new guidelines for the pharmacologic treatment of childhood MBD disorders, which if left unchecked, can emerge as more serious schizo-affective illnesses in adulthood.

Pediatric Psychopharmacology

Investigator: Robert L. Sprague
University of Illinois
Urbana, Illinois

Résumé by: Program Analysis Section, DERP, NIMH

Purpose: Drug therapy is a promising but controversial new approach to correcting behavior and learning problems in children. More information is needed before the effectiveness of this mode of treatment can be fully determined. This investigator is studying the effects of stimulants and depressants on memory and learning processes, activity, and physiological responses. He is also developing, testing, and refining measures of drug action to establish basic psychopharmacological characteristics of psychotropic drugs.

Subjects: Subjects are retarded and emotionally disturbed children 4 to 12 years old. Rats are also used.

Method: Two drugs, the stimulant, methylphenidate (Ritalin), and the minor tranquilizer, thioridazine (Mellaril), are being investigated. Although methylphenidate has a stimulant action in adults, it seems to have a depressant effect in children. In one experiment, the effects of both drugs on retarded children's acquisition and retention of a recognition response are studied. Another experiment examines the effect of methylphenidate on responses to light flashes, skin conductance, and heart rate in emotionally disturbed children. A third study concerns the effect of methylphenidate on motor activity in hyperactive children. Young rats are used to test the effects of methylphenidate on the formation of the myelin nerve sheath in the associative areas of the cortex.

Results: This research is in the data collection phase.

Implications: Results of this research may provide a better basis for clinical evaluation of the effectiveness and safety of psychotopic drugs for treating children's emotional and behavioral problems.

Effects of LSD-25 on Psychotherapeutic Communication

Investigator: Charles C. Dahlberg
William Alanson White Institute
New York, New York

Résumé by: The Investigator.

Purpose: The investigator is studying the effects of LSD-25 on verbal interaction in psychotherapy. He will compare the results of psychoanalytic therapy conducted with the aid of LSD-25 or d-amphetamine to the results of therapy without drugs.

Subjects: The subjects (neurotic, white middle-class men and women between the ages of 23 and 43) are screened to eliminate those with psychoses or physical disabilities that would contraindicate drug administration.

Method: Monthly sessions for each patient are divided equally among three experimental programs: seven LSD-25, seven amphetamine, and seven placebo sessions. The investigator does not know who gets which drug during a given session. The experimental session, 2 hours long, consists of psychoanalytically oriented psychotherapy. The patient is given a low to moderate dose of LSD, amphetamine, or placebo on an empty stomach and allowed to eat a light lunch an hour later. Several language evaluating instruments are used to assess changes in various aspects of the subject's behavior. Nurses' ratings and psychiatric evaluations are also made. All sessions are tape recorded.

Results: A total of 630 fifty-minute tapes have been recorded from subjects who have completed their experimental sessions. Recent results have shown that various drugs have different effects on speech rhythms during therapy sessions. As compared to placebo, d-amphetamine decreased average pause time and LSD increased it; thus, the patient's pause time may have been one of the subliminal cues utilized by the therapist to guess which drug the patient had received. The therapist noted that the typical LSD patient was more intolerant of interruption, regardless of whether the patient was withdrawn and silent or talkative and excited. Nevertheless, the patient wanted human contact. The therapist felt that the patient who had taken LSD was more preoccupied with inner experiences and harder to understand than before taking the drug, but he still needed some reassurance. LSD diminished interpersonal relatedness

and led to greater autonomy, which was reinforced by the therapist. Under LSD, the transference response also was more readily available for the patient's therapeutic use. When the patient became uncommunicative, he often had remarkable inner experiences which he reported at the next session.

LSD produced greater emotionality as measured by crying. The ability to understand language per se (as opposed to symbolic expressions) was not changed by LSD or dextroamphetamine. This fact was attributed to the power of the psychotherapeutic situation where verbal communication in the normal mode is expected.

Implications: The quantitative and qualitative measurements of verbal behavior under several drug conditions used in this study should provide objective information about the therapeutic usefulness of LSD.

An Approach to Rational Drug Therapy in Schizophrenia

Investigators: **Mervin Clark and Pushkar Kaul**
University of Oklahoma
Norman, Oklahoma

Résumé by: Program Analysis Section, DERP, NIMH

Purpose: A great number of drugs have been developed to help victims of schizophrenia, but probably the most widely used agent is the major tranquilizer, chlorpromazine. This project (a continuation of earlier studies of drug therapy in schizophrenia supported by MH 11666) focuses on the development of a sensitive procedure to accurately measure the amount of chlorpromazine and its metabolites in blood and other body fluids. The investigators hope this method will serve as a means to correlate blood and/or tissue and other body fluid levels with the clinical effectiveness of chlorpromazine.

Subjects: Blood and body fluids from persons given chlorpromazine are used in this research.

Method: Chlorpromazine and its metabolites are identified by a variety of analytical procedures including dansylation, quaternization, and, if necessary and feasible, a combination of gas chromatography and mass spectrometry. Procedures that are found most sensitive are selected for further study.

Results: The project is in its initial stages.

Implications: This research may produce new and more accurate ways to identify drugs in body fluids. It might also lead to the more efficient use of chlorpromazine in the control of mental illnesses.

Chlorpromazine Metabolism in Acute Schizophrenia

Investigator: **Samuel Gershon**
New York University
New York, New York

Résumé by: Program Analysis Section, DERP, NIMH

Purpose: The success of the major tranquilizer, chlorpromazine (CPZ), in treating schizophrenia can be predicted to some extent through behavioral ratings of the patient. This investigator is attempting to develop a laboratory method to provide a more precise prediction of improvement in individual patients. He is searching for a reliable assay procedure to measure the presence of CPZ and its metabolites in the blood and urine.

Subjects: Schizophrenic patients currently under treatment participate in this research.

Method: Various assay methods are compared to determine capacity to measure CPZ and its many metabolites in hospitalized patients. These methods include radioisotopic procedures; fluorescent labeling of demythylated CPZ metabolites with fluorescein isothiocyanate; application of gas and liquid chromatography with flame ionization detection; preparation of 2,4-dinitrophenyl derivatives of CPZ metabolites; a scan technique for color complexes of CPZ by spectrophotometry; colorimetric assays for urine; and plasma-solvent extraction and deproteinization by ethanol or methanol for blood plasma. An evaluation is also made regarding CPZ dosage levels, its metabolism, therapeutic benefits, and side effects.

Results: Findings indicate tentatively that the scan technique provides the most practical and versatile assay of CPZ. To date, 18 CPZ metabolites and CPZ itself have been analyzed by this method. Scan technology, which is currently undergoing further refinement, appears to be sensitive enough for more thorough investigations of CPZ in blood plasma.

Implications: Methods developed in this research may be extended to other psychoactive drugs. Research in this area may improve the understanding of drug action and brain function and contribute to the classification, diagnosis, and treatment of schizophrenia and other mental disorders.