Behavioral Consequences of Mild Hypertension

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SUMMARY Tests made of the sensory-perceptual, cognitive, and psychomotor abilities of untreated young patients with essential hypertension have revealed a pattern suggesting a slight functional impairment of the central nervous system. Reduced performance was most marked for those tasks requiring speed and psychomotor coordination, particularly when the behaviors observed were self-initiated. Lowered scores were more evident among female hypertensives; no differences in performance by race were noted. The deficits measured by these sensitive tests do not appear to be great enough to intrude on everyday activity nor to impair work ability. Changes that may result from blood-pressure-lowering therapies will require further study.

T HE relationship between behavior and hypertension has been investigated in a number of ways. Acute and chronic blood pressure responses to stress have been demonstrated in experimental studies with animals and in humans, and the way in which these pressor responses may be involved in precipitating and perpetuating hypertensive disease has been a subject of much discussion.1 A considerable effort also has been expended in developing the concept of a "hypertensive personality," a configuration in which anger is said to be inhibited in its behavioral expression and, instead, is channeled to an accentuated sympathetic nervous system response. Although particular behavioral characteristics seem to be present in the hypertensive patient, the concept that the constellation provides an etiologic nexus has been difficult to prove. Finally, certain experiments that we and others reported earlier have suggested that some aspects of the behavior of the hypertensive individual in interpersonal relationships may be consequences rather than causes of the hypertension.

The latter observations led us to undertake the present experiment, which was an attempt to demonstrate whether the hypertensive subject does demonstrate evidence of central nervous system (CNS) impairment, resulting from the elevated blood pressure, which in turn might affect behavior. Although several reports have suggested that such a deficit may be present, the subjects have usually been those with advanced hypertensive disease, and results are confounded by circumstances of age, severity of the disorder, and/or antihypertensive medication. To clarify this formulation, we undertook the survey of a broad range of neuropsychologic functioning in mildly hypertensive individuals who were relatively young and whose hypertension was of brief duration, at a time when no gross neurological or cerebrovascular change was detectable. We were, in fact, looking for indications of the earliest possible changes in CNS function, just as one looks for minor electrocardiographic changes or for a decrease in the filtration fraction to detect early signs of hypertension in the function of the heart and kidney respectively, before any clinical consequences become apparent.

Our study was motivated also by the probability that certain of the drugs used for lowering blood pressure in the treatment of the disorder may themselves evoke changes in behavior, and that a body of data collected prior to treatment of any kind would provide a baseline for subsequent investigations of one or another kind of antihypertensive therapy.
Methods

Subject Selection

The study sample consisted of 41 hypertensive patients (24 men and 17 women) and 41 matched control subjects (Table 1). In all subjects the hypertension was classified as mild (i.e., diastolic pressure of 90 to 105 mm Hg) and had recently been identified. At the time of behavioral testing, no patient was on therapy; earlier 14 had received thiazide diuretics and four, small doses of propranolol or alpha methyldopa, but these medications had been discontinued for at least 10 days prior to testing. The average blood pressure on the day of the behavioral tests was 150/93 mm Hg for the 24 men and 151/97 mm Hg for the 17 women, in contrast to levels of 125/77 mm Hg and 116/73 mm Hg for male and female controls respectively. Age, race, and education were the matching variables for patient-control pairings and were not different between groups. To achieve some degree of demographic uniformity, most control subjects were provided by the patients, who were asked to "bring a volunteer friend." All patients were medically evaluated and classified as primary (essential) hypertensives, and had no evident neurological signs, orthopedic defects, or uncorrected disturbances of vision or hearing. Patients and control subjects granted informed consent, as approved by the Human Use Committee of the University of Pittsburgh, and all received a small honorarium for their participation.

Behavioral Tests

All subjects were examined by a test battery consisting of four different types of tasks: sensory-perceptual; cognitive; psychomotor; and nonverbal communication. In the discussion of results, we will focus on the three sensory-perceptual, cognitive, and psychomotor functioning tests. The nonverbal communication cluster of tests were included to examine the hypothesis that hypertensive subjects receive interpersonal cues and social information in a way different than normotensive subjects, as communicated by standardized videotapes of facial and upper-body expressions of a person engaged in a problem-solving task. These tests failed to show any differences in the performance of normotensive and hypertensive subjects and will not be discussed further in the present report. The data were subjected to appropriate analysis of variance using disease and sex as the major variables.

Sensory-Perceptual Tests

The sensory-perceptual tasks consisted of the following:

1. Visual recognition threshold. Selected visual stimuli were presented for progressively longer time intervals until the subject could successfully identify them.
2. Perception of spaced stimuli. This task tested the ability to identify two letters presented simultaneously at a fixed tachistoscopic exposure interval, when the distance between the two was increased on each successive trial until both letters could no longer be recognized.
3. Critical flicker frequency. The threshold (frequency) at which a regularly flickering light was first perceived as fused or steady was determined at two levels of stimulus intensity.
4. Two-flash fusion threshold. The maximal interval of darkness separating two successive flashes of light that gave rise to an impression of only a single flash was also measured at two levels of stimulus intensity.

Cognitive Tests

The cluster of cognitive tests consisted of the following:

1. Digit-symbol substitution test. The subject's speed and accuracy in transcribing simple digits and symbols was tested.
2. Block design. The ability to duplicate patterns by arranging colored blocks was tested.
3. Memory for designs. The ability to reproduce abstract graphic designs after brief exposure and a fixed delay was tested.
4. Time judgment. Two components were examined, one being the subject's accuracy in pressing a key for a prescribed interval of 5, 10, or 15 seconds (method of operative estimation), the other the ability to duplicate the duration of a simple sensory stimulus presented, following a 5-second delay (method of reproduction).

Psychomotor Function Tests

Psychomotor functioning was appraised by several tests, selected to sample the main dimensions of fine psychomotor behavior (i.e., the smaller musculature of the extremities rather than the large muscle groups or whole body movements).
1. Lift and Jump Reaction Times. Lift reaction time tests the latency of a finger lifting movement following presentation of a tone. Jump reaction time requires both a lift response and a movement through space to depress a key placed some distance away.

2. Tapping Speed. The subject was asked to identify the rapidity of an oscillating movement, measured by the number of taps made alternately between two metal plates in 5 seconds time when they were located in a horizontal plane and perpendicular to the subject.

3. Transfer Coordination Speed. The speed achieved in a movement transferring a dowel from one closely-fitting socket to another was measured.

4. Traverse Time. The speed of a self-cued, forward, ballistic movement of the arm and hand was measured.

5. Movement Reversal Time. This test provides an index of the "turn-around time" required for a movement made first in one direction to be followed immediately by its opposite.

6. Handgrip Strength. Handgrip strength was measured for both the dominant and non-dominant hands.

Results

Sensory-Perceptual Tests

Sensory-perceptual ability, as reflected in performance on the tests, was somewhat deficient on all four tasks for the hypertensive subject (fig. 1), reaching a statistically significant level for Visual Recognition Threshold ($p = 0.05$), and for female hypertensives only (fig. 2) in the Perception of Spaced Stimuli ($p = 0.05$). Critical Flicker Frequency and Two-Flash Fusion Threshold were impaired in hypertensive patients as compared with normotensive controls, but not at a significant level.

Cognitive Tests

As illustrated in figure 3, the performance of hypertensive subjects was deficient in several of the cognitive measures, with the notable exception of the Memory for Designs test. All other tasks showed some deficit performance in the hypertensive group, reaching a significant level ($p = 0.01$) on the Digit-Symbol Substitution test. The Operative Estimation of Time, as shown in figure 4, was markedly impaired for the female hypertensive group ($p = 0.01$). This performance deficit occurred at all durations tested, with the female hypertensive subjects underestimating time by almost 50%, e.g., they estimated a 5-second tone as lasting only about 3 seconds. The same thing occurred to a lesser, nonsignificant extent in the Reproduction of Time tests.
Psychomotor Function Tests

Traverse Time and Transfer Coordination Time (both $p = 0.05$), as well as Tapping Speed ($p = 0.01$), all of which reflect movement speed in actions that require either self-cued or coordinated motions, were significantly slowed in the hypertensive patients (fig. 5). Movement Reversal Time and Reaction Time tended to be slower in the hypertensives than in normotensive controls, but not significantly so. Handgrip seemed to be stronger in hypertensives than controls, particularly in the nondominant hand, but this finding also did not reach significant levels.

Discussion

Findings from this varied array of performance tests demonstrated that young, mildly hypertensive individuals have significant behavioral impairments on some tests in all three of the spheres of central nervous system (CNS) function tested: sensory-perceptual, or "signal-input" activities; cognitive, or "central processing" behaviors; and psychomotor or "output" responses of several kinds. Behaviors that are most directly linked to environmental stimuli, such as reaction time responses, seemed to be relatively less affected, while those that are more obviously self-initiated or "self-cued" by the subject, such as Tapping Speed, were more affected. Performance on tasks that placed a demand on both speed and coordination for their successful execution, such as Traverse Time or Digit-Symbol Substitution, were also more obviously reduced below the levels achieved by matched normotensive controls. It is important to note that none of these patients was distinguished by any marked or obvious defect in everyday behavior and that it would not appear likely, at least at this early stage of hypertensive disease, that the deficits we noted would be intrusive or limiting to ordinary work or family and avocational activities. These special functional tests impose a "load" on the subject's ability to respond which, in their way, might be analogous to the use of treadmill pacing for probing more closely into the details of cardiac or respiratory functioning under mild stress.

Our observations obviously raise a number of puzzling questions. First of all, do the deficits reflect a situation that existed prior to the blood pressure elevation; are they the result of something innate to those individuals who later become hypertensive or do they...
correlate with the presence, duration, and severity of increased blood pressure? Repeated studies in normotensives, with and without an hereditary history of hypertension, may help to answer this question. The answer also must obviously relate to the pathogenesis of the CNS deficits. At this early stage of the hypertensive disease, we find it difficult to believe that the observed impairment in behavior could be the result of restricted cerebral blood flow, although it may be linked to cellular and metabolic changes that may be taking place within the CNS. The observation in rats by Dworkin et al. that raising blood pressure decreased reactivity to noxious stimuli also indicates a possible explanation for our results. Similarly, still another mechanism is suggested by preliminary data presented by deJong et al. and Zamir et al. that show spontaneously hypertensive rats (SHR) to have decreased pain sensitivity, which is eliminated by the opioid antagonist, naloxone.

Second, are these behavioral deficits progressive, becoming more evident with increased duration and severity of the high blood pressure? Some insight can be gained by comparing our results with those of other investigators who have studied samples of subjects with more severe hypertension of longer duration. For example, we found no significant impairment on the cognitive tests of Block Design and Memory for Designs tests, although in subjects with more severe hypertensive disease, cognitive deficits have been reported for the Category Test, Verbal and Performance Scale Scores for the Wechsler Adult Intelligence Scale, (WAIS) and for WAIS Block Design. Furthermore, Wilkie and Eisendorfer, in their study of the effects of hypertension in the aged, found evidence for intellectual deterioration in those with persistent blood pressure elevations. Similarly, no differences were found in our study between hypertensives and their normotensive controls on the tasks of Reaction Time or Critical Flicker Fusion, although previous studies with more severe cases of hypertension have demonstrated such differences. Thus, one might infer that greater effects would be expected as the disease persists over a longer period of time and/or becomes more severe.

A third question is: What happens to the deficits when these patients are actively treated for their hypertension? Some improvement in function may occur in certain of the behaviors affected when blood pressure is reduced, but it is also possible that specific antihypertensive drugs — particularly those that act through the CNS — may have the effect of aggravating certain deficits while improving others. This complex question is an ongoing feature of our studies.

One rather striking finding in this experiment was that the behavioral impairments in our hypertensive subjects were much more apparent in women than in men. In Visual Recognition Time, Perception of Spaced Stimuli, and in Time Estimation, the female hypertensives were significantly poorer in performance than all of the other groups. In general, on all of the tasks including those in which a significant disease X sex interaction was not present, scores of female hypertensives tended to be lower than those of male hypertensives or of male or female controls. We have no ready explanation as to why females should be more affected behaviorally by their hypertensive disease than males. It does not seem likely that the somewhat greater blood pressure difference between female hypertensives and controls than between male hypertensives and their controls (10/8 mm Hg; table 1), would produce such large differences in behavioral impairment. It may be that the males have compensated for their behavioral impairment in a way that the females have not, e.g., that the demands for keeping close track of time are more salient for a male than for a female subject and, therefore, he has more frequently verified his time estimates and overcome a slippage in this skill; this is highly speculative, however. Whatever the reason may prove to be in subsequent studies, the present results clearly suggest that effects of hypertension on the CNS were more extensive in female subjects.

The demonstration of behavioral deficits in hypertensive subjects may bear an interesting relationship to earlier psychosomatic theories concerning hypertension. Rather than an etiological role for the "hypertensive personality" in the development of hypertensive disease, the finding that hypertensive individuals do not perform as well in a variety of cognitive, psychomotor, and perceptual tasks suggests that the personality factors might be a consequence rather than a cause of elevated blood pressure. An individual who is slowed, particularly in self-cued behaviors where he or she perhaps does not perceive subtle cues as well as others, and whose cognitive processes are slightly impaired, may be perceived by others as somewhat different than normotensive individuals, or may cope less well with social situations requiring confrontation and expression of hostility. Thus, the "hypertensive personality" may, in fact, be a tacit recognition of the difficulties in performance that have been measured in these tests of CNS function.

To conclude, our study has revealed an intriguing pattern of mild CNS functional impairment early in the course of hypertensive disease. These findings are preliminary, and the precise mechanisms and relationships between the behavioral deficits and the chronic elevation of systemic blood pressure are as yet unknown. It remains to be determined to what extent normalization of the blood pressure by therapeutic intervention may, in fact, serve to correct these mild deficits.

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