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The Effects of Deanol on Cognitive Performance and Electrophysiology in Elderly Humans

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Abstract. Deanol (900 mg/day for 21 days) had no effect on learning a list of words when tested at weekly intervals. Tests of simple and complex reaction time and a test of continuous serial decoding of digits showed no enhancement with the drug. Several components of evoked potentials recorded from several scalp sites did show enhanced amplitude under drug treatment. These changes were not accompanied by changes in the EEG spectrum as are seen with some other psychoactive drugs. Deanol seems to be an ineffective treatment for the normal slowing of cognitive function seen in the normal elderly person or those elderly with only minimal cognitive decline and free of symptoms of dementia. Contrary to earlier reports, elderly persons were found to be able to benefit from warning signals in a complex reaction time task.

Key words: deanol – Electrophysiology – Reaction time – Human performance – Age

Older persons process information more slowly than younger persons, especially when memory search is required (Anders and Fozard, 1973; Craik, 1977; Welford, 1977). In an effort to assess a drug reputed to alleviate some of the mental deterioration of senility (Green, 1965; Lawrence and Leichman, 1965), several tasks were used to assess the information processing ability of older persons during deanol (Deaner, Riker Laboratories) treatment.

Deanol has been demonstrated to be metabolized and incorporated into the central nervous system (CNS) choline pool (Dormard et al., 1975a, b), probably by increasing the availability of choline, the rate limiting substance in acetylcholine (ACh) synthesis (Fonnum, 1975). Choline is also a component of cell membranes, the composition of which may be affected by deanol (Ansell and Spanner, 1962).

The choice of the drug was based on the well-documented sensitivity of elderly patients to anticholinergic drugs (Davis, 1974; Neubauer et al., 1966a, b). The central symptoms of anticholinergic intoxication are similar to those of organic brain syndromes (Drachman and Leavitt, 1974; Safer and Allen, 1971). It was hypothesized that deanol would effectively improve mental functioning in the elderly to the extent of their relative ACh deficiency.

It has been reported (Botwinick et al., 1957; Rabbitt, 1964, 1968; Talland, 1965) that a warning signal (WS) in a reaction time (RT) paradigm which delivered timing information or decreased the number of possible classes of imperative signals speeded RT in younger persons, but had no effect in older persons. Moreover, for the younger group, increasing the amount of information in the WS decreased RT significantly. We wished to test whether treatment with deanol would lead to better utilization of the WS information by older persons.

The strongest reported effect of a deanol ester has been on demented elderly subjects where it enhanced alertness and the ability to recognize those around them (Bohard and Guennoc, 1968). Thus, enhanced memory or learning ability could be a possibility in normal elderly people treated with the drug. The elderly usually have more difficulty with recall than with recognition tasks (Crenshaw, 1969; Erber, 1974; Schonfield and Robertson, 1966), thus, the task in the present experiment used recall as the major test of memory.

The average evoked potential (AEP) measures obtained in the present experiment were expected to give some indication of the subject's attentional state, response to stimuli and the drug, whether or not the subject pressed the response key (Hillyard et al., 1973, 1971; Schwent and Hillyard, 1975; Squires et al., 1973). The drug treatment was predicted to enhance amplitude of the N_{100} and P_{300}

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components, and to decrease the latency of the N_{100} and P_{300} peaks. An analysis of the EEG into the various spectral components was carried out, because it enabled further testing of the effect of the tasks on the subjects. Measurement of the changes in the EEG from nondrug to drugged state allowed testing of the drug for its potential stimulant and anxiolytic effects. Deanol was not expected to change the amount of beta activity, but was expected to enhance the percentage of alpha activity (8–12 Hz) by decreasing the percent occurrence of the lower frequencies: theta (7–4 Hz) and delta (4–1 Hz).

Materials and Methods

Subjects. Eleven male subjects were obtained from a pool of volunteer subjects maintained by the Duke University Center for the Study of Aging and Human Development. Five of these subjects were obtained from a large longitudinal study population ($N = 502$) and were selected by using the criterion that their Wechsler Adult Intelligence Scale (WAIS) digit-symbol scores had decreased by at least 20% over the past 6 years. The maximum and minimum scores are 19 and 0. The mean of the group was 5.4 at the last testing before being selected for this experiment. The digit-symbol subtest was chosen, since it is an age-sensitive test, as opposed to the verbal subtests which tend to remain stable with age. The subjects' age range was 54–71 with a mean of 65.8 years. All subjects were paid a flat rate of $80.00 for their participation. Our sample exhausted the pool of subjects who were available from the longitudinal study and met our criteria.

Procedure. All subjects were brought to the laboratory for a short physical examination. They were briefed on the procedures of the experiment and were then given several hours of practice on the tasks. They returned 1 week later for another practice session. Each practice session was a duplicate of the experimental sessions except more time was allowed for questions and explanations.

To provide experimental data, subjects returned at weekly intervals for four test sessions. All subjects were tested at the same time of day on each return to the laboratory.

Drug. Deanol (300 mg) (Riker Laboratories) was administered TID orally (100 mg tablets) for 21 days. Identical placebo tablets were taken the same way. The experimental design was double-blind without a crossover. No other medications were allowed during the experiment.

Drug or placebo condition was assigned randomly. Following the two practice sessions, the first test session (day 0) was performed with no drug administered. Drug or placebo treatment commenced the morning following this first test session. The ensuing three experimental sessions were thus carried out on days 7, 14, and 21 with the subjects on the active drug or placebo.

Apparatus. The first task used a keyboard with 9 keys. The center key was pressed and held down by the subject to indicate that he was ready for a trial. The imperative (or reaction) signal was the illumination of one of the other 8 keys; whenever one of these keys lit up, it was to be pressed as quickly as possible. Eighty trials (10 per key) were given in random order to obtain the mean lift RT from the center key and the mean press RT for each response key. All presentations were under computer control and no trial could be given until the subject had signalled his readiness by holding down the center key. Random intertrial intervals were 2–5 s long.

After a 5-min rest, a series of 105 trials were given using WS. The signals were of three levels and were randomly intermixed. The first level gave only time information: after a 1.2-s WS, one of the 8 response keys was illuminated. The second level signalled that in 1.2 s a key would be illuminated and it further indicated whether the response key would be to the left or right of the center key (i.e., it reduced the number of possible response keys from 8 to 4). The third level gave the usual 1.2-s WS and it also reduced the number of possible response keys from 8 to 2 by indicating whether it would be the two outermost left or the two outermost right keys. The WS were 3 light-emitting diodes, each 3 mm in diameter and 15 mm apart in a horizontal row. The WS for level 1 was illumination of only the center diode. Level 2 was indicated by illumination of the center plus either the left or the right diode. Level 3 was illumination of only the left or right outermost diode. There were 33 trials of each type. Five 'catch' trials were also included to test the effect of incorrect warning information on RT. Since lift RT (for the center key) should be more sensitive to aging effects than press RT, it was used as the single dependent RT measure. The above task was formulated to test the results of Rabbitt (1964, 1968), Botwinick et al. (1957), and Talland (1965) who had all reported that older subjects were unable to use WS information to improve their performances.

A continuous performance task (CPT) was used which was modelled after the test of Mirsky and Cardon (1962). Digits were presented for 100 ms via a seven-segment display made up from light-emitting diode elements. The dimensions of these digits were 9 mm in height and 6 mm in width, and were displayed 1.0 m in front of the subject at shoulder level. The subject held a small switch in his right hand to be pressed whenever two odd or two even digits were displayed consecutively. For the first task in this series, another duplicate key was held in the left hand. Pressing this switch was required for the presentation of each digit. Thus, a subject could present digits at whatever rate was confortable for him. Following this manual presentation of the digit series, a second series was run under computer control, using as a presentation rate the subject's average rate for the manual series. This allowed the comparison of self- and machine-initiated trials while holding the average rate of presentation constant. The final series was machine-initiated and run at the fixed, rapid rate of 1 digit/s. All series contained 300 digits with targets (to which the subject responded by a key press with his dominant hand) distributed randomly and occurring on the average once in every six trials. A target was defined as an odd or even digit which consecutively followed another of the same classification. The behavioral and physiological data were segregated according to signal detection theory and the parameters of d′ and log-β computed (McNicol, 1972).

For the verbal learning task, a list of 16 words was chosen randomly from the Thorndike-Lorge compendium of medium familiar words. These words were presented to the subject via a slide projector and screen arrangement with the screen 7 ft in front of the subject. The words were exposed for 2 s with a 4-s delay between word onsets. At the end of the list the subject was immediately asked to recall as many words as possible. The subject's responses were tape recorded for later analysis. This procedure was then repeated six times.

Before the second presentation and after the sixth presentation, a recognition procedure was inserted. This procedure presented 16 words; 8 from the list to be learned randomly mixed with 8 new items. The subject pressed a key as quickly as possible for all words he recognized as being from the list to be learned. The presentation rate was the same as the rate used for the list to be learned.

EEG data were obtained from scalp sites F_z, C_z, and P_z in the International 10–20 system (Jasper, 1958). Horizontal and vertical eye movements and blinks were recorded from electrodes above and below the left eye and at the outer canthus of each eye. Trials on which eye blinks occurred were omitted from analysis. All electrodes were referenced to linked mastoids and all impedances were below 2,000 ohms. A Grass (model 78) polygraph was used for amplification and a Hewlett-Packard FM seven-channel analog tape recorder was used to store the data. Off-line analysis into AEPs was by a PDP-11/03