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Review

Trends in drug discrimination research analysed with a cross-indexed bibliography, 1982–1983

I.P. Stolerman and P.J. Shine
Departments of Pharmacology and Psychiatry, Institute of Psychiatry, De Crespigny Park, London SE5 8AF, UK

The drug discrimination procedure has become one of the most widely used paradigms in behavioural pharmacology, a situation which is reflected in the appearance to date of more 600 publications, including the proceedings of a number of symposia. Advances in technique have made drug discrimination techniques among the most powerful available to behavioural pharmacologists, and a very large amount of information on a wide range of drugs from different pharmacological classes has been obtained under strictly comparable experimental conditions. Stolerman et al. (1982, in reference 34) compiled a bibliography of drug discrimination research for 1950–1981. This has now been extended to include the years 1982–1983. Analysis of the bibliographic information facilitates quantification of recent research activity in the field and makes apparent certain trends and omissions that might otherwise be difficult to perceive.

There follows a brief discussion of some of these trends, relating mainly to the types of drugs studied and the relative use or neglect of specific experimental procedures. The current bibliographic listing of 191 articles is then given, together with an index enabling papers dealing with specific aspects of the subject to be identified readily.

Growth of the Field

The development of the field may be gauged from Fig. 1, which shows the numbers of papers published during each of the last 33 years. After a period of relative inactivity, rapid growth began in 1971. The most recent data provide no clear indication that this stage has yet been passed: the present bibliography contains 82 and 61 entries for 1982 and 1983 respectively (excluding the individual papers in the drug discrimination symposium). The largest number of entries recorded previously was 64, in 1981. A small number of earlier articles is also included in the present listing, so that when it is used in conjunction with the earlier version, almost complete coverage is provided for the years 1951–1983.

It may be noted that during the 1960's, most research papers were concerned with demonstrating the basic phenomenon under study and with defining some of its fundamental characteristics. During the early 1970's different methods were evaluated and some degree of standardization developed. In the mid-1970's drug discrimination began to be widely applied in diverse areas where, most commonly, it provided a specific and quantitative behavioural assay in studies of the neuropharmacological mode of action of drugs. Now we are at a stage where discriminative effects of drugs are often used alongside classical techniques without serving as the primary focus of study. Indeed, authors do not always indicate the use of drug-discrimination methodology in the titles of their papers, making it increasingly difficult for such work to be identified. There is a trend apparent for the full potential of drug discrimination techniques to be obscured by the emphasis on the neuropharmacological application. Virtually no work has been reported on the possible discriminative effects of naturally-occurring substances (e.g., neurotransmitters and hormones) at physiological concentrations, and the significance of the purported relationship of discriminative drug effects with subjective effects remains in doubt.

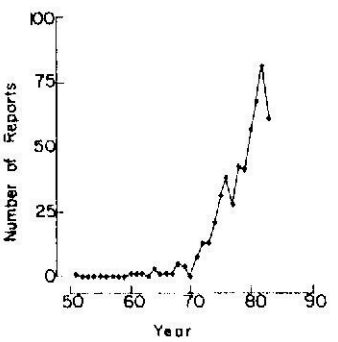

Fig. 1. Growth of the literature on drug discrimination research over 32 years since the first report appeared. Abstracts, research papers, reviews, and books were included to produce this diagram. Individual papers in several books devoted primarily to drug discrimination research were excluded because they distort the trends shown in the figure

Pharmacological aspects

The indexing of articles according to drugs used for training discriminations makes it easy to quantify research activity directed to different pharmacological classes. In the period 1982–1983, the largest numbers of investigations involved

Offprint requests to: I.P. Stolerman

training subjects to discriminate sedative-hypnotic drugs including alcohol [57]. The figures in square brackets indicate total numbers of citations on a topic. Within this class, there were 24 studies of benzodiazepine discrimination, 22 of barbiturates and 13 of ethanol. Diazepam and pentobarbitone seem to have been regarded as prototypical agents and have been used as training stimuli more frequently than other compounds: the reasoning behind this remains obscure and, with certain exceptions, these studies seem rather far removed from present knowledge of the drugs' mode of action at the neurochemical level.

Opioid drugs formed the basis of 48 studies. The most popular agents for training have been morphine [15] and fentanyl [11], compounds generally regarded as agonists at the mu-subtype of opioid receptors. Relatively few studies have used kappa-agonists such as ethylketocyclazocine [7] or sigma-agonists such as SKF 10,047 [5], or have used compounds selected primarily for their opioid-antagonist effects [8]. Nevertheless, despite the overwhelming popularity of the putative mu-agonists, drug discrimination techniques have provided some of the best behavioural evidence for the existence of opioid receptor subtypes and generally, this is an area where the neurochemical and behavioural work seems to have been particularly well co-ordinated. Opioid peptides have received less attention than might be expected: no such compound seems to have been used to establish a discrimination and in only a few studies have they been used in generalization tests.

Drug discrimination techniques also appear to have been much favoured by researchers interested in hallucinogenic agents [50]. The greatest emphasis seems to have been placed on the dissociative anaesthetics, phencyclidine, and ketamine [30], followed by the LSD- and DOM-like compounds [27]. Particularly strong correlations of discriminative effects with certain neurochemical actions have been reported for the LSD-DOM class. This level of research activity is interesting when considered in relation to the lack of therapeutic value of hallucinogenic agents.

The only other class of drug which has been the subject of fairly widespread research has been the psychomotor stimulants [22], including studies with (+)-amphetamine [17] and cocaine [9]. The use of these compounds seems to have declined, perhaps because they were studied so intensively in earlier years and because their mode of action seemed so well understood. Interest in nicotine seems to have been maintained [11] and may grow as the importance of central nicotinic mechanisms is increasingly recognized. Agents from the wide spectrum of analeptic (convulsant) drugs were used as training stimuli in only 10 studies. Some of these compounds have anxiogenic effects, and the potential value of their discriminative stimulus properties for providing animal analogues of anxiety suggests that this area may develop rapidly. Antidepressants, neuroleptics, and muscarinic-cholinergic antagonists have been almost completely ignored as training stimuli in recent years, generating only two studies each.

Antidepressants and neuroleptics have proved more difficult than most types of drug to study with existing discriminative techniques. The low level of interest in the anticholinergics is more surprising, especially in view of the important role they played in drug discrimination studies in the early years of the field and the current interest in cholinergic mechanisms in memory and Alzheimer's disease. Cannabis derivatives also seem unfashionable [2]!

Methodological aspects

Although drug discrimination techniques have a lot in common with each other, the relative merits of different approaches have been much debated over the years. The use of maze-running techniques has declined [7]. Almost all other studies used an operant conditioning paradigm involving response choice, such as the two-bar procedure or a development of it such as a three-choice technique. Rats were the subjects most widely used [128], followed by birds [26] and monkeys [23]. Of mice and men there were two studies each.

There were large variations in the schedules maintaining the baselines of behaviour upon which drug discriminations were developed. Food was the preferred reinforcing event [126], followed by shock escape-avoidance [25], water [11], electrical stimulation of the brain [3] and money [1]. Fixed ratio schedules predominated [103] followed by variable intervals [24]. Continuous reinforcement was used mainly in connection with shock escape-avoidance, whereas small bands of enthusiasts continued to show their preference for tandem variable interval fixed ratio schedules [9], fixed interval schedules [1] and interlocking schedules [1]. One innovation has been the introduction of second order schedules together with a colour-tracking procedure [4]. More work has been done with fixed ratio schedules of food presentation [87] than with any other schedule, and most of these studies used rats [51].

There have also been examinations of the time-courses of drug action [24], the role of training dose [18], drug versus drug discriminations [13] and chronic effects such as tolerance and dependence [10]. Fewer studies have looked at discriminations between different doses of the same drug [5] or at interactions of drug-produced stimuli with exteroceptive cues [5].

Using the bibliographic index

The list of references is followed by an index which refers back to the numbers of articles in the list. The index is primarily pharmacological, although species, and procedural variables are also included. Each drug in the index is followed by a list of articles where its use as a training drug was reported. Additional entries in the index show when the drug was used in cross-tests (generalization tests), or as a pretreatment in attempts to modify discriminative drug effects. This feature makes it very easy to obtain comprehensive lists of studies where a selected drug or class of drugs has been used in a particular way, and it has been found very useful when planning research or preparing manuscripts. It is possible to carry out a limited number of more specific searches using combinations of two or more keywords, or to supply the data base itself to people with access to suitable computing facilities. Readers interested in either of these possibilities, or who might like to obtain a combined listing for 1951–1983, with index, should contact the senior author.

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Index