Pharmacology Biochemistry & Behavior, Vol. 18, pp. 541–544, 1983. © Ankho International Inc. Printed in the U.S.A.

Effects of Methylphenidate on the Fixed-Ratio Performance of Mentally Retarded Children[1]

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Received 12 August 1982

POLING, A. AND S. E. BREUNING. *Effects of methylphenidate on the fixed-ratio performance of mentally retarded children.* PHARMACOL BIOCHEM BEHAV 18(4) 541–544, 1983.—The effects of methylphenidate on the lever-pressing of 12 mentally retarded children maintained under fixed-ratio 5, 10 and 20 schedules of food delivery were examined. For five children, methylphenidate at oral doses of 0.3, 0.7 and 1.0 mg/kg produced generally dose-dependent decreases in response rates, whereas for the other seven children the two lower doses increased response rates while the highest dose decreased responding. The differential effects of methylphenidate across participants could not be attributed to differences in control response rates or demographic factors. However, each child whose rate of fixed-ratio responding was increased by methylphenidate also demonstrated a therapeutic response to the drug.

Methylphenidate Fixed-ratio schedule Lever-press response Children Mental retardation

DRUG effects in mentally retarded humans has become a topic of interest as it has become apparent that little is known concerning the clinical efficacy or basic behavioral effects of many drugs in this population, and that findings with other populations (e.g., the mentally ill) do not necessarily generalize to the mentally retarded [4, 5, 6].

Methylphenidate (Ritalin) is one drug whose effects in the mentally retarded are little known. This drug is a stimulant frequently used to treat hyperkinesis (now generally referred to as attention deficit disorder), a behavioral syndrome of children "characterized by short attention span, aggressive behavior oriented toward peers, impulsiveness, and restlessness" [11]. A large number of clinical investigations have examined the therapeutic efficacy of methylphenidate and other stimulants, and it appears that the problem behaviors of many (but by no means all) hyperactive, non-retarded children are beneficially affected by stimulant medications (for reviews see [1, 2, 13]). Fewer successes have been reported when methylphenidate was used with mentally retarded children who exhibited problem behaviors similar to those associated with hyperkinesis [11].

Methylphenidate's behavioral pharmacology in mentally retarded humans is largely speculative. For example, the manner in which the drug affects schedule-controlled behavior in this population is unclear. One study [8] reported that a 0.5 mg/kg dose of methylphenidate had no effect on the rate of bar-pressing or rocking of 10 mentally retarded subjects when these responses were maintained under a fixed-ratio 15 (FR 15) schedule of candy delivery and analyzed statistically on a group basis. When examined on an individual basis, the response rate of some subjects increased when drug was given, while that of others decreased. Since only one dose of methylphenidate was evaluated, and no further reports in this vein have appeared, these results are difficult to interpret.

The present study examined the effects of oral doses of 0.3, 0.7 and 1.0 mg/kg methylphenidate on the lever-press responding of mentally retarded children when responding was maintained under FR 5, 10 and 20 schedules of food delivery. These doses were selected since they fall within the suggested therapeutic range and, in hyperactive non-retarded children, "doses between 0.3 and 0.7 mg/kg appear

[1]This research was supported by USPHS Grants MH/HD 37449 to Stephen E. Breuning and MH 30915 to the Clinical Research Center for Affective Disorders and Western Psychiatric Institute and Clinic. Costs of manuscript preparation were partially defrayed by a Faculty Research Grant awarded to Alan Poling by Western Michigan University. Requests for reprints should be addressed to Dr. Alan Poling, Department of Psychology, Western Michigan University, Kalamazoo, MI 49008, or Dr. Stephen E. Breuning, John Merck Program for Multiply Disabled Children, Department of Psychiatry, Western Psychiatric Institute and Clinic, University of Pittsburgh School of Medicine, 3811 O'Hara Street, Pittsburgh, PA 15213.

TABLE 1
SUBJECTS' DEMOGRAPHIC CHARACTERISTICS

Subject	Sex	Age (yrs)	Weight (kg)	IQ	Initial CTRS
1	F	11.2	38.6	56*	16.7
2	F	12.6	42.1	44†	15.8
3	M	14.3	56.6	43†	15.9
4	M	14.1	50.1	29‡	16.4
5	M	9.6	32.3	59*	18.1
6	F	7.4	22.4	54†	15.4
7	M	10.0	32.5	63*	17.5
8	M	8.2	24.7	25‡	16.7
9	F	9.3	30.3	49†	19.3
10	M	10.2	34.8	51‡	15.8
11	M	6.8	23.4	61†	16.3
12	F	8.7	26.2	37*	16.4

*Wechsler Intelligence Scale for Children—Revised.
†Stanford-Binet.
‡Leiter International Performance Scale.

to increase academic and learning behaviors, while large doses (i.e., above 1.0 mg/kg) seriously impair these same behaviors" [11]. Reported data were collected as part of a larger investigation designed to assess the effects of methylphenidate on several clinically relevant measures, including time spent on-task, parts assembled in a workshop task, and teachers' evaluations of behavior. The abbreviated Conners Teachers Rating Scale (CTRS), described elsewhere [12], was used to quantify teachers' evaluations.

PROCEDURE

Subjects

Twelve hospitalized mentally retarded children (mean intelligence quotient=48, range=25 to 63; mean age=10.2 years, range=6.8 to 14.3 years), seven boys and five girls, participated in the study. The sex, age, weight, intelligence quotient (IQ) and CTRS score of each child at the onset of the investigation is shown in Table 1. Participants were selected on the basis of having mental retardation due to unknown etiology with no other neurological disorders and scoring above 15 (the accepted cutoff for hyperactivity with non-retarded children) on the CTRS. CTRS scores were used in screening participants because methylphenidate is useful in managing the behavior of hyperactive, non-retarded children, which allows a clinically reasonable argument to be made for evaluating the drug's effects in mentally retarded children who behave similarly (i.e., whose CTRS scores fall above 15), although not necessarily in other mentally retarded individuals. Parental consent to participate in the study was obtained for each child.

Apparatus

Testing was conducted in a room 4 m wide, 5 m long, and 2.5 m high. The room was equipped with a chair, in which the participant sat facing a table. A work panel located on the table was equipped with a metal response lever that projected outward 10.2 cm, and a food dispenser that delivered small edibles (M & M's, Mars, Inc., Hackettstown, NJ, or Reese's Pieces, Reese's Co., Hershey, PA). Solid-state and electromechanical equipment located in an adjacent room recorded responses and arranged food deliveries.

Procedure

Each child initially was trained to press the lever under a FR 1 schedule, where every press was followed by delivery of a single piece of candy. Training involved verbal instruction, modeling, and physical guidance if necessary. After initial training, the child was left alone (although constantly monitored via a one-way mirror) and instructed to keep pressing the lever to earn candy. During the first session, which like all subsequent sessions terminated after 30 min, the FR value initially was set at one and gradually increased across time. This procedure was continued across sessions until all participants consistently earned food when it was available under a FR 20 schedule. At that point, the experiment proper began.

The experiment was conducted in alternating seven-day phases of methylphenidate and placebo administration. Three oral doses of methylphenidate hydrochloride (CIBA Pharmaceutical Co., Summit, NJ), 0.3, 0.7 and 1.0 mg/kg, were examined. These doses, like placebo, were administered in capsules of identical appearance 90–100 min prior to the experimental session. Double-blind conditions were in effect throughout the study; neither the participants nor the experimenter were aware of the drug given. Each participant received each dose of methylphenidate during one seven-day block, with the order of exposure counterbalanced across participants. As noted above, a seven-day block in which placebo was given preceded and separated each series of drug administrations.

In each experimental session, a participant was exposed to FR 5, 10 and 20 schedules of food delivery. Each FR value was in effect for 10 min; the order in which the schedule values appeared alternated irregularly across sessions and no exteroceptive stimuli were associated with the individual FR values. Thus, a mixed FR 5, FR 10, FR 20 schedule of food delivery was in effect during all sessions. Response rates during each component of this schedule (i.e., under each value of the FR) were recorded separately.

RESULTS

Figure 1 depicts the rate of responding of each child under all experimental conditions. Control values (0 mg/kg) represent mean response rates during the last session of each of the three placebo phases; each drug data point indicates the response rate during the final session of exposure to a particular methylphenidate dose.

During control sessions, children responded most rapidly under the FR 20 component, and least rapidly under the FR 5 component. Drug effects differed across participants, with two major patterns of sensitivity being evident. For five children, methylphenidate generally failed to increase responding relative to control values. In these individuals, the drug typically was associated with dose-dependent rate decreases at each FR value.

The 1.0 mg/kg methylphenidate dose also decreased response rates in the remaining seven children. However, the two lower doses generally increased response rates in these individuals. The magnitude of this effect typically was greatest under the FR 20 schedule, least under the FR 5 component. In five children, the highest rates of responding were associated with the 0.3 mg/kg dose, although the 0.7

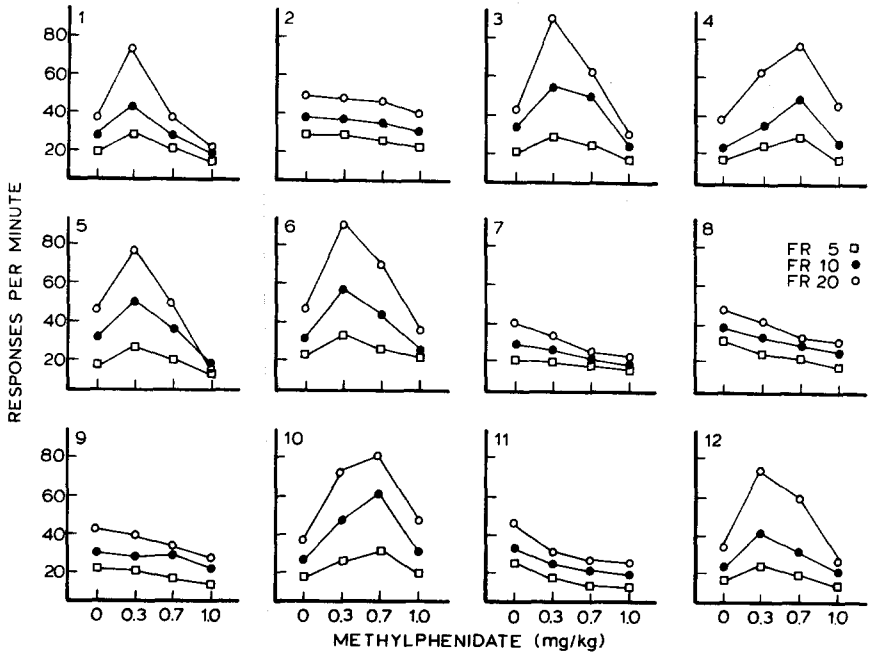

FIG. 1. Effects of methylphenidate on the FR performance of mentally retarded children. Each control (0 mg/kg) data point represents the mean rate of lever-pressing across three sessions as explained in text. Each drug data point represents performance during the final session of exposure to the indicated dose.

mg/kg dose was associated with the most rapid lever-pressing in two individuals.

DISCUSSION

In the present study, methylphenidate did not similarly affect the FR performance of all participants. However, data were not disorderly, and therefore uninterpretable. Rather, two separate patterns of sensitivity were evident. This may be of interest, especially if the variables responsible for the differential effects across participants can be disclosed.

One variable that investigations with nonhumans have revealed to influence the effects of stimulants on schedule-controlled performance is the control (drug absent) rate of responding. These drugs generally increase low-rate operants at doses that decrease high-rate operants [10]. Given this, it might be expected that those participants for whom methylphenidate increased FR response rates in the present study responded at far lower control rates than those for whom the drug decreased responding. This was not the case: Whether methylphenidate increased or decreased the FR responding of mentally retarded children was not related in any obvious way to control response rates. The drug's effects also were not related to the age, sex, or intelligence of participants, or the sequence of exposure to the three doses of methylphenidate. Thus, the factors that account for the two patterns of sensitivity observed in this study are unknown.

Retrospective analysis of the measures taken to determine the clinical efficacy of methylphenidate did reveal that each child for whom 0.3 and 0.7 mg/kg doses of the drug were associated with increased rates of FR responding also evidenced a therapeutic response to the drug. This was shown by increases in time spent on-task and parts completed in a workshop assembly task, and decreases in teachers' ratings (CTRS) of hyperactive behavior. The five children whose rates of FR responding were highest when 0.3 mg/kg methylphenidate was administered had mean CTRS scores of 16.5, 7.2, 9.6 and 19.7 for the 0, 0.3, 0.7 and 1.0 mg/kg conditions, respectively. The two children whose rates of FR responding were highest when the 0.7 mg/kg dose was given had mean CTRS scores of 16.1, 9.3, 6.9 and 21.2 across these same four conditions. The CTRS scores of the remaining five children, whose FR responding was decreased by methylphenidate, increased as the drug dose increased. Thus, each child whose FR response rate increased in the presence of methylphenidate manifested a therapeutic response to the drug, while each child whose FR responding decreased in the presence of the drug failed to manifest such a response. Further, for the former individuals, the greatest rates of lever-pressing occurred at the dose (i.e., 0.3 or 0.7 mg/kg) which led to the greatest therapeutic control of hyperactivity. This finding suggests that Davis' [8] findings, discussed earlier, may have been due to some of her subjects being therapeutic responders while others were not. Unfortunately, the variables that determine whether methylphenidate produces a desirable clinical outcome with mentally retarded children are elusive.

The present findings suggest that mentally retarded individuals showing therapeutic responses to methylphenidate may also show increased rates of adaptive behavior. This stands in contrast to the results of recent studies showing dose-dependent decreases in adaptive behaviors of mentally retarded individuals receiving neuroleptic drugs regardless of whether there is a therapeutic response to the drug [3,7], and may be of clinical significance given that the rationale for using a neuroleptic versus methylphenidate with mentally retarded children appears to often be tenuous (see [9]).

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