during the first 30 minutes and only a small proportion (< 20 percent) of the radioactivity remaining after 50 minutes could be attributed to radioactively labeled metabolites. The unchanged peptide disappeared from the focal infusion site with a time course similar to that observed for the behavioral response after DiMe-C7 administration (Fig. 2B). The disappearance of DiMe-C7, however, appears largely to be due to diffusion away from the injection site rather than metabolic degradation, because unchanged peptide appeared in the adjacent substantia nigra and in hindbrain with a time delay of about 20 minutes after injection of DiMe-C7 into the VTA (Fig. 2B). The delayed appearance of DiMe-C7 in adjacent brain areas may help to explain various additional behavioral responses that occur after administration of this analog into the VTA (*12*).

These results support the suggestion that DiMe-C7 represents a metabolically stable and biologically active analog of SP in the central nervous system. It should prove useful for future studies of the functional role of SP in various regions of the central nervous system.

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11. Rats under Equithesin anesthesia (3.75 ml/kg) were prepared with stereotaxically implanted 23-gauge stainless steel guide cannulas (12 mm) ending 3 mm above the VTA. Coordinates for the placement were, in millimeters, 3.5 posterior to bregma, ± 0.5 lateral to the midline, and 5.6 below skull [L. J. Pellegrino and A. J. Cushman, *A Stereotaxic Atlas of the Rat Brain* (Appleton-Century-Crofts, New York, 1967)]. Locomotor activity was recorded in cages (35 by 25 by 25 cm) fitted with a pair of photocells (130 mm apart and 10 mm above the cage floor). Interruptions of the beam were recorded on line with a Rockwell AIM 65 microprocessor. The rats were habituated to cages 2 hours daily for 3 days before testing and 2 hours on the test day. Data were recorded in 10-minute intervals for 90 minutes after infusion.
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13. We thank R. Wade and D. Brundish, Ciba-Geigy, Horsham, England, for the labeled peptides. M.R.H. is a Helen Hay Whitney Foundation postdoctoral fellow and S.P.W. is a Medical Research Council scholar.

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Reduced Sympathetic Nervous System Responsivity Associated with the Relaxation Response

Abstract. *Sympathetic nervous system activity was assessed in experimental and control subjects who were exposed to graded orthostatic and isometric stress during monthly hospital visits. After the first session, the experimental subjects practiced a technique that elicited the relaxation response. Their concentrations of plasma norepinephrine during subsequent graded stresses were significantly higher. No such changes were noted in the control group. These results were then replicated in the control group in a crossover experiment. The groups did not differ in their heart rate and blood pressure responses. These observations are consistent with reduced norepinephrine end-organ responsivity after regular elicitation of the relaxation response.*

The relaxation response is defined by a set of integrated physiological changes that are elicited when a subject assumes a relaxed position in a quiet environment, closes his or her eyes, engages in a repetitive mental action, and passively ignores distracting thoughts (*1–4*). These behaviors are associated with physiological changes that include decreased oxygen consumption, heart rate (HR), arterial blood pressure (BP), respiratory rate, and arterial blood lactate (*4–6*). In addition, there are slight increases in skeletal muscle blood flow. All of these changes are different from those reported during sleep or quiet sitting (*4, 5, 7*). Although the physiological changes associated with the relaxation response are consistent with decreased sympathetic nervous system (SNS) activity, direct measurements of plasma norepinephrine (NE) levels have been reported to be either unchanged (*8*) or variable (*9*). In the current prospective, crossover investigation, we measured SNS reactivity in experimental subjects before and after they regularly elicited the response and compared the results with those of control subjects.

Medical histories were taken and physical examinations performed on 32 subjects. Two were excluded because of chronic illness. Informed consent was obtained from the remaining 30 subjects, who were randomly assigned to either an experimental or a control group. Nineteen subjects completed the entire investigation with ten in the experimental group (seven males, three females) and nine in the control group (four males, five females). The average age of the experimental group was 25.2 ± 3.5 years and of the control group, 25.5 ± 3.2 years.

The subjects were admitted to the Clinical Research Center of the Beth Israel Hospital in the early evening so that a 10- to 12-hour adaptation period preceded testing the next morning. During this adaptation period, maximum handgrip-tension levels were established for each subject. Each subject was awakened approximately 30 minutes before testing and had a 21-gauge intravenous catheter inserted in the antecubital vein of the nondominant arm. Sequential blood samples (10 ml each) were drawn for plasma NE analyses at five different times (−10, 0, +5, +10, and +15 minutes). When the first two samples (−10 and 0) were taken, the subjects were supine; the subjects then stood up. After 5 minutes of standing, the +5 sample was drawn. For the next 5 minutes, the subjects remained standing and also gripped at a tension corresponding to 30 percent of maximum. At the end of this 5-minute period, the +10 sample was drawn. In the subsequent 5 minutes, subjects remained standing and gripped at 100 percent of maximum grip tension. The +15 sample was then drawn. Immediately prior to each blood drawing, HR was measured by palpation of the radial pulse and BP by auscultation.

Blood samples were kept on ice

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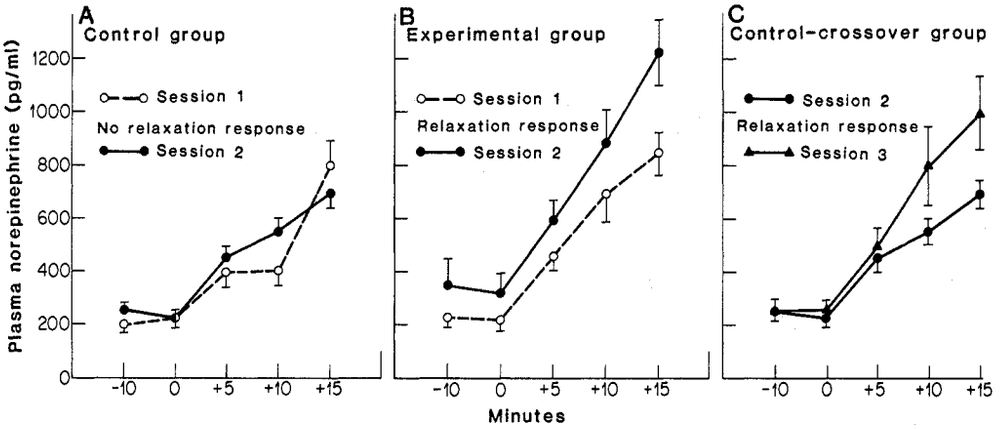

Fig. 1. Plasma NE concentrations ($\bar{X}$ ± standard error of the mean) corresponding to graded levels of orthostatic and isometric stress. The control group (A) practiced a control relaxation technique that does not elicit the relaxation response between sessions 1 and 2. The experimental group (B) practiced a relaxation technique that elicits the relaxation response between sessions 1 and 2. The control-crossover group (C) elicited the relaxation response between sessions 2 and 3.

throughout the testing procedure in order to retard enzymatic degradation of plasma NE. At the end of the procedure, the samples were centrifuged at 20,000 rev/min for 20 minutes. Plasma samples were separated by suction from the packed red cells and frozen at −80°C until the assays were completed. The radioenzymatic assay of Lake *et al.* (*10*) was used to determine plasma NE.

After this initial admission, subjects who had been assigned to the experimental group were instructed to practice twice daily (20 minutes per session, 40 minutes per day) for 30 days a technique that elicits the relaxation response (*7*). Subjects who had been assigned to the control group were instructed to practice twice daily (20 minutes per session, 40 minutes per day) for 30 days a control technique of sitting quietly that does not elicit the relaxation response (*7*). The primary differences between the instruction sets were the use of a repetitive word or phrase and adoption of a passive attitude in the experimental group. After practicing their respective techniques for 30 days, during which they kept diaries of their practice, the subjects returned to the Clinical Research Center for session 2. All subjects in the experimental group had practiced the technique at least once daily, and all but two of the control group had sat quietly for a comparable period of time. Two of the control subjects sat quietly, on the average, for less than one period daily. Plasma NE concentrations were again determined during the graded stresses. The test procedures were identical to those of session 1.

After session 2, six subjects from the control group entered the crossover group and were instructed to practice twice daily (20 minutes per session, 40 minutes per day) the technique used by the experimental group. After 30 days, these crossover subjects returned for retesting in session 3. The subjects in the experimental group were not asked to practice the control technique, because we have learned that it is difficult to sit quietly and not elicit the relaxation response once it has been learned (*11*).

The HR, BP, and plasma NE data of the experimental and control groups were compared by a three-way (groups by visits by graded stresses) analysis of variance (*12*). The data of the crossover group during sessions 2 and 3 were compared by a two-way (visits by graded stresses) analysis of variance. Within-subject comparisons at different stress levels were accomplished with the Dunnett's multiple comparison test (*13*).

The supine and graded stress plasma NE levels in the experimental and control groups were not significantly different during the first visit (Fig. 1). Plasma NE increased significantly in both groups as a function of the five graded stresses [$F(4, 64) = 112.61$, $P < .001$].

On session 2, however, after eliciting the relaxation response for 30 days, the experimental group displayed significantly greater NE concentrations with graded stress than on session 1 [$F(1, 16) = 5.45$, $P < .05$] (Fig. 1). Further, the control and experimental groups differed significantly at each level of stress [$F(4, 64) = 7.88$, $P < .002$] and had significantly different patterns of NE responses on the two sessions [$F(4, 64) = 8.20$, $P < .001$]. The mean NE concentrations increased from the first to the second session in the experimental group at stress level +15 [Dunnett's test, $q'(45) = 2.57$, $P < .05$]. Increased NE concentrations were seen in eight of the ten experimental subjects. There were no significant differences in the mean NE concentrations in the control group between sessions 1 and 2, and only one of the nine control subjects displayed increased NE.

In the six control subjects who entered the crossover condition, the mean plasma NE responses to graded stress were

Table 1. Blood pressure and heart rate responses ($\bar{X}$ ± standard error of the mean) to graded levels of stresses at minutes −10, 0 (supine), +5 (standing), +10 (standing + 30 percent hand grip), and +15 (standing + 100 percent hand grip).

Minute	Control group		Experimental group		Control-crossover group	
	Session 1	Session 2	Session 1	Session 2	Session 2	Session 3
			Systolic blood pressure (mmHg)			
−10	106 ± 2	106 ± 5	120 ± 5	108 ± 3	106 ± 5	101 ± 3
0	106 ± 2	106 ± 5	117 ± 5	108 ± 3	106 ± 5	103 ± 2
+5	110 ± 3	112 ± 6	111 ± 3	110 ± 5	112 ± 6	106 ± 5
+10	118 ± 3	122 ± 5	126 ± 8	119 ± 5	122 ± 5	115 ± 6
+15	138 ± 5	134 ± 6	133 ± 8	131 ± 7	134 ± 6	136 ± 8
			Diastolic blood pressure (mmHg)			
−10	72 ± 3	68 ± 4	75 ± 4	70 ± 3	68 ± 4	67 ± 4
0	70 ± 3	69 ± 5	73 ± 4	69 ± 3	69 ± 5	68 ± 3
+5	79 ± 3	82 ± 4	78 ± 4	79 ± 2	82 ± 4	77 ± 5
+10	87 ± 2	89 ± 5	87 ± 6	85 ± 3	89 ± 5	85 ± 6
+15	101 ± 4	101 ± 5	88 ± 6	90 ± 5	101 ± 5	93 ± 7
			Heart rate (beats/min)			
−10	60 ± 2	64 ± 4	60 ± 3	57 ± 2	64 ± 4	65 ± 5
0	59 ± 2	62 ± 3	57 ± 3	57 ± 2	62 ± 3	66 ± 3
+5	74 ± 3	76 ± 3	78 ± 5	72 ± 4	76 ± 3	81 ± 3
+10	84 ± 5	81 ± 3	84 ± 7	79 ± 4	81 ± 3	85 ± 3
+15	95 ± 7	90 ± 5	94 ± 5	87 ± 4	90 ± 5	93 ± 3

significantly greater after regular elicitation of the relaxation response [$F(1, 10) = 6.80$, $P < .05$]. This pattern was evident in four of the six crossover subjects. The differences were significant during stress level +15 [$q'(25) = 1.84$, $P < .05$].

Systolic and diastolic BP increased progressively with graded stresses in both the control and experimental groups (Table 1). During the first session, BP did not differ between groups in any condition. Further, despite the significantly augmented release of plasma NE in the experimental group on session 2, there were no parallel increases in systolic or diastolic BP. Systolic and diastolic BP tended to be lower on session 2 in the experimental group and on session 3 in the crossover group, but the differences were not statistically significant.

Heart rate also increased progressively with graded stresses (Table 1). The two groups were similar on session 1. On session 2, HR levels were not distinguishable from those of session 1 in either group. There were also no changes when sessions 2 and 3 were compared in the crossover group.

In the experimental subjects, after they had regularly elicited the relaxation response for 30 days, the plasma NE response to graded stress was augmented over and above that of the control subjects. Measured concurrently with plasma NE, HR and BP did not change in either group. This result was replicated within this investigation when six of the nine control subjects subsequently elicited the relaxation response for 30 days in a crossover extension.

In accordance with earlier reports (*8, 9*), our study revealed that plasma NE levels under low-stress conditions (supine posture) did not change after subjects elicited the relaxation response. On the other hand, under high-stress conditions (upright posture and isometric stress), the relaxation response was associated with augmented plasma NE. The cardiovascular responses to postural and isometric stresses are largely mediated by SNS activity. Plasma NE concentrations, the index of SNS activity in our study, increased disproportionately over HR and BP. These data suggest that in subjects eliciting the relaxation response more NE is required to produce the normal compensatory increases in HR and BP.

The elicitation of the relaxation response may reduce adrenergic end-organ responsivity. The mechanism for such a change in this responsivity is not clearly identified (*14*). These data are consistent with an earlier study (*15*) suggesting that subjects eliciting the relaxation response may be less responsive to stress.

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Integrating Visual Information from Successive Fixations

Abstract. *One of the classic problems in perception is how visual information from successive fixations of a scene is integrated to form a coherent view of the scene. The results of this experiment implicate a process that integrates by summing information from successive fixations after spatially reconciling the information from each glimpse. The output of this process is a memory image that preserves the properly reconciled information from successive fixations.*

One of the great puzzles in the psychology of perception is that the visual world appears to be a coherent whole despite our viewing it through a temporally discontinuous series of eye fixations. In a sense, the problem is that our data about a scene consist of individual "snapshots," and yet our perception consists of a single panoramic view (*1*). We have empirically demonstrated the existence of a briefly lasting memory in which temporally separate glimpses of a display are stored simultaneously and spatially reconciled with one another. With this memory serving as the basis of perceptual experience, the observer literally sees a coherent view of a display that is constructed from the individual glimpses of which it is made. Such memory could subserve the translation of information originally coded by retinal coordinates into information coded by spatial coordinates, the way we ultimately experience it.

To empirically establish this phenomenon of information integration across fixations, we used an experimental task modeled after one used by DiLollo (*2*). The task required subjects to localize a missing dot in a 5 by 5 dot matrix. The 24 dots that were included in the matrix were presented in two frames of time. In the first, a randomly selected 12 dots were shown; after a brief interval, the second frame was displayed. In order for a subject to determine the location of the missing dot, his visual system had to integrate the two separate frames into a single representation of the matrix. We modified DiLollo's version of this task by manipulating the presentation of the two frames of dots. Subjects viewed the first frame while they fixated one location on the screen, and they saw the second frame (in the same spatial location as the first) only after they had shifted their gaze to another screen location (Fig. 1). With this procedure, the two frames of dots were presented in the same spatial area, but subjects viewed them during different fixations. Hence, the images of the two frames fell on different retinal areas. With this modification, successful integration of the frames required that subjects make use of the spatial overlap of the frames to overcome their lack of retinal overlap.

To assess the quality of performance in this condition, we included a control condition in which subjects did not execute a saccade; the frames were presented to the same retinal areas as in the

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