chloride (BUP) in a 30% (v/v) ethanol solution given daily for 16 days. Six hours following BUP administration on days 14, 15 and 16, subjects were randomly assigned to receive a single intravenous (IV) or intramuscular (IM) injection of hydromorphone hydrochloride (HDM), 0, 2 or 4 mg. Using a parallel groups design, subjects were randomly assigned to one of two groups (A or B). Group A continued to receive 8 mg of BUP daily for another 18 days (days 17 through 34); Group B received 8 mg every other day (alternating with placebo) over the same 18-day period. Six hours following BUP administration on days 29 through 34, subjects again received a randomly determined single daily IV or IM injections of HDM, 0, 2 or 4 mg. The last BUP dose was given to each group on day 34, and placebo continued through day 54. Six hours following BUP placebo administration on days 51 through 54, subjects received a randomly determined single daily IV or IM injection of naloxone hydrochloride (NAL), 0, 3, 6 or 12 mg. Physiological and behavioral observations were performed at −1 and −0.5 (preHDM/NAL) as well as 0.5, 1, 2 and 4 hr following HDM or NAL administration. Physiological observations included measurements of supine and standing blood pressure and heart rate, respiratory rate, pupil diameter, and body temperature. Subscales of the Addiction Research Center Inventory, Observer and Subject Drug Effect Questionnaires, and the Withdrawal Symptom Questionnaire were used to rate behavioral signs and symptoms of acute opioid effect and withdrawal.

INVITED ADDRESS

Food Effects on Brain and Behavior
Richard J. Wurtman, Massachusetts Institute of Technology, Cambridge, MA
Chair: *Peter B. Dews,* Harvard Medical School, Boston, MA

SYMPOSIUM

CNS Stimulants, Aggression and Prosocial Behavior: ADD Children and Animals
Chair: *James M. Swanson,* Child Development Center, University of California, Irvine, CA
Discussant: *Markus Kreusi,* National Institute of Mental Health, Bethesda, MD

AMPHETAMINE'S EFFECTS ON THE SOCIAL BEHAVIOR OF GROUP-LIVING MONKEYS. Larry D. Byrd and Euclid O. Smith. Yerkes Regional Primate Research Center, Emory University, Atlanta, GA.

The chronic administration of sympathomimetic drugs, e.g., *d*-amphetamine and methylphenidate, has become a primary pharmacological treatment for children exhibiting the behavioral syndrome, Attention Deficit Disorder (ADD). The acceptance of this treatment strategy has derived largely from the outcome of case studies involving human children. However, variability in therapeutic efficacy suggests the need for an animal model that is more amenable to a systematic analysis of the variables that can influence drug effect. An interest in the behavioral effects of sympathomimetic and other stimulant drugs within a social context led us to undertake studies with group-living nonhuman primates to identify and characterize changes in several behavioral measures as a function of dose of *d*-amphetamine. In adult male stumptail macaques living within a heterogenous social group, *d*-amphetamine (0.003–0.56 mg/kg) decreased affiliative (prosocial) behavior. In contrast, *d*-amphetamine either increased or had little effect on aggressive behavior as a function of the monkey's dominance position in the group. Moreover, *d*-amphetamine increased aggression initiated by adult male monkeys against nonadult monkeys in the group and decreased aggression toward adult members. Also, the drug increased aggression toward kin-related members of the group and decreased aggression toward nonkin monkeys. The results indicate that *d*-amphetamine can modify the behavior of drug-treated members of a group, and that the drug can indirectly affect other members of the group even though they did not receive the drug. (Supported in part by USPHS grants DA-02128 and DA-01161, and NIH grant RR-00165 from the Division of Research Resources to the Yerkes Primate Research Center.)

ROLE OF BIOGENIC AMINES IN MAINTAINING HYPERACTIVITY IN NEONATAL RATS. Lewis S. Seiden. University of Chicago, Chicago, IL; Frederick E. Miller. University of Illinois, Chicago, IL; and Thomas G. Heffner. Parke Davis-Warner Lambert Drug Co., Ann Arbor, MI.

Monoamine neurotransmitters play an important role in the treatment and possible etiology of Attention Deficit Disorder with Hyperkinesis (ADDH). Evidence for the involvement of monoamines stems from both clinical work and studies exploring animal models of the ADDH syndrome. The primary pharmacological treatment of ADDH involves the use of sympathomimetic drugs such as *d*-amphetamine, methylphenidate and pemoline. The fact that these agents act to increase the synaptic concentration of monoamines has been one of the major reasons for the focus on monoamines in research on ADDH. Normally, rats are very inactive between 0 and 9 days postpartum. Between days 10 and 15, locomotion in the form of ambulation increases greatly, reaching a peak of activity on day 15, and between days 15 and 30, they gradually return to normal activity. However, when rats were depleted of forebrain dopamine by administration of the neurotoxin 6-hydroxydopamine (6-OHDA), the normal developmental pattern of locomotion was altered dramatically. Although the early developmental pattern was relatively normal, when the 6-OHDA rats reached the 15-day peak, their activity declined much more slowly, if at all, when compared to rats treated with vehicle. The degree to which the activity returned to normal depended on the extent of destruction of the catecholamine system. The results suggest relationships between the dopamine and serotonin systems in the expression of hyperkinesis and its treatment with amphetamine and related compounds.

AGGRESSION AND PROSOCIAL BEHAVIOR IN ADD CHILDREN: EFFECTS OF METHYLPHENIDATE. Stephen P. Hinshaw. University of California, Los Angeles, CA.

Stimulant medication, the most prevalent treatment regimen for Attention Deficit Disorder (ADD), has consistently been shown to reduce many of the core symptoms of the disorder, including problem behavior in the social realm. Yet two response domains that are of critical prognostic importance for children—prosocial behavior and aggression—are inconclusive with respect to medication response. First, although stimulants have repeatedly been shown to diminish socially disruptive and noncompliant behavior, their ability to decrease actual aggression has been demonstrated less

conclusively, particularly with regard to systematic observations (rather than ratings) of aggressive acts. Second, whereas stimulant medication leads to increases in social compliance, the question of its effects on explicitly prosocial behavior (e.g., social initiation or leadership) is indeterminate. To help resolve such questions, we recently investigated stimulant effects on (a) compliant vs. prosocial behaviors and (b) disruptive vs. aggressive behaviors in a naturalistic summer research program for boys with ADD. The 25 participants, aged 6–12, were placed on a double-blind trial of placebo, 0.3 mg/kg or 0.6 mg/kg methylphenidate hydrochloride over a 3-week period, in a within subjects/crossover fashion, with each dosage lasting for one week. Scan-sampling procedures were used to record ongoing social behavior in naturalistic classroom and playground settings, and reliable observations of the distinct social behaviors in question were made. Clear medication effects on aggression were found. An overall main effect was clearly significant, and individual response patterns showed that all subjects clinically appraised as both hyperactive and aggressive showed at least a 50% reduction of aggression on medication. Interestingly, for only several subjects did the 0.6 mg/kg dosage provide any greater benefit than did the low (0.3 mg/kg) dose. Effects on prosocial behavior were less striking, although for certain older (ages 9–12) boys who had presumably learned basic prosocial skills previously, medication effects were dramatic. The clinical and methodological significance of these findings include the importance of analysis of individual response patterns in addition to group means.

METHYLPHENIDATE AND ADD CHILDREN'S SOCIAL BEHAVIOR: INDIVIDUAL DIFFERENCES, DOSE RESPONSE. William E. Pelham, Jr. Western Psychiatric Institute and Clinic, University of Pittsburgh School of Medicine, Pittsburgh, PA.

A number of studies have evaluated the dose effects of psychostimulants on ecologically valid measures of functioning in Attention Deficit Disorder (ADD) children. Typical studies have included evaluations of doses ranging from 0.15 to 0.75 mg/kg methylphenidate (MPH) or equivalent, and they have focused on a variety of dependent measures, tapping both social and cognitive spheres. Despite relatively similar dose ranges and dependent measures, however, these studies have yielded somewhat inconsistent results. For example, some report only linear effects of stimulants on measures of cognitive functioning, while others report that beneficial stimulant effects peak at relatively low doses. Similarly, some studies report beneficial stimulant effects on ADD children's social behaviors, both prosocial and antisocial, but other studies have failed to support these findings. It is the thesis of this paper that the discrepancies result from individual differences in drug effects, both across children within response domains and across dependent measures within children. Data to support this argument are reported for 17 ADD children who underwent a within-subject evaluation of placebo, 0.3 and 0.6 mg/kg MPH, with dose randomized over days. Dependent measures were gathered over 5 to 9 days per condition, and included observations of classroom and playground behavior, measures of classroom seat work, mathematics and reading performance (completion rate and accuracy), and frequency counts of positive peer interactions, negative verbalizations, conduct problems, rule-following behavior and noncompliance to adult requests. Analyses of group data consistently revealed linear effects of MPH, within the dose range evaluated, across most dependent measures. However, very few children exhibited the linear trends that characterized the group data. On some dependent measures, not a single child's data were reflected in the group mean. Furthermore, the shapes of the dose-response curves across the dependent measures consistently varied within children. The results have implications for psychopharmacology with ADD children, particularly regarding the notion of a "medication responder."

INVITED ADDRESS

Substance Abuse Treatment and Policy: Contributions of Behavioral Pharmacology

Thomas J. Crowley, University of Colorado Health Sciences Center, Denver, CO

Chair: *John Grabowski,* University of Texas Health Sciences Center, Houston, TX

SYMPOSIUM

Progress in Understanding the Behavioral and Neurobiological Effects of Cocaine

Chair: *Steven I. Dworkin,* Louisiana State University School of Medicine, Shreveport, LA

Discussant: *John Grabowski,* University of Texas Health Sciences Center, Houston, TX

LONG-TERM EXPOSURE TO COCAINE: OVERVIEW AND SOME CURRENT DATA. William L. Woolverton. University of Chicago, Chicago, IL.

(Abstract not available)

REPEATED COCAINE ADMINISTRATION AND SCHEDULE-CONTROLLED BEHAVIOR. Marc N. Branch. University of Florida, Gainesville, FL.

Recent research has shown that effects of repeated cocaine administration can be altered by behavioral variables. Among the recently discovered important factors are the parameters of schedules of positive reinforcement. Tolerance to effects of repeated cocaine administration has been found to depend strongly on the parameter value of fixed-ratio schedules, but not at all on the parameter value of fixed-interval schedules. Variable-ratio and variable-interval schedules have produced intermediate effects, i.e., for some subjects, tolerance has been schedule-parameter dependent, whereas for others, it has not.

REINFORCING AND CARDIOVASCULAR EFFECTS OF COCAINE IN MONKEYS AND HUMANS. Charles W. Schindler, Jonathan R. Katz, Steven R. Goldberg, Ro Nemeth-Coslett and Jack E. Henningfield. National Institute on Drug Abuse Addiction Research Center, Baltimore, MD.

The effects of IV cocaine administration were determined in both squirrel monkeys and human volunteers. In monkeys, the ability of cocaine to maintain self-administration behavior and the cardiovascular effects of cocaine were determined in separate groups. In humans, self-administration and cardiovascular measures were taken concurrently. In monkeys, where higher doses could be administered, cocaine produced significant increases in blood pressure at