enjoying the hospitality of Departamento de Personalidad, Evaluaciòn y Tratamiento Psicologico at the University of Granada. The expert help of Andrée Houyoux in editing *à distance* is kindly acknowledged.

Though I might have missed the work of other people (in which case I apologize and would welcome their informing me, so that I can correct the mistake), it seems that the origin of psychopharmacological research using operant techniques on the European continent can be traced back to the work carried out at the University of Liège (Belgium) from 1959. As in the life of an individual, the development of a science is often a matter of chance and of favorable circumstances concurring at a given time, rather than deliberate planning. This was the case for the birth of operant psychopharmacology in continental Europe. A short account of it requires some reference to my own personal background.

In September 1959, I returned to Belgium, after having spent 1 year at the Department of Experimental Psychology at Harvard. This had been the final step (and a decisive one indeed) in a long period of university education that had started in Liège with a degree in Philosophy and Letters, was followed by a degree in Psychology in Geneva, then dominated by Piaget, and continued with a year of interdisciplinary field research in central Africa (which eventually provided the topic for a doctoral thesis). I was offered a position that could be compared to that of a British lecturer, associated to the chair of General Psychology that was part of the Faculty of Philosophy and Letters. I had been impressed at Harvard by B. F. Skinner's theoretical and methodological achievements and was determined to import operant techniques ("Canonical papers," 1984; Richelle, 1976, 1978, 1988, in press; Skinner, 1938, 1969, 1972, 1987). In spite of all his generous support that enabled me to start a laboratory, Professor J. Paulus could not provide me with space and technical facilities. I had to turn to some university department more prepared to host an experimental psychologist. Here is where chance comes into the picture. A friend of mine, recently trained in the United States, was a member of the Pharmacology Department at Liège, where he did experimental work on the cat's brain. He was looking

for cooperation with a behavioral scientist. He suggested that I join him and persuaded Professor M. J. Dallemagne, a renowned expert in calcium metabolism, to admit me to his laboratory. Dallemagne was an exceptionally friendly and open-minded man, who was ready to give any truly devoted young researcher a chance to develop new areas of research. As a professor of pharmacology, he was aware of the recent developments and of the future prospects in the field of neuropharmacology. I found myself immediately sharing whatever space was available as well as technical facilities, and had the first homemade operant chamber built in the shop. Jean Schlag (my neurophysiologist friend), like many brain experts in those days, used cats in his acute experiments; I trained cats to depress a lever, and continued to use them for many years. On-line control circuits were electromechanical devices, modeled after those I had seen in Mem Hall and at the Waltham Hospital operant conditioning unit (where I had spent many stimulating hours with Ogden Lindsley), but they were homemade assemblies of pieces purchased from the U.S. Army surplus stores.

Being a guest in a medical school laboratory, courtesy dictated that I would give something in return to my hosts. Operant techniques had recently been applied to the rapidly developing field of experimental psychopharmacology in the United States. While at Harvard, I had had the occasion to meet P. Dews, W. Morse, and other pioneers. It seemed obvious that I should start some drug experiments. The operant procedure was all the more welcome because Schlag and another researcher, J. Faidherbe, were at that time painstakingly trying to automate a shuttle box for cats for studying psychotropic drugs. They were easily persuaded that the operant conditioning chamber was a far more efficient device for that purpose. By December 1959, the ship was launched, and I could leave for another 6 months' stay in central Africa, while Faidherbe conducted experiments with the first continental cats employed in behavioral pharmacology.

First Publications in Behavioral Pharmacology

The first paper to result from this research, co-authored by Faidherbe, Schlag, and Richelle, was published in French in the *Archives Internationales de Physiologie et de Biochimie* in 1961, mentioning the date of receipt of the manuscript as December 6, 1960. It was a study of the effects of methylphenidate on operant responding in what could be described as a multiple schedule involving a 75-s extinction period followed by a signaled continuous reinforcement period that terminated with the first (reinforced) response. The emphasis was on the drug's effects on the acquisition phase—stable behavior being little altered—and on interindividual differences. The use of the term "operant"—a neologism in French, with no accent on the e—was briefly legitimated in a footnote. References were made to earlier contributions of operant techniques to psychopharmacology, namely Dews (1965), Sidman (1959), Brady (1959), and, of course, Ferster and Skinner (1957).

This paper was soon followed by another study (Richelle, 1962) submitted by February 1, 1962, to the *Archives Internationales de Pharmacodynamie,* again in French and on cats. It was the first exploration in our laboratory of the action of a compound in the recently created class of benzodiazepines, namely chlordiazepoxide, on operant behavior controlled by a fixed-interval schedule. It was also the first appearance of the expression *régulations temporelles—temporal regulations of behavior* as we have come to use it in English as well—to designate the patterning of behavior typically observed in temporally defined schedules, and the origin of a line of research on time in nonhuman and human behavior that was to develop steadily since then in our laboratory (see Richelle, 1968b, 1972, 1977; Richelle & Lejeune, 1979, 1980a, 1980b, 1984, 1988; Richelle, Lejeune, Perikel, & Ferry, 1985).

The first two papers in English appeared in the same year. One, in the *Journal of the Experimental Analysis of Behavior,* was a short observation on nonconsumption of the reinforcer under drug action, incidentally made in the study on cats treated with methylphenidate (Faidherbe, Richelle, & Schlag, 1962). The other reported results on rats trained on a fixed-interval schedule under chlordiazepoxide (Richelle, Xhenseval, Fontaine, & Thone, 1962). It was published in the first volume of the newly created *International Journal of Neuropharmacology.* This publication was significant in two respects. It was the first research carried out in association with students attracted by the new field; these were medical students who

came to behavioral pharmacology as an addition to their normal assignments. Two of them eventually became psychiatrists, and were to contribute in a decisive manner to the development of behavior therapy in Belgium. O. Fontaine is still affiliated with our laboratory as a senior researcher while teaching behavior therapy; he has been the founder and the President of the Belgian Society of Behavior Therapy and Behavior Modification and the President of the European Society. Second, the paper was reissued in 1970 in *Readings in Behavioral Pharmacology,* edited by Thompson, Pickens, and Meisch (Richelle, Xhenseval, Fontaine, & Thone, 1970). This we took as recognition of the quality of our modest contribution to the field and a valuable encouragement to pursue further work.

From 1962, research on minor tranquilizers and drug effects on temporal regulations continued to develop, but other lines of investigation were also followed. Among these, studies on behavioral effects of chronic treatments (chlordiazepoxide, diazepam, meprobamate, morphine, dextromoramide, etc.) deserve mention, including a replication of the self-administration technique designed by Weeks (1961) and by Thompson and Schuster (1964), adapted to dogs (Fontaine & Richelle, 1964). Self-administration was discontinued, for various reasons related to financial and human resources. I still think that this was a mistake.

An Ethological Digression

In the meantime, a new department of psychology was created in Liège, with a curriculum that was very innovative compared to what was offered then in other continental universities. I had been appointed as associate professor in 1962, then as full professor in the Chair of Experimental Psychology in 1965. From 1962, psychology students would become the main population of the laboratory. After initial training in their practical work in experimental psychology in general, some of them eventually turned to behavioral pharmacology as the topic of their master's thesis or, later, of their doctoral thesis. They were systematically encouraged to complete their training abroad, with the consequence that some of them settled down there. Themes of research were progressively diversified, psychopharmacology keeping its place, but with, in addition, temporal regulation, cognitive development, language, neuropsychology, mental retardation, and others. Special mention should be made of early studies combining operant conditioning and the ethological approach. These were favored by my friendship with J. C. Ruwet, the colleague who held (and still holds) the Chair of Ethology and Animal Psychology at the Biology Department, most of his teaching being addressed to psychology students (ethology was already a compulsory subject in their curriculum). One of the best master's theses we ever had concerned the use of operant conditioning to analyze hoarding behavior in the Syrian hamster in a seminatural environment. The student, J. Godefroid, had designed a terrarium based on a model used by Eibl-Eibesfeldt that permitted easy observation of the galleries and specialized territories dug into the ground by a pair of hamsters living permanently in the huge experimental device. Around-the-clock recording of operant activity enabled a chronobiological analysis. Data were unambiguous and new in several respects; more important, the approach was original and opened new perspectives toward joint research projects with ethologists. The paper, coauthored by Godefroid, Ruwet, and myself, was eventually rejected by the *Journal of the Experimental Analysis of Behavior,* in spite of a concise and enthusiastic review by one of the referees, who thought the paper had "a fresh ethological flavor" and should be published with some minor improvements in style. Changes required by the other referee would have taken all the substance out of it, and we were not ready to make them. In the meantime, Godefroid had moved to Canada, and Ruwet and I had other priorities. The paper is still in our files. I still think it would have been one of our best contributions, but it was probably untimely in the American context of behavior analysis. As early as 1969, a small (by invitation only) international symposium was organized in Liège by Ruwet and myself on methodological issues in the comparative study of behavior (Richelle & Ruwet, 1972). Among the participants were H. S. Terrace, P. Broadhurst, Baerends, members of K. Lorenz's group, and French ethologists and psychophysiologists. Although most of the sessions were in English, the publication was in French (Richelle & Ruwet, 1972). American readers will understand how outdated and strange to our European minds appeared the

somewhat bitter debate over the phylogenic aspects of behavior that took place in the late 1970s between R. J. Herrnstein and Skinner.

Propagating the Behavior Analysis Approach in Pharmacology

Being, I presume, the importer of operant methodology to continental Europe, or at least to the French-speaking area, I felt responsible for its dissemination, and of its potentialities in various fields of application, including psychopharmacology. An introduction of operant conditioning for French readers that included a chapter on psychopharmacological applications was published in book form (Richelle, 1966). It provided illustrations from American pioneers in the field as well as from our laboratory. B. F. Skinner, who loved the French language, published a review of the book in *JEAB* (Skinner, 1967), which Catania (1989) mentions as the first book review published in that journal.

The links with the department of pharmacology were extremely favorable for informing our medical colleagues. I was asked to lecture for various audiences of pharmacists or physicians. In 1963, the local medical journal—a scientifically serious periodical produced by the medical faculty—published a general paper on experimental psychology and psychopharmacology (Richelle, 1963). In 1968, I was offered the opportunity to present an address to the annual meeting of the international association of French-speaking physiologists that took place in Lyon. I took the occasion to deliver a methodological paper on the integration of behavior as a variable, both dependent and independent, in pharmacological research; an extended, 50-page version was to appear in the *Journal de Physiologie* (Richelle, 1968a). It referred to more than 150 papers, including two dozen from our laboratory. In 1969, I was asked to coconvene, with E. Jacobsen from Copenhagen, who was the chief editor of *Psychopharmacologia,* a symposium on behavioral approaches in an international meeting on neuroleptics that was organized in Liège by J. Bobon, the psychiatrist who had carried out the first clinical tests on haloperidol (Buser et al., 1970).

Participation in multidisciplinary meetings as a representative of behavioral science continued to be and still is for me more rewarding than attending exclusively psychological meetings. Special mention should be made of the unusually informal and, therefore, perhaps unusually stimulating group of individuals, initially based in Marseilles, with extensions over France, Belgium, Switzerland, Austria, Germany, Italy and Spain, that labeled itself *Association pour la Méthodologie de la Recherche en Psychiatrie.* For more than 20 years, it has promoted scientific contacts between psychiatrists and scientists in various other fields, including behavioral psychopharmacology. Whatever they might owe to me, I owe much to the colleagues met there.

Behavioral Pharmacology in Belgium

This general context explains the peculiarities of the propagation of the experimental analysis of behavior in Belgium. Although Belgium is a small country, where contacts between university laboratories are easier to promote and maintain than in the Boston area, and although personal relations between experimenters have usually been friendly, psychological laboratories other than those in Liège showed little interest in operant techniques; they were more concerned with the then-growing area of cognitive psychology, and had little or no tradition of nonhuman research. One exception was the Laboratory of Experimental and Comparative Psychology headed by Georges Thinès at the Catholic University of Louvain, where operant techniques were used for psychopharmacological purposes. In addition, these techniques also found their place in neurophysiological laboratories, mainly in the same university, in Michel Meulders' group, where studies on brain self-stimulation were conducted in the late 1960s, and where behavioral pharmacology research took place soon after, and later in the psychophysiology laboratory at the Flemish University of Leuven.

However, the main expansion of operant research was to take place in the drug industry. Paul Janssen, who was to become a prominent European figure in neuropharmacology, had founded a company in which research laboratories had a privileged place, covering the traditional range from chemistry to physiology, but with an emphasis on behavior that was not the rule on the continent in those days. From the late 1960s, intensive explorations of the properties of butyrophenones included

highly automated screening in operant chambers. C. Niemegeers has been especially responsible for that area. With the success of various compounds, Janssen's company eventually became an international success, and still more resources were invested in basic research. Operant procedures were further put to work, by F. Colpaert, in drug-discrimination research, among other areas.

Operant research units of a more modest size were also established in other industrial laboratories in Belgium, in *Union Chimique Belge,* under the initiative of C. Giurgea, and at Labaz, where it was discontinued for organizational reasons, neuropharmacology being concentrated in the French plants (now part of the SANOFI group).

The French Connection

The picture was quite similar in France. The invited lecture that I gave at the 1967 physiology meeting, or the paper published thereafter, had seminal value, as testified to later by some investigators who started using operant techniques. One of them, a veterinarian, R. Dantzer, was soon to build his own operant chambers for pigs at the Toulouse laboratory of the French National Institute for Agricultural Research, and to engage, in the early 1970s, in the study of anxiolytic drugs. Incidentally, Dantzer had initially come across operant techniques at the Institut Marey, the neurophysiological laboratory of the College de France, headed by A. Fessard and his wife, S. Albe-Fessard, where a young psychophysiologist, Jean Delacour, had included them in his doctoral research on learning mechanisms. Dantzer eventually completed his thesis in 1977, acknowledging his debt to, besides myself and Delacour, David Sanger and Giorgio Bignami. He was later to join the *Institut National de la Santé et de la Recherche Médicale* neurobiology group in Bordeaux and is one of the founding members of the European Behavioral Pharmacology Society.

In spite of my close personal relationships with French colleagues, operant conditioning techniques never became very popular in French psychological laboratories. It is typical that Dantzer was not trained as a psychologist. Most users of operant methods, like Delacour, were neurophysiologists or psychophysiologists who had been convinced of their efficiency, or were psychologists affiliated to neurobiology laboratories. For instance, in the late 1960s, in the Strasbourg laboratory developed by Mandel and later headed by P. Karli, a young psychologist, Bruno Will, was conducting experiments on operant conditioning in rats focusing on inter- and intraindividual variability in simple motor responses, a major aspect of behavior that was completely neglected by many well-established researchers in those days. He had made contact with us at the Liège laboratory, and I served on his thesis jury. He is now a renowned expert on the neurobiology of ontogenic development and head of the Strasbourg laboratory. One of my students, J. Maurissen, trained in neurochemistry in Strasbourg after completing his degree in psychology in Liège, before moving to Rochester where, as a graduate student, he studied behavioral toxicology in V. Laties' and B. Weiss' department. He was trapped in the brain drain, and is now established at Dow laboratories in Michigan.

Operant techniques were soon in use at the important CNRS neurophysiology and psychophysiology laboratory that was developed in Marseilles in the early 1960s under Jacques Paillard's directorship. In fact, the first lecture I gave outside Belgium on operant techniques, reporting on our early pharmacological studies, was in Marseilles, in 1961, at the invitation of J. Paillard, before his Institute was built. A few years later, one of my first students, Françoise Macar, moved to Marseilles, where she developed research on physiological aspects of timing behavior in cats, extending her previous work in Liège on purely behavioral aspects. The Marseilles laboratory was soon to become familiar with operant procedures in refined psychophysiological studies on psychomotor performances in nonhumans, especially monkeys, carried out mainly by J. Requin's group.

Among other psychopharmacological laboratories where operant techniques were used, P. Buser's in Paris, P. Cardo's in Bordeaux, and V. Bloch's CNRS group at Gifsur-Yvette deserve mention. In Buser's laboratory, studies of EEG correlates of conditioned behavior were conducted by A. Rougeul-Buser; Cardo has contributed to the study of electrical brain self-stimulation; Bloch and his co-workers have been focusing on memory processes and sleep, among other themes.

Temporal regulations of behavior, our label

for timing behavior and time estimation tasks, had become by that time one major theme of research in our laboratory, and this remains one of our main interests. Shared interest in the psychology of time, besides a number of other circumstances, was to favor a close and fruitful relationship with Paul Fraisse in Paris, who encouraged one of his students, Viviane Pouthas, to start animal research using differential-reinforcement-of-low-rate schedules. This evolved into a long-term cooperation involving our "Time Group," expertly headed by the most dedicated co-worker, Helga Lejeune, who was partner in many of our joint ventures on time in animals and humans (Lejeune, 1990). Twinning projects involving Liège, Marseilles, Paris, and later Manchester (with John Wearden) developed and received support from various national and international agencies, including the European Training Programme in Brain and Behavior Research that gave a decisive impulse to many cooperative projects involving behavioral sciences in the 1960s and 1970s (and continues to do so under the administration of the European Science Foundation in Strasbourg).

As in Belgium, but with a delay of several years, operant techniques were adopted in pharmacological laboratories. In Paris, P. Simon's group was probably the main INSERM-University team to develop sophisticated behavioral studies, mainly conducted by P. Soubrié and M.-H. Thiébot. Drug companies took more time before including specialists in nonhuman behavior in their research team, R. Porsolt being the first, at Synthélabo, followed much more recently by D. Sanger in the same company, and in the late 1980s, by F. Colpaert, who moved from Janssen in Belgium to Servier in Paris (and has very recently moved on to Pierre Fabre Medicament at Castres), and by the transfer of Soubrié from the university context to one of the research laboratories of the SANOFI group in Montpellier.

The Dutch and Italian Links

In Holland, operant chambers seem to have been introduced first in the early 1960s by Jacques van Rossum at the Department of Pharmacology of the University of Nijmegen. In 1964–1965, J. Slangen introduced them in Utrecht at the Rudolf Magnus Institute. Early work was on eating and drinking behavior; self-administration studies followed, and more recently drug discrimination has become a major theme. Slangen played a central role in developing behavioral pharmacology through his teaching of psychophysiology and through his research at the University of Utrecht, Faculty of Social Sciences. Operant techniques are now widespread in Dutch laboratories in various fields of the neurosciences, with a special place devoted to neuropharmacology.

In Italy, the origin of behavioral pharmacology can be traced back to the 1950s in work done in Nobel Prize winner Daniel Bovet's laboratory in Rome and at the Milan Institute Mario Negri, with L. Valzelli and S. Garattini. The latter group initially focused on social interactions in rodents. In Rome, Bovet, together with G. L. Gatti, pioneered the study of drug effects on acquired behavior, using pole climbing, mazes, and various discrete trial tasks. They soon turned to the study of drug effects on acquisition proper, leading to their description of facilitative effects of nicotine. Operant techniques were used from the early 1960s. In 1966, Gatti published results in an Italian journal showing differential effects of haloperidol and chlorpromazine on response rates in multiple fixed-ratio fixed-interval schedules in pigeons (Gatti, 1966). Continuous signaled avoidance was used in studies aimed at distinguishing behavioral effects of compounds previously impossible to distinguish behaviorally (Gatti & Bovet, 1963). G. Bignami joined Bovet's group in the early 1960s. In a joint project with P. L. Broadhurst, Bignami performed the initial selection experiment that led to the Roman High Avoidance (RHA) and Roman Low Avoidance (RLA) strains of rats (Bignami, 1965; Bignami & Bovet, 1965). In 1964, these strains were moved to Broadhurst's laboratory in Birmingham, where the selection was continued and the strains used in a number of experiments in behavioral genetics, including pharmacogenetics. Gatti and Bignami headed the research group at the *Istituto Superior di Sanita* after Bovet left in 1965. They continued to pursue behavioral research in an unusually refined way for pharmacological laboratories. Their contributions have been on the central antimuscarinic syndrome, on the multiple systems believed to be involved in response activation and response suppression as affected by

antimuscarinic and anxiolytic agents, on the comparative effects of benzodiazepines and barbiturates on continuous avoidance, and, more recently, on early ontogenetic aspects of exposure to drugs (Bignami & Gatti, 1969; Gatti, 1967). The latter area of research was selected by one of my students, E. Tirelli, for a doctoral thesis under joint supervision of G. Bignami and myself, presented in Liège in 1987 (Tirelli, 1989, 1990).

The above-mentioned laboratories and individuals, as underlined in the first paragraph, became part of a network of interactions materializing in exchanges of students, joint projects, reciprocal visits, and common involvement in scientific meetings. As might be expected, the First European Meeting on the Experimental Analysis of Behaviour, organized in Liège in 1983, included one important symposium devoted to behavioral pharmacology (Lowe, Richelle, Blackman, & Bradshaw, 1985). A satellite symposium held in French was devoted to depression, and included some behavioral contributions. In the second European meeting, held in Liège in 1988, behavioral pharmacology was given its place, with C. R. Schuster being a special American guest, and with a satellite symposium on drug addiction.

Behavior in Pharmacology, Still a Challenge

Let me come back to the activities of Liège laboratory and conclude with some reflections on the current state of, and trends in, behavioral pharmacology.

As already mentioned, being responsible for the development and teaching of experimental psychology in the Institute (later Faculty) of Psychology, I was not expected to confine myself and my students exclusively to the field of psychopharmacology. A number of other topics were developed through time. Some of them have been evoked above, because of their close relation with operant research and behavioral pharmacology. Others will be ignored here, because they are more distant from our present concern, although they implied genuine combinations of experimental analysis of behavior and other experimental and theoretical traditions. For example, research carried out from the late 1960s on dealt with Piaget-type problems in cognitive development using progressive errorless training procedures, or, in a different vein, with creative behavior. Further developments eventually led to more recent studies on the theme of behavioral variability.

Research in behavioral pharmacology continued, notwithstanding, with an emphasis on behavioral effects of benzodiazepines, including tolerance after chronic treatment, potentiation in combination with other agents (such as amphetamine) up to the study of contextual effects in tolerance and withdrawal in doctoral research currently in progress (Jodogne, 1990; Jodogne & Tirelli, 1990). Antidepressant drugs were also explored (Emilien, 1984), current research bearing upon their possible actions on anticipation and timing mechanisms. Other fields of research that have received attention more recently include early treatments with drugs in infancy and effects of stress on immune reactions. In the field of temporal regulation of behavior, the emphasis has been put recently on a developmental approach, that is, subjects in early stages of growth (birds from eclosion, rats from the 16th day) and senescent subjects (Lejeune, 1989; Lejeune, Jasselette, Nagy, & Perée, 1986; Lejeune & Nagy, 1986). These topics converge with an increased interest among psychopharmacologists for drugs that act on cognitive capacities, reflecting a general concern for aging in modern societies and a widespread obsession with mental deterioration in individuals facing ever-longer life expectancy.

The development of this new area of investigation in behavioral pharmacology suggests some concluding reflections as to the role of the experimental analysis of behavior at the present stage of neuropharmacological science. Neuropharmacology has largely benefited from the exploding progress in the neurosciences in the last 40 years. The study of behavioral aspects has been more and more integrated in refined studies at the neurochemical and neurophysiological levels, either as a tool for identifying and differentiating mechanisms of action or as a complementary verification of hypothesized processes involving drug action in relation to brain chemistry of neurotransmitters, neurohormones, neuropeptides, and the like. We are, undoubtedly, very far from early studies pointing to the straightforward effects of psychotropic drugs on behavior or demonstrating the importance of drug–behav-

ior interactions. However, looking at the current state of the art, it would seem that, in spite of exceptional developments in all directions, or perhaps because of these exceptional, and to some extent unmanageable, developments, very simple things need to be pointed out repeatedly with respect to behavior. One early lesson from behavior analysis was that different drug effects can be observed depending on the schedule of reinforcement. Therefore, one should avoid any general qualification of the properties of a given drug (e.g., in terms of anxiety reduction, sedation, antidepressant action, activation, etc.) on the basis of results obtained in one single test. This now sounds like a rather trivial statement for an introductory textbook. However, overgeneralizations are still frequent, especially (curiously enough) in those areas where the sophistication of psychological research would normally lead to more subtle views. For example, it is not rare that, in their quest for cognition-enhancing compounds, psychopharmacologists turn to exceedingly simple and single tests, such as one-trial passive avoidance, to draw conclusions about positive effects on memory. It is evident, however, that because it has such far-reaching implications for the future of our societies, the study of drugs and cognition requires the sort of critical refined approach, at the behavioral level, that characterized early contributions of the experimental analysis of behavior to pharmacology. Appropriate procedures are available and have been used extensively in basic psychological research, but it remains to introduce them into psychopharmacology and to apply them to the exploration of new compounds potentially active on memory processes, problem solving, attention, and the like. There is still a place, right now, for an essentially behavioral analysis of drugs in the future that is by no means exclusive of a more strictly integrated "brain and behavior" approach, the fruitfulness of which is evident. But for the sake of neuropsychopharmacology and its clinical applications, warnings against the temptation of "the flight from the (behavioral) laboratory" are still appropriate.

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