The Effect of Methylphenidate on Test Performance in the Cognitively Impaired Aged

THOMAS CROOK1 *, STEVEN FERRIS2, GREGORY SATHANANTHAN2, ALLEN RASKIN1, and SAMUEL GERSHON2

1 Psychopharmacology Research Branch, Division of Extramural Research Programs, National Institute of Mental Health, 9-101, 5600 Fishers Lane, Rockville, MD 20857, U.S.A.
2 Neuropsychopharmacology Research Unit, Department of Psychiatry, New York University Medical Center, New York, New York, U.S.A.

Abstract. It was hypothesized that a central nervous system stimulant with relatively weak peripheral effects would facilitate test performance in the cognitively impaired aged. Twelve elderly subjects participated in a counter-balanced, crossover comparison of 10 mg methylphenidate, 30 mg methylphenidate and placebo. All treatments were administered double-blind as a single dose of oral medication. Neither dosage of active medication was found to effect psychomotor or psychological test performance, subjective report, heart rate or blood pressure. A subsequent open trial of 45 mg methylphenidate resulted in heart rate, blood pressure and subjective changes in two of eight subjects but no effects on test performance. The results suggest that cognitive performance in the moderately impaired aged is unimproved following administration of methylphenidate, and perhaps similar sympathomimetic amines, below a dosage level associated with clinically significant peripheral effects.

Key words: Methylphenidate — Central nervous system stimulant — Peripheral drug effects — Aging — Cognition — Psychological test performance.

The behavioral change which has most consistently been found to occur with advanced age is a decline in performance on fast-paced tasks (Jarvik and Cohen, 1973). Indeed, much of the early evidence suggesting a decline with age in verbal learning ability seems to have resulted from the speeded nature of the learning tasks employed to compare the performance of old with young subjects (Botwinick, 1967). Birren (1974) has suggested that the general slowing of response speed seen in advanced age reflects a decrease in the speed with which the central nervous system (CNS) processes information and that increased processing time underlies age-related deficits in diverse aspects of cognitive function.

Substantial evidence exists to support the hypothesis that the slowing of response speed with age is attributable to altered CNS functioning rather than sensory-perceptual or peripheral neuromuscular factors (Botwinick, 1973). Lowered electrocortical reactivity has been held by Surwillo (1963) to account for a large proportion of the response speed decrement. However, decreased cortical reactivity in the aged may be accompanied by decreased reactivity of some peripheral autonomic end organs and increased reactivity of others. For example, the frequency of spontaneous galvanic skin responses in the elderly is below the range associated with optimum performance (Shmavonian and Busse, 1963), while plasma free fatty acid levels (FFA) are higher (Troyer et al., 1966). Eisdorfer and his colleagues have demonstrated that test performance of aged subjects can be improved by pharmacologically blocking feedback to the CNS from the peripheral effects of heightened autonomic arousal (Eisdorfer et al., 1970), perhaps thereby increasing CNS activation (Thompson and Marsh, 1973).

Direct pharmacologic stimulation of the CNS would seem to offer the possibility of decreased response time and, consequently, improved cognitive test performance in the elderly. However, since both FFA mobilization (Eisdorfer, 1967) and increased blood pressure (Birren, 1963) are factors associated with performance decrement in the aged, the drug of choice would seem to be a CNS stimulant with relatively weak cardiovascular and sympathomimetic effects. Methylphenidate (Ritalin) would seem to be a central stimulant worthy of investigation since it exerts relatively weak peripheral autonomic effects (Meir et al., 1954).
In the present study we predicted methylphenidate would improve the performance of cognitively impaired elderly subjects on measures dependent upon perceptual, motor, or information processing speed. In non-fatigued, young adults the drug would be expected to exert a disinhibiting effect which would facilitate performance on reflexive stimulus-response tasks but impair performance on tasks which involve inhibition or delay of initial response tendencies and mediation of higher processes (Broverman et al., 1968; Jarvik, 1972). Thus, performance on measures such as disjunctive reaction time or the Digit Symbol Substitution subtest of the Wechsler Adult Intelligence Scale (Wechsler, 1958) would not be expected to improve in alert young normals, while improvement would be expected on such measures as simple reaction time and finger tapping speed. The former, higher order, tasks are those on which performance reliably declines with age (Botwinick, 1967), and on which clinically significant change would likely be reflected.

METHODS

Subjects

Subjects were six males and six females between the ages of 65 and 80 years who resided with a family member in the community and complained of diminishing memory and intellectual function. The mean age of study subjects was 72 years and all subjects were described by their families as having significant memory impairment of more than 1 year but less than 5 years duration.

An age-corrected scaled score of at least 8 on the Vocabulary subtest of the Wechsler Adult Intelligence Scale (WAIS) was required for study admission as an indication of both adequate premorbid intellectual function and ability to complete the required psychological testing. Subjects were also required to score more than one standard deviation below the mean established for their age group and WAIS Vocabulary level on at least three of five subtests (excluding digit span) on the Guild Memory Test (Gilbert et al., 1968). The latter criterion was imposed to ensure memory loss significantly greater than expected in the normal aging process. Persons were excluded from the study on evidence of medical contradictions, or a history of seizure disorder, alcoholism or psychiatric disorder requiring hospitalization. Also excluded were persons who required medications which might influence the effects of methylphenidate.

Procedure

Two separate drug trials were conducted. The design of each is outlined as follows:

Study 1

The first study employed a single factor, counterbalanced, crossover design in which three treatments, each consisting of a single dose of oral medication, were administered double-blind. The treatments were 10 mg methylphenidate, 30 mg methylphenidate, and placebo. One male and one female were assigned to each of the six possible sequences in which the treatments could be ordered. Prior to the study all subjects were brought into the psychological laboratory twice, tested, and familiarized with the test equipment and personnel. This procedure was undertaken in order to diminish anxiety attendant to psychological test performance. Drug administration began following the second day of familiarization. Medication was administered on the morning of study day 1, day 3, and day 5. One day was allowed between each administration in order to reduce the likelihood of residual effects. Psychological testing began 45 min after ingestion of medication.

Study 2

A second study was to be undertaken with a higher dose of medication if no untoward drug effects occurred in any subject during study 1. Study 2 was designed as an open trial of 45 mg methylphenidate. Subjects were tested before and 45 min after ingestion of the medication.

Measures

Heart rate and blood pressure were recorded at baseline and at 30, 60, and 90 min following ingestion of medication. The psychological test battery was composed of the following measures:

1. Finger Tapping Speed. Subjects were instructed to depress a key with the index finger as many times as possible in a 15-s interval. The number of responses was recorded separately for the dominant and non-dominant hand.

2. Reaction Time. Performance was recorded on both a simple visual reaction time task and a disjunctive task involving a three light choice situation. In both cases a variable preparatory interval of 1 – 3 s was employed with an auditory warning signal.

3. Perceptual Speed. The test measures the speed with which an individual can find a well known symbol embedded in a mass of material (Moran and Mefford, 1959). The subject is presented with a page of random numbers in which the left most number in each row is circled. The 150-s task of the subject is to cross out every digit in a row identical to the digit circled in that row.

4. Speed of Closure. The test measures the subject’s ability to rapidly unify an apparently disparate perceptual field into a single percept (Moran and Mefford, 1959). The task of the subject is to find within 150 s as many four letter words as possible embedded in 22 lines of continuous capital letters.

5. Digit Symbol Substitution Test. The test is the most sensitive of the 11 WAIS subtests to age related cognitive decline (Botwinick, 1967). The 90-s task measures the subject’s ability to learn new material involving the relationship of symbols (Wechsler, 1958).

6. Memory for Faces Test. The test provides a measure of initial recall of meaningful non-verbal material (Moor et al., 1960). The task of the subject is to inspect a stimulus panel composed of 16 facial photographs for 60 s. Immediately after this exposure the subject is presented with a response panel containing 32 photographs and asked to identify those 16 which he has already seen.

7. Digit Span. Forward and backward digit span were recorded as measures of immediate rote memory.

8. Associate Learning. The associate learning subtest of the Wechsler Memory Scale (Wechsler, 1945) was employed to provide a measure of learning and recall of paired associates.

9. Paragraph Recall. An index of both immediate and delayed recall of meaningful verbal material was obtained using the paragraph recall subtest of the Guild Memory Test.