Cognitive dysfunction with cardiovascular disease*

JAMES W. McDANIEL

University of Colorado School of Medicine, Denver, Colo. 80220

Recent investigations have suggested that cerebral hypoxia due to cardiac insufficiency may produce cognitive impairment. Experimental evidence confirming cognitive dysfunction in persons having cardiovascular disease has, however, not been thoroughly developed. Cognitive and visual-motor impairment with cardiovascular disease in men has been confirmed in the present study; this is apparently related neither to aging nor to hypertension.

The reduction of cognitive efficiency in patients with cardiovascular diseases has been suspect for some time but has been a complicated problem for investigation due to the confounding effects of aging and other physiological variations. Spieth (1965), however, partially reconciled the issues through the finding that cardiovascular disease imposes further performance decrements upon those normally attributable to aging. Spieth's interpretation was that circulatory insufficiency within the nervous system was the most likely cause of cognitive dysfunction. Reports that electroencephalographic abnormalities with cardiac disease are related to hemodynamic factors (Jouve et al, 1961) have added support to this hypothesis. Jacobs et al (1969) have concluded that any factor capable of altering cortical oxygen supply, for example, blood flow, hemoglobin level, and arterial oxygen pressure, can affect cognitive functioning, in particular short-term retention and conceptual activity. Previous research has documented difficulties in gross motor coordination (Fowler & Gardner, 1963) and psychometric test performance (Zaks et al, 1963) among cardiac patients, but there have been few controlled laboratory investigations of cognitive functioning in clinical research relative to cardiovascular disease.

The investigation reported here has attempted to clarify the extent of cognitive dysfunction among individuals with cardiovascular diseases under conditions that are reliably identical for all Ss. Results are provided in terms of traditionally interpreted indexes of rate of learning or acquisition of a new response pattern in an environmentally and experimentally controlled situation.

METHOD

The Ss for this investigation were 20 male patients whose mean age was 48.4

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years. All had confirmed myocardial infarctions, but with varying degrees of myocardial damage and functional incapacity. A control group of 12 males whose mean age was comparable (44.5 years) and a larger control group of 20 younger Ss (mean age 23.2 years) also served as Ss.

An automated technique for visual discrimination learning was employed with both experimental (N = 20) and control Ss (N = 32). This method and apparatus has been described in detail elsewhere (Vaughn & McDaniel, 1969). The task presented the S is a match-to-sample problem during which response latencies and error rates are tabulated throughout the task.

A pursuit-rotor tracking task was also employed during which Ss had alternate 20-sec work-rest periods, tracking at a speed of 45 rpm. The apparatus was a Lafayette Model 2203, and time on target was recorded to the .01 sec for 15 work trials with right and left hands.

RESULTS

Visual Discrimination Learning

Since the older age control group did not differ significantly from younger Ss on the acquisition of this task, data for controls have been pooled for comparison with experimental Ss. Cardiac Ss had a significantly greater error rate than controls at every stage of the match-to-sample task, as indicated in Table 1. All Ss first were required to match stimuli on the basis of color alone, then by geometric shape, and subsequently by the number of designs present in the sample stimulus, the sequence being repeated twice. Although only error rates are presented here, identical results were determined for times required by cardiac vs control Ss to arrive at the solution to each problem.

It was expected that some correlation could be determined between blood pressure and task performance among cardiac patients, but this was not confirmed. Task performance in terms of mean errors and mean solution search times did not correlate significantly with systolic or diastolic pressures.

Visual-Motor Tracking

All Ss, cardiac and controls, received their first trials using the right hand and after 15 switched to the left hand for an equal number of trials. A criterion of 95% accuracy was established, defined as the number of trials to reach this percentage of time on target in a 20-sec work period. This required significantly greater mean number of trials with both right and left hands for cardiac Ss than for comparably aged controls, as indicated in Table 2. To illustrate these differences in performance, data for the right-handed trials are presented in Fig. 1.

DISCUSSION

Results of this research indicates a rather profound degree of cognitive and visual-motor dysfunction among males with cardiovascular disease that is attributable neither to aging nor hypertension. In visual discrimination learning, cardiac Ss have demonstrated greater errors and times required in arriving at a problem solution. These Ss likewise required significantly more trials than did controls to reach the same level of performance efficiency in visual-motor tracking. Recent research has suggested that hemodynamic factors responsible for inadequate oxygen transport to the cerebral cortex may cause these deficits. If this relationship proves valid, remediation may be possible. Jacobs et al (1969) have found, for example, that increasing the arterial oxygen tension by means of hyperbaric oxygenation over a period of 15 days significantly increased the cognitive efficiency of the aged Ss with cerebral arteriosclerosis. Recent treatment methods emphasizing the physical reconditioning of cardiac patients may also offer some promise, and research designed to improve the cognitive efficiency of persons with cardiovascular diseases should definitely be integrated with other clinical research oriented toward cardiac rehabilitation.

Table 1
Differences Between Mean Error Rates on Match-to-Sample

Subgroup	Color 1	Form 1	Number 1	Color 2	Form 2	Number 2
Cardiac	13.8	7.3	10.5	8.3	8.1	5.9
Control	5.8	4.4	4.3	5.6	3.3	2.6
t (df = 50)	10.47*	3.66*	6.75*	2.65**	11.46*	6.56*

*p < .001, **p < .05

Table 2
Differences in Mean Trials to 95% Efficiency
in Pursuit-Rotor Tracking

Subgroup	Right Hand	Left Hand
Cardiac	7.3	7.5
Control	3.8	4.6
t (df = 28)	4.60*	8.17*

* $p < .001$

REFERENCES

- FOWLER, W., & GARDNER, G. The relation of cardiovascular tests to measurements of motor performance and skills. *Pediatrics*, 1963, 32, 778-789.
- JACOBS, E., WINTER, P., ALVIS, H., & SMALL, S. Hyperoxygenation effect on cognitive functioning in the aged. *APA Proceedings*, 1969, 4, 721-722.

- JOUE, A., GERARD, R., GRAS, A., REGIS, H., BENJAMINE, R., & Malfroy, P. Hemodynamic and electroencephalographic correlations in hypoxic heart diseases. In H. Gastaut and J. S. Meyer (Eds.), *Cerebral anoxia and the electroencephalogram*. Springfield, Ill: Charles C Thomas, 1961. Pp. 590-596.
- SPEITH, W. Slowness of task performance and cardiovascular diseases. In N. T. Welford and J. E. Birren (Eds.), *Behavior, aging and the nervous system*. Springfield, Ill: Charles C Thomas, 1965. Pp. 366-400.
- VAUGHN, A., & McDANIEL, J. Electromyographic gradients during complex visual discrimination learning. *Psychonomic Science*, 1969, 16, 203-204.
- ZAK, M., COSTELLO, J., KEZDI, P., & BOSHER, B. The influence of physiological impairment in cardiac patients on neurological and psychological functioning. *American Psychologist*, 1963, 18, 396. (Abstract)

The effects of scopolamine on the extinction of a continuously reinforced response*

W. A. McKIM

Lakehead University,† Thunder Bay, Ont., Canada

Thirty-five rats were injected with varying doses of scopolamine, methyl scopolamine, and saline before extinction of a continuously reinforced response. Methyl scopolamine and low doses of scopolamine speeded extinction, whereas higher doses of scopolamine led to responding similar to that of saline controls. It is suggested that the relatively weak tendency to respond after CRF training and the drastic switch to extinction from CRF maximized the disruptive peripheral effects of scopolamine, and as a result higher doses were required to show prolongation of extinction.

One of the more interesting effects of anticholinergic drugs on behavior is that they retard or block the extinction of a previously reinforced response. Herrnstein (1958), after injecting rats with doses of scopolamine from .05 mg/kg to 1.6 mg/kg, found increased responding during two phases of a four-ply multiple schedule that had never been associated with reinforcement. Stone (1964) and Carlton (1963) both examined the effects of scopolamine on the extinction of a Sidman avoidance response. Stone used an alternating avoidance-acquisition procedure and with dosages ranging from 1 to 20 mg/kg, demonstrated increased responding during the extinction periods.

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†Presently at the University of Western Ontario, London, Ontario, Canada.

Carlton, who examined terminal extinction, injected his rats with .6 mg/kg before each extinction session and found no decrease in response rate after 10 sessions. Hearst (1959) used doses of .6 mg/kg of scopolamine given before each session and found no evidence of a decrease in response rate in a discrete-trials discrimination task, even after food had been withheld for 40 sessions.

The above studies all involve either some situation in which the organism has had experience with nonreinforcement or the use of shock motivated behavior; both procedures are known to increase resistance to extinction (Jenkins & Stanley, 1950; Solomon & Wynne, 1954). The purpose of the present study was to extend these earlier results with a procedure involving terminal extinction of a previously continuously food-reinforced response. Dose-response relationships for this drug effect were also examined.

It has been demonstrated in a number of studies that peripheral anticholinergic effects are similar for both scopolamine and methyl scopolamine, whereas methyl scopolamine has very weak central effect, if any (Goodman & Gillman, 1965). Janssen & Neimegeers (1967) have shown that the median effective dose (ED50) for production of miosis in rats with scopolamine is .004 mg/kg and .003 mg/kg for methyl scopolamine, but for central effects the ED50 for scopolamine is .016 mg/kg and for methyl scopolamine is greater than .3 mg/kg. Samuel, Kodamma, & Menear (1965), claim scopolamine to be from 10 to 316 times more effective than methyl scopolamine in producing central effects as measured by the ED50 for the disruption of avoidance behavior.

Using related anticholinergics, atropine and methyl atropine, Whitehouse, Lloyd, & Fifer (1964) showed equal decrements in eating behavior at equal doses of both drugs, yet demonstrated disruption of a discrimination task with atropine and not with equivalent doses of methyl atropine.

It has been assumed in this study as in many others (Bohdanecky, Jarvik, & Carley, 1967; Carlton, 1963) that at equal doses methyl scopolamine will have similar peripheral effects as scopolamine but will have minimal central effects and thus will serve as a control for the influence of peripheral anticholinergic blocking on behavior.

SUBJECTS

Ss were 35 male Long-Evans hooded rats between 100 and 150 days old. They were kept on a 23½-h food-deprivation schedule; they were permitted to eat ad lib for ½ h each day after each experimental session. Water was available at all times in the home cage and during experimental sessions.

DESIGN

A 7 by 7 Latin square design with five independent replications was utilized (Edwards, 1950). Each replication involved seven different rats and continued for 7 consecutive days during which time each of seven drug dosages were given. Three doses of scopolamine hydrobromide¹ (.1, .3, and 1.0 mg/kg), three doses of scopolamine methyl bromide (.1, .3, and 1.0 mg/kg), and a saline control dose were given in a random sequence to each animal with the restriction that, within each replication, all seven doses were given on each day of extinction.

APPARATUS

Seven Electrocraft Skinner boxes that delivered a 45-mg Noyes pellet each time the animal depressed a lever that protruded from one wall of the chamber were used. The manner of operation of the feeder permitted the animal to receive pellets at a maximum rate of one every 3 sec. The