

# ISGIDAR

INTERNATIONAL  
STUDY  
GROUP  
INVESTIGATING  
DRUGS  
AS  
REINFORCERS

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### ABOUT ISGIDAR NEWSLETTER

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## MEETING OF WORKING COMMITTEE

The working committee of ISGIDAR met in Chicago on November 16, 1973. The following active members of the committee were in attendance: R. L. Balster, A. T. Dren, J. R. Goldberg, R. A. Meisch, H. Wakeley and M. Wilson. W. Wuttke, an ISGIDAR member, represented F. Hoffmeister. Other members of ISGIDAR also attended, namely, R. Grove, T. Harwood, C. Johanson, N. A. Krasnegor, M. W. Tischman and E. C. Tocus.

A considerable period of time was spent reviewing the objectives of ISGIDAR. The role that investigations on the properties of drugs responsible for their ability to act as reinforcers for self-administration may play in predicting abuse liability was recapitulated. This discussion, though valuable, did not lead to conclusions not already defined in the first ISGIDAR newsletter.

The main order of business was to review the extensive evaluation of information supplied to the working committee by its members in the questionnaires mailed out with the first ISGIDAR Newsletter. The committee was indebted to the University of Chicago group, particularly to Dr. Chris Johanson for organizing these data and subjecting them to analysis. Pulling together the data obtained from such diverse procedures and drawing conclusions and making inference from these analyses was a Herculean task, well performed. A very brief review resumé of the treatment of the responses to the questionnaire will be described below for general distribution to ISGIDAR members. Members of the Working Committee who were unable to attend the meeting will receive copies of print-outs of the composite data and its analyses along with this issue of the Newsletter. Drs. Schuster and Johansen, with assistance from other members of ISGIDAR, will attempt to arrive at major conclusions from the

analysis of these data for presentation at the Mexico City meeting of the CPDD.

It was agreed that the next meeting of the Working Committee would be held in Mexico City at 9:00 AM on Sunday, March 3; the day preceeding the Annual Meeting of the CPDD. J. E. Villenreal was to be asked to arrange for a place for the committee to meet.

There was a considerable discussion about drugs that might have been studied as reinforcers for self-administration and not reported on the questionnaires as well as some obvious drugs that appear not to have been studied. It was the consensus that it would be highly advantageous to have negative data now in the files of the ISGIDAR members as well as to have additional compounds studied. Members present who had such data expressed a willingness to the committee to provide it to the committee. In addition, some of the members agreed to study a few compounds which are generally accepted as either not being subjected to abuse or to have only trivial abuse potential. The committee felt it would be important to know the extent to which a wide variety of compounds known to have actions involving diverse mechanisms but still referable to the CNS, would or would not serve as reinforcers under different test situations.

Arrangements will be made, prior to the Mexico City meeting and finalized there, to dispense test drugs to members of the Working Committee willing to examine one or more of them. The drugs to be studied will be selected as one or more of the most widely used representatives of major classes of centrally acting drugs and which have not yet presented any major problems in terms of street use. Committee members who have data on such compounds were encouraged to provide it to the committee in order to avoid unnecessary redundancy in testing. At present, C. R. Schuster will manage the acquisition of the drugs and arrange for their coding and probable distribution by Dr. E. May. We have seven investigators who are willing to study one or more such drugs, provided they have not already done so. There were several members who were not present whom we assumed might also be willing to study at least one such compound. The investigators would each get one compound blind with information on its solubility and mouse CD<sub>50</sub>. Hopefully the work would be finished in time for a fall meeting in Ann Arbor.

It would be very helpful to the committee if its members would assemble a complete list of currently marketed drugs which they have studied. When this list is received by C. R. Schuster he could tick off those compounds the committee would like the critical information about. He would return the list along with a questionnaire form that would provide him with such information as would be required for analysis and putting into a form suitable distribution to other interested groups. ISGIDAR would act as a clearing house for such information and the ISGIDAR newsletter would serve as a means to dispense such information to all investigators who might find it useful.

The committee members and guests deeply appreciated the fine dinner sponsored by the Abbott Laboratories on the evening before the meeting.

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Epitome of Data Analysis by K. Johanson and Others

Data supplied to the committee on questionnaires was encoded in order to separate it for treatment by: (1) Investigator, (2) Test Drug, (3) Baseline Drug (that for which Test Drug was substituted in substitution studies, (4) Session time (hrs), (5) Fixed Ratio Used, (6) Number of animals studied per dose, (7) Doses, (8) Number of reinforcing doses/session and (9) Whether or not rate of SA exceeded rates for saline controls.

Some data was provided on 39 drugs. For many of these there was inadequate information to justify analysis. For others the information was supplied from a single laboratory. The data was entered on mag tape and programmed into a PDP-8 which then produced a graphic display of number of infusions/session on the ordinate and the unit dose in mg/kg on the abscissa. The data supplied by investigators who used multiple test sessions per day was lumped together and treated as a single test session.

Three examples of such dose-response curves have been appended in this new letter. The data were also treated in terms of numbers of infusions/hour vs. dose. The most notable finding was the exceptionally good agreement between laboratories in estimation of the unit dose of the drug which gives the maximum number of infusions per session. As might have been expected, when multiple short sessions and very small doses were used, these tended to produce higher rates of self administration. However, doses producing maximum effect were still found to be in the same range.

It was obvious from some of the print-outs that some of the investigators were using too high doses to establish the optimum unit dose using their particular test procedures.

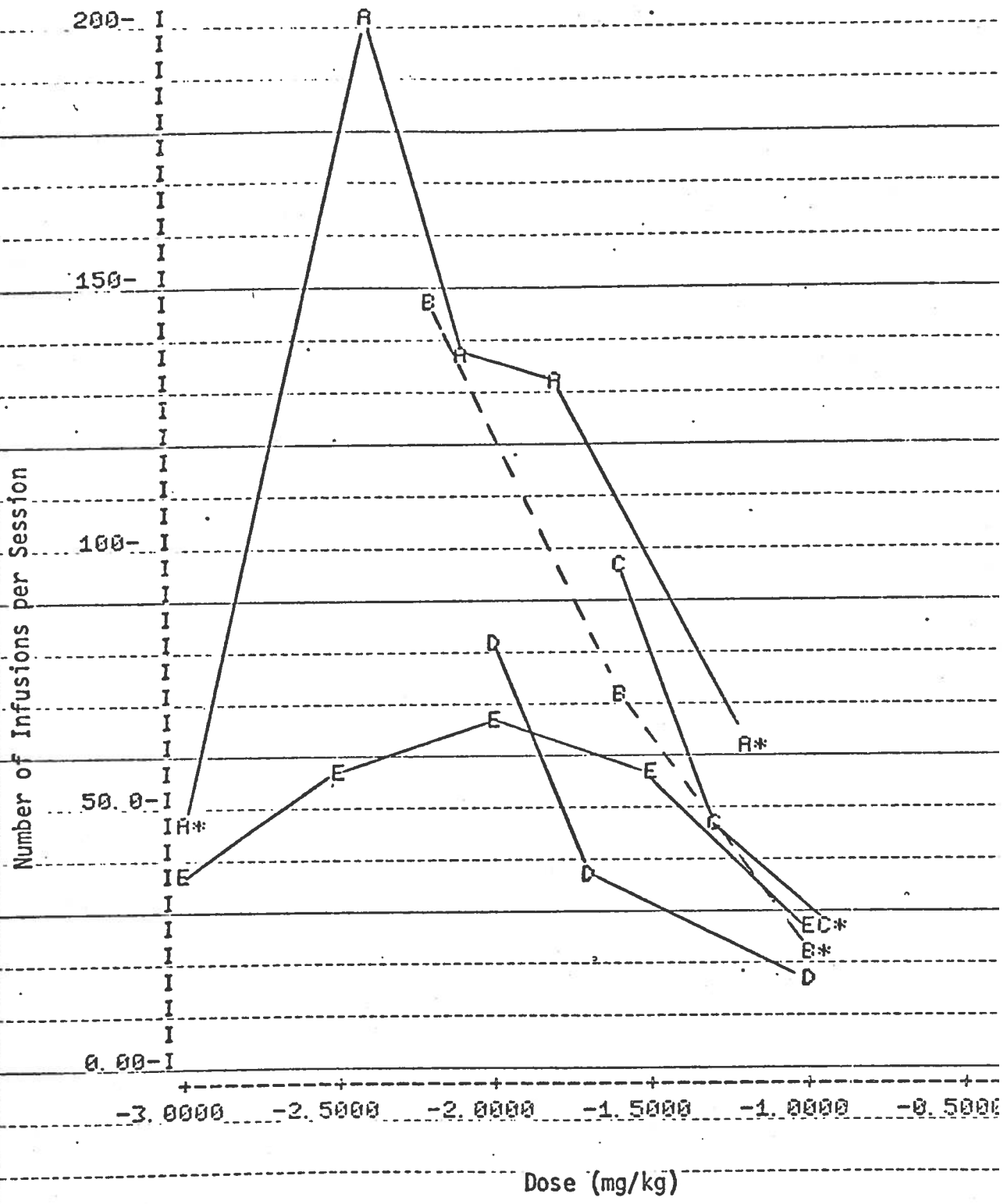
As would be expected, heroin produced obviously higher response rates at lower unit doses than did codeine or morphine. While no between-drug comparisons were made, visual examination of the composite graphs clearly indicates that codeine is more reinforcing than morphine at about the same range of unit doses. There appears to be fairly good general agreement between laboratories supporting this already reported observation.

Stimulants were found to be highly reinforcing by all laboratories, but again most had failed to extend their low dose range down sufficiently to detect optimum unit dose for any particular test procedure. Methamphetamine, cocaine, d-amphetamine, methylphenidate, pipradol and phenmetrazine all showed self-administration rates in excess of those expected from saline controls.

Data obtained from studies on pentozocine, d-propoxyphine and cyclazocine were also examined. While pentazocine and d-propoxyphine were obviously reinforcing regardless of the laboratory in which they were studied. Cyclazocine was not found to be reinforcing. Likewise, aspirin and sodium salicylate were not found to be reinforcing under the test situations used by the two investigators who each studied one of these two drugs.

The data on self-administration of pentobarbital remains the least clear when just a visual comparison was made between data obtained by different laboratories.

With the thiobarbiturates and barbiturates, the drug training history of the test animal may be of critical importance in defining the willingness of the animal to accept those drugs as reinforcers. This remains one of the important areas for further research, and one that is of undoubted importance in a global analysis of the psychopharmacologic aspects of drug abuse.



A	6.0000	3.0000	McCarthy: Methamphetamine
B	3.0000	1.0000	Yanagita: SPA
C	4.0000	6.0000	Balster: Cocaine
D	4.0000	7.0000	Dren: Cocaine
E	4.0000	5.0000	Woods: Cocaine

