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Creation and First 20 Years of the Society for the Stimulus Properties of Drugs (SSPD)

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OVERTON, D. A., J. A. ROSECRANS AND H. BARRY, III. *Creation and first 20 years of the society for the stimulus properties of drugs (SSPD).* PHARMACOL BIOCHEM BEHAV **64**(2) 347–352, 1999.—Clinical observations and novels in the 19th century recognized that memory of some events can be retrieved only under the influence of the same drug condition that was present during the event. This dissociative effect of drugs probably reflects the same drug effects that were later called the discriminative stimulus effects of drugs. The Society for Stimulus Properties of Drugs (SSPD) was founded in 1978 as a forum for communications and periodic meetings on this drug effect. During its early years many of its members were psychologists, but subsequent to that time the most frequent research application has been for the pharmacological purpose of identifying new drugs that have the same discriminative stimulus attributes as a prototype training drug. The majority of members have been in the United States, but several major international meetings have been in Europe. The methods used by the society's members involve both neuropharmacological and psychological processes, allowing them to make unique contributions to the study of both mind and brain. © 1999 Elsevier Science Inc.

SSPD Drug discrimination History Stimulus properties of drugs

MEMBERS of the Society for Stimulus Properties of Drugs (SSPD) are interested in a specialized topic that combines concepts from psychology and pharmacology. The authors of this historical account were the first three presidents of the SSPD, and hope that our memories and records of the creation and early history of this society may provide useful information for those interested in the society.

EARLY RECOGNITION OF THE DISSOCIATIVE EFFECTS OF DRUGS

Reports of dissociation produced by drugs date from the first half of the 19th century. European physicians were fascinated with dissociative phenomena. Medical textbooks devoted entire chapters to amnesia, fugue states, and cases of multiple personality. Combe (12) reported in 1830 that a reversible amnesia could be produced by drugs. The first novel to popularize amnesia due to a change in drug condition was published in serialized form in a London newspaper for popular amusement by Collins in 1868 (7). Before the end of the century, Ribot developed a comprehensive theory that attributed both drug-induced dissociation and the clinically observed dissociative amnesias to interoceptive stimuli (37). All of this exuberant interest was based on clinical observations, and we know of no experimental studies on this topic in the 19th century.

The high level of interest in dissociative processes and the stimulus properties of drugs apparently disappeared at the beginning of the 20th century. Perhaps amnesia then came to be attributed to dynamic repression of urges from conscious awareness as suggested by Freud (15). Freud's ideas certainly altered the conceptual frameworks of the clinicians who, in the 19th century, had been the main source of the reports of amnesia produced by drugs and by other events. For whatever reason, published references to dissociation produced by drugs disappeared from the literature around 1900.

Interest in state-dependent learning was revived shortly before the middle of the 20th century. American psychologists were persuaded that sensory stimuli controlled behavior. Notably, Guthrie, in 1935, popularized a model under which all sensory stimuli played a role in controlling behavior (21). If so, the subjective effects of drugs might alter memory retrieval, and what appeared to be an effect of a drug on performance might, in fact, be an effect of the stimulus properties of the drug on memory retrieval.

Another impetus for the studies on state-dependent learning also appeared in the 1960s. Physiological psychologists were making new models for how the brain might work, and some of these models predicted that drug effects would dissociate learning. When Girden and Culler reported the first ex-

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perimental demonstration of state-dependent learning in 1937, they proposed one such model (18) that was described in contemporary textbooks. Hebb, Overton, and Sachs also published models that predicted that drugs could directly control memory retrieval without the intervening action of drug-produced stimuli (23,31,39).

After the pioneering report by Girden and Culler, the next several experiments explicitly designed to test for the occurrence of state-dependent learning were inspired by Neal E. Miller. Their purpose was to control for drug stimulus effects in studies designed to identify the effects of drugs on behavior. These experiments were performed by several of Miller's students, including Auld, Conger, Grossman, and Barry (1,4, 13,20). Additional reports indicating that drug-induced stimuli could exert behavioral control came from Belleville, Barry, Harris, and Balster, among others (3,5,22). As a group, these reports initiated the scientific study of the stimulus effects of drugs. A curious feature of this era is the fact that the 20th-century investigators of stimulus properties of drugs were apparently unaware of the 19th-century interest in the same topic (35,36). Siegel eventually corrected this oversight by workers in the field, and reestablished an appreciation of the 19th-century contributions to the area (43,44).

TRAINING DIFFERENTIAL RESPONSES TO DRUG STIMULI

The most effective method for measuring the stimulus properties of drugs is to reinforce different responses, depending on whether the animal is in a drug or nondrug condition. Obstacles to this technique include the limitation of using only one of the conditions, drug or nondrug, in training sessions on any given day, and uncertainty whether the drug stimulus will be strong enough to enable the differential choices to be learned in a reasonably small number of sessions. Although Conger was the first to use a drug-discrimination training procedure, subsequent reports by Overton attracted much more scientific attention, perhaps because they linked drug discrimination to the then more striking phenomenon of state-dependent learning (31,32). Overton used a T-maze task, in which rats had to run in one direction when drugged and in the opposite direction when undrugged. Drug control of responding was demonstrated with high doses of several psychoactive drugs.

Overton's findings were followed by improvements in the technique. Several investigators used a choice between two levers in a chamber, with food as the reinforcement for hungry rats (6,22,24,28,29). In this preparation, tests of lever selection at the beginning of each session, prior to the first food reinforcement, allowed the determination of whether and how rapidly the animals learned to discriminate drug from nondrug conditions. With this procedure, discriminative responses could be established with low doses of drugs. Soon after, Schuster and Brady, using rhesus monkeys, and Colpaert, using rats, started using a fixed ratio schedule on both levers (9,42). This induced a high rate of responding, which was exclusively on one lever during the test prior to the first reinforcement. Overton, using these techniques and the additional procedure of training with progressively lower doses, demonstrated discrimination of very low doses of several drugs (34).

UTILIZATION IN PHARMACOLOGY AND MEDICINAL CHEMISTRY

The attractiveness of evaluating drug actions via discriminative stimulus control of behavior by a drug, rather than via less specific procedures such as drug effects on unconditioned behavior, was demonstrated early in the 1970s by several pharmacologists including Hirschhorn, Rosecrans, Schechter, and Winter (25,41). The goal of research in their laboratories was to determine mechanisms of drug action, and especially those of drugs that induced a high level of dependence in humans including nicotine, alcohol, and morphine.

Medicinal chemists such as Glennon also began to use the discriminative stimulus procedure to evaluate chemical analogues of specific training drugs (17). The discriminative stimulus procedure provided the chemist with a selective and specific tool by which to evaluate structure–activity relationships or medicinal mechanisms of action of compounds within a given pharmacological class. For some, the potential to evaluate mechanisms and sites of drug action in the brain appeared to be enormous (38).

DRUG DISCRIMINATIONS AND ABUSE LIABILITY

Attention to the discriminative stimulus properties of drugs by investigators interested in drug abuse has passed through several distinct phases. The first contact involved investigators such as Goodwin, who thought that the state-dependent effects of alcohol might be the cause of alcohol-induced blackouts and related to the abuse liability of ethanol (19). Later, Overton argued that drug discrimination results with a variety of drugs might predict, or at least provide information about, the subjective effects of drugs presumed by many to underlie their abuse (33). From that time forward, many laboratories working on drug abuse included drug discrimination studies among the approaches that they employed. The third point of contact between drug abuse researchers and the SSPD involved investigators who believed that drug discrimination studies in humans might provide better, or at least different, information about the effects that caused abuse of drugs than could be obtained by asking drugged subjects about their subjective experiences. This orientation led to drug discrimination studies in human subjects. For example, Kallman published the first study to show that humans could detect different levels of nicotine using a two-lever operant procedure (27).

COMMUNICATION BETWEEN USERS OF DRUG DISCRIMINATION

Most of the early research on stimulus properties of drugs was by psychologists. They reported their findings at psychological meetings and published them in the standard psychological journals. However, this did not entirely meet their needs. They were young investigators creating a new field. They wanted to popularize their innovative work and meet one another to swap ideas. How could this be accomplished?

One solution was to schedule informal discussions of stimulus properties of drugs at professional meetings. Overton organized about a dozen such discussions during the 1970s. Additional workshops and satellites were organized by Rosecrans at the Society for Neuroscience in 1975, and at the Committee on Problems of Drug Dependence (1976–1980). Stolerman was instrumental in holding several informal meetings at the meetings of the European Neuroscience Association.

Another solution was to request larger blocks of program time at the regular meetings. An important event of this type was a symposium on state dependent learning at the 1972 meeting of the Federation of American Societies for Experimental Biology (FASEB). Another such symposium, on the topic of nonpharmacological state-dependent learning, was held at the meetings of the American Psychological Association 2 years later. Both the formal and informal meetings

were important to the overall growth of the area, and the attendance at these meetings increased each year.

The desire to transform the study of stimulus properties of drugs into an independent and recognized field also led to symposia on the topic, meetings convened for the sole purpose of exchanging information on the stimulus effects of drugs. The first was held at the University of Minnesota in 1969 (45), and it was followed by two others organized in the mid 1970s (26,30). The symposium organized by Lal (30) was the first to attract international attendance. Increasingly, it appeared that an organization was needed to sponsor meetings and publications on the stimulus properties of drugs.

CREATION OF THE SSPD

The decision to create the SSPD occurred in 1978, during one of the informal gatherings of drug discrimination researchers concurrent with a meeting of the FASEB. Participants included the three authors of the present narrative, among others. Overton wrote proposed bylaws and mailed them to investigators active in the field, requesting comments and approval. Barry agreed to preside at the first official SSPD meeting a few months later at the meeting of the Committee for Problems on Drug Dependence (CPDD) in Baltimore. The bylaws were approved. The society was created. It was that simple. The intended function of the SSPD was limited to service as an umbrella organization for its members. The SSPD meetings were to be concurrent with and at the location of meetings of major national societies to reduce travel time and expense.

Overton, the first president, was elected by mail ballot shortly after the initial meeting. The dues were set at the nominal amount of $5 per year. Table 1 lists the meetings subsequently held by the society and identifies its successive presidents. The president's term is 1 year, although one president, Bennett, served for 2 consecutive years. The only other officer of the society is the secretary-treasurer, and Table 2 lists the successive members who have served in that position. The secretary's term of 2 years has the advantage of providing greater continuity than the briefer terms of the presidents. Further continuity has resulted from the fact that some of the secretary-treasurers have subsequently been elected president. One secretary-treasurer, David V. Gauvin, served for 2 consecutive terms.

EARLY DEVELOPMENT OF THE SSPD

Difficult questions soon arose. Should the SSPD meetings be satellites to psychology conventions, pharmacology conventions, or physiology conventions? Should the SSPD meet

TABLE 1

SSPD MEETINGS, IDENTIFYING THE SOCIETY SPONSORING THE MEETING, LOCATION, DATE, AND THE PRESIDING PRESIDENT*

Year and Society	City	Date	President
1978 CPDD	Baltimore	3 June	Donald A. Overton
1979 FASEB	Dallas	2–4 April	"
1979 CPDD	Philadelphia	4 June	John A. Rosecrans
1980 FASEB	Anaheim	13–14 April	"
1980 CPDD/ISGIDAR	Hyannis	16–17 June	Herbert Barry, III
1980 SFN	Cincinnati	12 November	"
1981 FASEB	Atlanta	14 April	"
1981 CPDD	San Francisco	13 July	James B. Appel
1982 FASEB	New Orleans	20 April	Beng T. Ho
1982 SFN	Minneapolis	3 November	James L. Howard
1983 SFN	Boston	8 November	"
1984 SFN	Anaheim	10 October	Robert L. Balster
1985 ISGIDAR	Baltimore	9 June	"
1985 SFN	Dallas	21 October	Ronald Browne
1986 CPDD/ISGIDAR	Lake Tahoe	16 June	"
1986 SFN	Washington, DC	10 November	Harbans Lal
1987 CPDD/ISGIDAR	Philadelphia	14 June	"
1987 SFN	New Orleans	17 November	Debra A. Bennett
1988 SFN	Toronto	15 November	Debra A. Bennett
1989 SFN	Phoenix	31 October	Michael W. Emmett-Oglesby
1990 SFN	St. Louis	20 October	T. U. C. Jarbe
1991 SFN	New Orleans	12 November	Stephen G. Holtzman
1992 SFN	Anaheim	27 October	Alice M. Young
1993 SFN	Washington, DC	7 November	William W. Woolverton
1994 SFN	Miami Beach	6 November	Andrew J. Goudie
1995 SFN	San Diego	14 November	Nancy A. Ator
1996 SFN	Washington, DC	19 November	Frank A. Holloway
1997 SFN	New Orleans	24–25 October	Kathryn A. Cunningham
1998 SFN	Los Angeles	10 November	Ian P. Stolerman

*Abbreviations: CPDD – Committee on Problems of Drug Dependence (Collegium on Problems of Drug Dependence); FASEB – Federation of American Societies for Experimental Biology; ISGIDAR – International Study Group for the Investigation of Drugs as Reinforcers; SFN – Society for Neuroscience.

TABLE 2
SECRETARY-TREASURERS OF THE SSPD AND THEIR DATES OF SERVICE

Edward C. Krimmer	1978–80
James L. Howard	1980–82
Ronald Browne	1982–84
Debra A. Bennett	1984–86
Michael W. Emmett-Oglesby	1987–88
Alice M. Young	1989–90
Gerald J. Schaefer	1991–92
Frank A. Holloway	1993–94
David V. Gauvin	1995–98

once a year or more frequently? Successive SSPD presidents struggled with these issues, and their solutions have varied. Initially, enthusiasm was high. Several meetings per year were scheduled, and these were not all brief meetings. For example, at the 1979 meeting with FASEB, Overton, then president, scheduled three evenings of SSPD sessions, and all were well attended.

Later, interest appeared to decrease. Members were presenting their work at the larger conventions and not at SSPD. In 1983, James Howard scheduled a meeting with FASEB but had to cancel it because no articles were submitted.

Debra Bennett, as Secretary-Treasurer, initiated a successful format in 1986, which has been repeated in subsequent years with occasional modifications. Meetings are held once each year at the end of a day at the annual meeting of the Society for Neuroscience. Snacks are provided so that the participants can work a few hours longer and defer supper until after the SSPD meeting.

THE DUAL ROLE OF THE SSPD

The SSPD has served two very distinct constituencies. In the 1960s, and early 1970s, most of the individuals interested in stimulus effects of drugs were psychologists. Many of these scientists had no particular interest in the pharmacological actions of drugs. However, a transformation took place in the 1970s as pharmaceutical companies discovered that the drug discrimination procedure provided a useful assay. Increasingly, pharmacologists used drug discrimination to study neuropharmacological issues. For them, the stimulus properties of drugs were tools rather than mysteries. Their core agenda was to understand the neurochemistry of the brain. As these other disciplines began to see the relevance of the drug discrimination method, articles were increasingly published in pharmacology journals such as *Psychopharmacology* and *Pharmacology, Biochemistry and Behavior.* By 1979, only 15 of 81 articles were published in psychology journals, reflecting the increasing interest in drug discrimination research among pharmacologists and neurochemists (40).

Throughout its history, the SSPD has straddled the divide between these two groups of scientists and made program decisions intended to serve both. Probably no one has been entirely happy with all the decisions that have resulted, but both groups have continued to participate.

RENEWED EUROPEAN LEADERSHIP

The early experimental literature on stimulus properties of drugs was exclusively produced in North America. Probably this resulted from the theoretical orientations of the time. European psychologists, influenced by the ethologists, were busy observing naturally occurring behavior, and interest in stimulus control, which led to many of the early studies on drug stimuli, was mainly limited to North American psychologists. Since the 1970s, however, European members of the SSPD have played a major role in the development of research on drug discrimination. Some of the most productive drug discrimination laboratories have been those of Colpaert in Beerse, Belgium, Jarbe in Uppsala, Sweden, and Stolerman in London, England.

Another major contribution of the European researchers on drug discrimination has been the organization and sponsorship of most of the international meetings on the stimulus properties of drugs. These have been stellar occasions, which raised the morale of every participant. Although not for the most part organized by SSPD, these meetings have contributed greatly to research on and publicity about the stimulus properties of drugs. The first international meeting was held at Janssen Pharmaceuticals in Belgium, and subsequent meetings have been at approximately 4-year intervals. Francis Colpaert played a central role by both organizing and arranging

TABLE 3
INTERNATIONAL MEETINGS ON STIMULUS PROPERTIES OF DRUGS AND THEIR PUBLISHED PROCEEDINGS

3–4 July 1978	First International Symposium on Drugs as Discriminative Stimuli, Beerse, Belgium (10)
30 June–3 July 1982	Second International Symposium on Drugs as Discriminative Stimuli, Beerse, Belgium (11)
5–7 July 1986	Third International Meetng of Drug Discrimination and State Dependence, Beerse, Belgium (8)
26–27 June 1988	Fourth International Drug Discrimination Meeting, Cape Cod, MA. (Articles in Drug Development Research, v 16, 1989)
25–27 June 1990	Fifth International Drug Discrimination Meeting, Noordwijerkhout, The Netherlands (16)
30 Aug–1 1998	Sixth International Meeting on Drug Discrimination, Beerse, Belgium (Articles in this issue.)

TABLE 4
SUCCESSIVE SATELLITE MEETINGS OF THE EUROPEAN STUDY GROUP FOR INTERNAL STIMULUS CONTROL

Year	Society	Location	Organizer
1979	British Association for Psychopharmacology (BAP)	Birmingham, UK	I. P. Stolerman
1980	European Neuroscience Association (ENA)	Brighton, UK	J. Slangen
1981	European Neuroscience Association (ENA)	Liege, Belgium	I. P. Stolerman
1983	European Neuroscience Association (ENA)	Hamburg, Germany	I. P. Stolerman
1984	International Union of Pharmacology (IUPHAR)	London, UK	I. P. Stolerman

sponsorship for many of these meetings, and Tables 3 and 4 list the international meetings and the European satellite meetings. Throughout, there has been continuous and active cooperation between the North American and European members of the SSPD.

To round out the roster of European contributions, mention should be made of the valuable Drug Discrimination Database created by Stolerman, which is now available on the Internet (40). This database is an extremely useful and important tool for the drug discrimination researcher.

CURRENT STATUS OF SSPD

With a membership of almost 200 scientists, the SSPD is alive and well and healthy. Even though not every research endeavor undertaken by earlier scientists succeeded, their enthusiasm has been replaced by a more focussed and sustained effort to exploit the stimulus properties of drugs for what they can tell us about drugs, and about the operation of the brain. One indicator of the continued enthusiasm of the members is the fact that two separate meetings were organized to commemorate the 20th anniversary of the society. The 2-day 1997 SSPD meeting, largely organized by Frank Holloway, was the first such meeting. The Sixth International Meeting on Drug Discrimination was the second. About 80 scientists attended each of these meetings.

FUTURE PROSPECTS FOR SSPD

Prediction of the future is always difficult and hazardous. Some psychologists might pessimistically assert that the drug discrimination method provides an expensive assay that addresses no underlying scientific issues of interest. But they are incorrect, and a more optimistic projection would be that drugs are physiological manipulations of the brain that eventually can model many aspects of control of behavior by interoceptive stimuli. This optimistic position suggests that drug stimulus research is strategically positioned at the boundary between psyche and physiology. The SSPD, therefore, can help its members to make major contributions to understanding how the brain creates both mind and behavior.

An article by Fowler et al. (14) provides some support for the optimistic position. Rats reared and housed alone in small cages were compared with others that lived in a large group in an enriched environment. The rats in the isolated environment were more sensitive to the discriminative effects of low doses of the indirect dopaminergic agonists, cocaine and amphetamine. The modification of drug discrimination by the difference between an isolated and enriched environment suggests that drug discrimination can measure effects of a variety of physiological and emotional conditions.

One thing is certain. As the amount of research on the stimulus properties of drugs has increased, so has its degree of acceptance by and integration into the adjacent fields of science. Even as late as 1978 when the SSPD was created, drug discrimination research was at the fringes of both pharmacology and psychology. Now behavioral pharmacology has entirely incorporated our interests and methods, a change that is very unlikely to be reversed. In the American Psychological Association, drug discrimination research is prominent in the history of the Division of Psychopharmacology and Substance Abuse, founded in 1966 (2). Both the American Society for Pharmacology and Experimental Therapeutics and the Society for Neuroscience sponsor many drug discrimination reports at their annual meetings. Drug discrimination articles are published regularly by core journals including *Psychopharmacology, Pharmacology Biochemistry and Behavior*, the *Journal of Pharmacology and Experimental Therapeutics*, *Behavioral Pharmacology*, the *European Journal of Pharmacology*, as well as in a variety of other behavioral and neuroscience journals. At least in the foreseeable future, the SSPD will continue to have an important role—that of facilitating the work of the many investigators who now work on the topic of stimulus properties of drugs.

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