

## The Analysis and Indexing of the Psychopharmacological Literature\*

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### INTRODUCTION

Several years ago, the Psychopharmacology Literature Project was inaugurated to develop techniques for the comprehensive indexing of the experimental and clinical world literature concerning the effects of psychopharmacologic agents in animals and man. All effects of well-known psychopharmacological drugs were to be indexed, not only their behavioral effects. Side effects were considered to be of great importance, although this complicated matters somewhat, particularly with regard to vocabulary control.

An index based on keywords or descriptors, leading the searchers to abstracts or original papers, was not contemplated. Instead, the approach to information storage would follow that of the Chemical-Biological Coordination Center (1, 2) and would also resemble the "index-abstract" approach (3, 4) developed for the Cardiovascular Literature Project which has, during the past eight years, been utilized for the analysis of over 45,000 scientific papers. It was not assumed, however, that the finished product would necessarily resemble the series of "Index-Handbooks of Cardiovascular Agents" (5, 6). For one thing, there would be even longer entries containing more information. Each index entry might begin to resemble a short abstract or annotation.

**Subject Headings.** The development of a thesaurus or glossary of approved terms is one of the major problems facing designers of indexing systems, particularly when true "indexing-in-depth" is contemplated. In psychopharmacology, as in other new and rapidly developing fields, terminology was found to be in a rather confused state. As a result, vocabulary control became a major goal of the present undertaking and occupied a great deal of our time and effort. All chemical substances, incidentally, are subject headings; that is, our thesaurus is "open-ended" in this respect.

Using available dictionaries and indexes, a list of several hundred nonchemical terms was compiled. Generally, these represented the following subject-matter categories: (a) anatomy, *e.g.*, reticular formation, thalamus, etc.; (b) physiology, *e.g.*, reflexes, etc.; (c) psychology, *e.g.*, imprinting, learning, etc.; (d) psychopathology, *e.g.*, schizophrenia, anxiety, etc.; (e) side effects, *e.g.*, nausea, vomiting, etc.

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The sections on psychology and psychopathology were most troublesome, as was to be anticipated. Numerous discussions with knowledgeable psychologists and psychiatrists convinced us that arbitrary decisions frequently would be necessary, and we would have to define terms in detail so that our indexers could use them accurately, even if the experts could not themselves get together on adequate definitions. We were aided in this endeavor by our part-time, nonresident indexers who represented various points-of-view, depending on their subject-matter training and background. They were assigned a number of representative papers from the available literature for indexing, using our vocabulary. An active correspondence ensued covering the adequacy of various terms. By this means, we attempted to bring together the vocabulary employed by the many experimental and clinical psychopharmacologists represented in the literature and our own terminology. Numerous changes were made in our thesaurus, and our indexing manual, containing instructions and suitable examples, was extensively rewritten and modified many times. Finally, after more than 1,000 papers, selected from some 188 journals, had been indexed, we felt that the thesaurus was, more-or-less, in good shape. That is not to say that further improvements are unnecessary.

A total of 246 terms are used, with extensive "see also" references and scope notes. Less frequently used concepts which represent synonyms or near-synonyms of these terms are cross-referenced to them under the usual "see" headings. The thesaurus is divided into four sections, available as appendices to our manual:

1. Appendix A entitled "Psychological and Psychiatric Terms" such as "Agitation," "Conversion Reaction," "Orienting Response," the various "Psychoses," etc.

2. Appendix B, "Miscellaneous Terms," contains 12 headings which are used for the indexing of review papers, such as "Diagnostic Aid" and "Enzyme," where "indexing-in-depth" is unnecessary.

3. Appendix C, "Side Effects of Drugs," entries, such as "Agranulocytosis," "Cardiac Rate," "Insomnia," etc.

4. Appendix D, "General Classification of Drugs," contains only seven terms, such as "Antidepressant" and is used only under special circumstances.

**Use of the Subject Heading List.** The following is taken from our instruction manual concerning some of the uses of the thesaurus.

"Within Appendix A, some subject headings have been given definitions and annotations. Some of the terms are defined only because of nomenclature differences in this

field of study and the definitions used indicate the project's interpretation. Other terms have been given rather lengthy definitions and annotations to allow for our own interpretations in these areas where more than one subject heading may be applicable. These definitions and annotations have not been taken from dictionaries, nor do they represent academic distinctions, but have been prepared for this project's specific use.

"Various laboratory tests have been designed to study and measure the physiologic response in terms of the psychological factors involved or from the other viewpoint, the psychological response in terms of the physiological factors involved. Regardless of the viewpoint taken, they represent a difficult indexing assignment. It is only through careful study of the paper being indexed that the proper subject headings can be determined and this is within the indexer's province.

A number of examples, with comments, are included rather than more elaborate instructions.

Indexing is done in the form of simple declarative sentences with the entity to be retrieved, the subject heading, placed first, as

CHLORPROMAZINE—Schizophrenia, contr.,  
anxiety in hosp. pts.

SCHIZOPHRENIA—Chlorpromazine, contr.,  
anxiety in hosp. pts.

In this example, the information would be recovered either under schizophrenia or chlorpromazine. Additional entries may be necessary to complete the indexing, as

CHLORPROMAZINE—Anxiety, contr., in  
hosp. schiz. pts.

ANXIETY—Chlorpromazine, contr.,  
in hosp. schiz. pts.

Any chemical compound which has an effect, or is tested for an effect, is indexed under the chemical and the effect. These appendices contain the only nonchemical terms which may be used as subject headings with the single exception of review articles as described in Appendix B.

Appendix C is the side effect, pharmacology, and toxicology list. This list has been compiled to reflect the importance and the quantity of data actually being published. The objective has been to facilitate retrieval. Items which occur frequently in the literature, or are important side effects, have been given specific subject headings. For example, *Blood Pressure* and *Cardiac Rate* are given separate entries since they are so often measured, both clinically and in pharmacologic trials. Conversely, there is a single entry for *Cardiac Activity* which includes the less frequently determined measurements such as cardiac rhythm and EKG. Actually, cardiovascular measurements are made so often that there are about ten individual subject headings available. In marked contrast to this we have found that the single subject heading *Respiration* is perfectly adequate for the entire system. The reason is simply that respiratory measurements are rarely made and respiratory side effects are infrequent.

An effort has been made to preserve important or dangerous side effects as separate entries.

Several headings are provided for recording the general effect of toxicity as it is frequently found in the literature. These are *Acute Toxic Symptoms*, *Local Toxic Symptoms*, *Chronic Toxic Symptoms*, and *Death*. *Acute Toxic Symptoms* is used specifically for listing the test procedures used to establish proper dosage in laboratory animals. *Acute Toxic Symptoms* can be used with the correct verb to index in one line the type of paper which mentions that a few of the subjects treated had nausea, headache, or dizziness following drug administration. As reported, we do not consider these minimal side effects to be of sufficient importance to warrant separate index lines. Care must be taken to index these actions separately, however, if the author indicates they are important. This heading is also used for those frequent cases of clinical reporting in which it may be stated that alkaline phosphatase levels, P.B.I. determinations, and blood studies were routinely done and no significant deviations were noted.

Appendix D is a list of preferred names for classes of drugs. There are some situations in which it is not reasonable or possible to enter specific drug names. This situation arises in indexing reviews in which a general term such as "ataractic drug" is used. These terms are also useful in indexing epidemiological studies of hospital populations before and after the introduction of tranquilizers. Actually, any collective chemical name may be used when necessary. When there is a choice of terms, *Tranquilizer* is preferred to *Ataractic* and *Antidepressant* is preferred to *Neuroleptic*, etc., as indicated in Appendix D.

The term *Placebo* is used as a chemical subject heading if the effect of placebo is reported. A paper on the effect of a placebo in anxiety is indexed as if placebo were an active drug (since this is the way in which it is being used). This does *not* mean that a line for placebo must be included for every paper in which placebo controls are used. The entry is made only if the effect of the pharmacologically inactive material is determined, not when such material is given only as a control.

There is a list of approved abbreviations in Appendix E.

**Special Indexing Problems.** Our first task, a survey of the available literature, described in a previous paper (7), indicated its great complexity. Experimental results and clinical findings were not as "straightforward" or arrived at as objectively as is the case in cardiovascular pharmacology, for example. This is due, in part at least, to a bewildering array of experimental methods and approaches and to that great bugaboo, biological variability. Here, to a greater extent than in most biomedical fields, the investigator intrudes upon the problem. His mere presence may alter his experimental results. Other strange things happen, such as the placebo effect, and complicated experimental procedures, such as the "double-blind" study, must be developed to get meaningful results. Relatively few investigators are fully trained in such methods. Accordingly, results vary greatly from laboratory to laboratory and not many experiments can be accurately duplicated.

Inevitably, the variability in the quality of the data presented in the literature leads to problems in indexing. Papers vary from the highly sophisticated evaluation of a group of patients with carefully defined characteristics to the most free-wheeling, impressionistic studies of miscellaneous, poorly characterized patient groups. No

rules can cover all situations, and indexers must be able to make sound judgments about the amount of detail which should be recorded for a given paper. It is this factor, more than any other, which makes it necessary for indexers to be trained, critical scientists.

A paper on a group of patients consisting of schizophrenics, senile psychotics, chronic brain syndromes, and manic depressives would be indexed according to the value of the data. If there were 20 patients in all and the evaluation consisted of the author's statement that the patients "did well", then a single entry using the nonspecific *Psychosis* would be all that would be justified. In contrast, if there were 200 patients and the evaluation were objective, with data presented separately for each diagnostic category, then each category would be indexed separately.

An extension of the example above is found in reports on drug treatment of ward populations among which there are representative types of mental disorders plus patients whose illnesses remain undiagnosed or tentatively diagnosed. Some clinical trials are well designed and adequately formulated to show an improvement in ward behavior and patient cooperation, but no specific drug action on a given diagnostic category can be distinguished. For these situations the subject heading *Mental Illness* has been provided. It was at first considered that an entry for *Patients* might be used, particularly since some test groups will include the rehabilitated, community-established former mental patient. However, the use of broad categories in an index system is apt to provide convenient "waste-baskets" and thus the entry *Mental Illness* was chosen and includes such patients with the indication of their status to be recorded in the experimental conditions column. For example, a paper in which the patients are described as 16% psychotic, 57% psychoneurotic, and 27% having psychophysiologic and personality disorders, would be indexed under the *Mental Illness* heading. The indexer is referred to Appendix A and this subject-heading for further notation. Again it might be pointed out that the Subject-Heading and Action columns do not stand alone but are made meaningful through the test details recorded in the remaining columns on the index sheet.

When indexing the side effects of drug treatment the quality of the data must be similarly evaluated. The statement that two patients complained of headache while taking a drug in an uncontrolled study would not be indexed because the effect is minor and not clearly related to the drug. If the study were controlled and there were more headaches in the treated group, then this would be indexed. Or, if the effect were of serious proportions, as the recent reports of devastating headache with neurological symptoms during the antidepressant treatment, then even a single case based on circumstantial evidence would be indexed.

The foreign language literature always presents a problem to a small indexing project since subject matter competence must be coupled with language fluency. In psychopharmacology, this problem is aggravated by the complex terminology. Frequently, for example, there is no adequate equivalent in English for some involved German psychiatric concept.

**Subject Matter Coverage.** One of the problems, which small, specialized abstracting and indexing services must solve, concerns the scope of coverage. In our case, it was

absolutely necessary to carefully define what sort of information we were to collect and to analyze or we would soon find ourselves covering such related fields as neuropharmacology, neurophysiology, and neurochemistry. On the other hand, we could not become too restrictive or we would omit many valuable studies relating to the mechanism of action of psychopharmacological agents.

After many discussions and after many papers had been indexed, we were able to develop some rules which would enable us, and our nonresident indexers, to determine which documents were pertinent to our undertaking. For example, we excluded all hypnotics and sedatives, analgesics such as morphine, etc., for to do otherwise would dilute our collection with a great deal of extraneous, yet related, material. It was decided to index all effects of three major classes of behavioral drugs, the tranquilizers, the antidepressants and hallucinogens or psychotomimetics upon (1) mental illness, including the psychoses and neuroses, symptoms as well as the entire disease (it is not always easy to differentiate between these two entities); (2) normal behavior in animals and man under a variety of experimental conditions, especially when well-known, reasonably objective psychological tests can be employed; (3) physiological and biochemical effects on animals and man, especially upon enzymes and enzyme systems, blood and tissue constituents, etc., including all recorded side effects, with particular emphasis upon toxicology; (4) experimental conditions produced in animals and man by drugs and other means (e.g., model psychoses, etc.). In addition, the metabolism of these agents was stressed, although this required a somewhat modified type of indexing.

**Drug Combinations and Interactions.** In some experiments two compounds may be administered together for an adjunctive therapeutic effect on a single symptom. In such cases where there is no intent that one compound modify the effect of the other, four index lines are prepared. The following example illustrates the indexing.

Trifluoperazine—Anxiety, rel., in psych., pts.,  
when admin., with amylobarbitone  
Anxiety—Trifluoperazine, rel., in psych., pts.  
when admin., with amylobarbitone  
Amylobarbitone—Anxiety, rel., in psych., pts.  
when admin., with trifluoperazine  
Anxiety—Amylobarbitone, rel., in psych.,  
pts. when admin., with trifluoperazine

If, however, the purpose of the paper is to demonstrate an interaction between drugs, a different method is used. For example, if it is thought that thioridazine might potentiate the action of chlorpromazine, the indexing would be

Thioridazine—Chlorpromazine-induced therapeutic  
effect, did not potentiate, in controlled  
study of 86 chronic schiz., pts.

This line is not reversed; i.e., it is listed only under thioridazine. Similar entries, using a drug-drug type of statement, can be made for antagonistic, synergistic, and additive effects.

# ANALYSIS AND INDEXING OF PSYCHOPHARMACOLOGICAL LITERATURE

INSTITUTE FOR ADVANCEMENT OF MEDICAL COMMUNICATION - WASHINGTON BRANCH

Author(s): Gwynne, P.H., M. Hundziak, J. Kavtschitsch, M. Lefton and S. Passamanick  
 Reference: J. Nervous Mental Disease 134, 451-455 (1962)  
 Title: Efficacy of trifluoperazine on withdrawal in chronic schizophrenia

Page 1/1  
 Language \_\_\_\_\_  
 Indexer \_\_\_\_\_  
 Checker \_\_\_\_\_  
 Classifier \_\_\_\_\_  
 Cypist \_\_\_\_\_  
 Proofreader \_\_\_\_\_

| Subject Heading        | Sub-heading              | Action                   | Experimental Conditions   | Route of Administration                                 | Collateral Information   |
|------------------------|--------------------------|--------------------------|---|---|--|
| TRIFLUOPERAZINE        | → Schizophrenia, chronic | amel., decr. withdrawal, | in 26 long term hosp. pts. in d. bl. contr. study eval. by Lorr Scale | upon p.o. admin. in doses up to 40 mg. daily for 4 mo.  | Other factors of the Lorr Scale were not alt.  |
| SCHIZOPHRENIA, CHRONIC | ← Trifluoperazine        | "                        | "   | "   | "  |
| CHLORPROMAZINE         | → Schizophrenia, chronic | did not alt.,            | "   | upon p.o. admin. in doses up to 400 mg. daily for 4 mo. | There was special interest in the "withdrawal" rating which was decr., by trifluoperazine. |
| SCHIZOPHRENIA, CHRONIC | ← Chlorpromazine         | "                        | "   | "   | "  |

Figure 1. General format of "index-abstract."

**Index Sheet.** Figure 1 illustrates the general format of our "index-abstracts."

The top of the sheet is reserved for bibliographic information, including the translated title of the paper, if it is in a foreign language.

There are four horizontal columns on each sheet so that four separate observations can be entered. Each observation in sentence form is divided into six parts, each recorded in a separate column: subject heading, sub-heading, action, experimental conditions, route of administration, and collateral information.

Our format is amenable to publication in more-or-less conventional columnar form. The word "columnar" should be stressed since it enormously facilitates the scanning of an index, particularly when there are a great number of entries under the same subject heading. The alphabetized subject heading enables easy access to the information collection, but the other columns must be searched sequentially.

Our format, with some modification, such as further standardization of the terminology used in columns other than those devoted to the subject heading and subheading, can be permuted. The difficulty here, however, is largely one of bulk, for the number of entries in the printout would be three times as great.

## CONCLUSIONS

It might be instructive to list several hypothetical questions which our system was designed to answer.

1. What is the effect of a specific drug upon depression in the adolescent when administered orally? At what dosage level?
2. What is the effect of a specific drug upon a toxic psychosis produced by pretreatment with another drug?

3. What drugs have been tested and with what results in the treatment of anxiety neurosis in the human adult?

4. What are the effects of piperazine tranquilizers upon dreaming? How do they compare with chlorpromazine in terminating LSD-25 reactions?

The above represent but a small sample of the kinds of questions which may be answered by our approach. Frequently, as in the case of a negative test data, it is wholly unnecessary to have recourse to the original documents from which index entries have been generated.

Our main shortcoming is our inability to answer questions dealing with the effects of chemical structure and structure alterations upon biological activity, such as, for example: What are the effects of compounds containing a phenothiazine nucleus, a dimethylaminoethyl substituent upon the nitrogen, and chlorine atoms in various positions on the nucleus, upon depression? Such questions can be answered only if chemical structures are coded and if storage and retrieval of such data are mechanized.

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