effective dose, enough to bind 2.5 times the amount of CCK-OP secreted per minute. Although the antibodies used in these experiments bind gastrin (*13*), it is unlikely that binding of gastrin in the CSF [which is reportedly present only in the neuro- and adenohypophysis (*1*)] contributed to the increase in food intake, since we had previously found that only very high doses of pentagastrin, when injected into the LV, decreased food intake in sheep, and these doses caused abnormal behaviors (*6*). In addition, desulfated CCK-OP had no effect on feeding at doses equivalent to those that decreased feeding at least 80 percent when sulfated CCK-OP was used. Caerulein, CCK-OP, and CCK-33 were all effective in decreasing feeding (*9*). Therefore there appears to be a strict structural requirement for CCK-like peptides to elicit satiety, making it unlikely that gastrin in the CSF would influence feeding behavior.

We propose that the food intake increase caused by CCK-AB was a direct result of the binding of CCK peptides in the CSF by the antibody molecules, preventing them from binding to receptors involved in satiety. This finding supports our hypothesis that, during feeding, CCK-OP or another CCK peptide in the brain is released into the CSF and then travels to the site of action for eliciting satiety. The inability to demonstrate a similar response in rats suggests that CCK-OP may function as a neuromodulator of satiety in some species but not in others.

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Stress-Induced Analgesia in Humans: Endogenous Opioids and Naloxone-Reversible Depression of Pain Reflexes

Abstract. *The cumulative effects of a repetitive stress induced by anticipation of pain (noxious foot shock) were studied on the threshold of a nociceptive flexion reflex of the lower limb. The threshold of the nociceptive reflex progressively increased with the repetition of the stress. This effect was reversed by naloxone, which even produced hyperalgesia, since a rapid and significant decrease in this threshold, below the initial values, was noted. The data provide evidence for involvement of endogenous opioids in the phenomenon of stress-induced analgesia in normal man.*

Some specific psychological conditions, stress and anxiety, can modify the perception of pain and spinal excitability (*1*). These modifications have been partly explained in terms of activation of central nervous structures such as reticular formation or limbic system (*2*). The progress made in understanding the anatomy and physiology of pain modulation led some investigators to examine the effects of stress in relation to endogenous opioids in animals. Rats subjected to intermittent and inescapable stress, noxious foot shock, showed a significant increase in the opiate-like activity of the whole brain as well as in an analgesia, as judged by the increase in the latency of tail flicking (*3*). These effects were partially blocked by strong doses of naloxone.

Our study, performed in humans, gives further evidence for involvement of opioid mechanisms in stress-induced analgesia, since we observed a naloxone-reversible depression of nociceptive reflexes with intermittent and repetitive stress (anticipation of inescapable and very noxious foot shock). For this study, six healthy adults (four men and two women, 22 to 35 years of age) were volunteers.

The neurophysiological procedure for eliciting and recording nociceptive reflexes from the lower limb has been described (*4*). Briefly, the sural nerve was stimulated with surface electrodes placed on the scratched and degreased skin (2 cm apart) at its retromalleolar path. The stimulus consisted of a train of ten shocks of 1 msec duration each (300 Hz of internal frequency) delivered by a constant-current stimulator at a rate of 0.2 cycle per second. Nociceptive flexion reflexes were recorded from a flexor muscle of the lower limb (biceps femoris muscle) by a pair of surface electrodes placed on the skin above the muscle. The reflex threshold was then defined as the stimulus intensity eliciting 70 to 80 percent of the responses in the biceps femoris muscle. This method was chosen because the threshold of the nociceptive reflex from the biceps femoris muscle is homogeneously stable at 10 ± 1 mA in normal trained volunteers and is well correlated with a pricking pain sensation elicited by a noxious sural stimulation (*4*). Thus, this method could allow the study of suprasegmental influences on nociceptive reflex activity as an objective index of pain behavior in humans (*5*).

The stress was induced by a 2-minute warning period announcing the rapid occurrence of a very noxious and inescapable electrical stimulation (70 mA) applied to the sural nerve. Subjects then received either the expected stimulus or a tactile one randomly distributed. This stressful anticipation of incertitude of pain was preceded by a 2-minute resting period during which the subjects were ordered to relax. These rest-stress periods were repeated 19 to 20 times during sessions of 80 to 90 minutes. All subjects were tested at least three times at weekly

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intervals during three randomized situations: a control session in which no injection was given and sessions in which either naloxone (5 mg, 10 cm^3) or a placebo (0.9 percent saline, 10 cm^3) were administered intravenously by a coded technique. The injections (naloxone or placebo) were given 45 to 50 minutes into each session so as to obtain a certain degree of hypoalgesia in the subjects as well as a significant increase in the threshold of the nociceptive flexion reflex.

Under these conditions, the cumulative effects of repetitive periods of stress were studied on the threshold of nociceptive reflex from the biceps femoris muscle in the successive resting states. The numerical values of the threshold were studied by an analysis of individual and global means and variances by steps of 30 seconds. The significance in the variations as a function of repetition of the stress in time was calculated from a regression analysis by the least-squares method. The significance in the variations within and between individuals and within and between each situation was determined by a factorial analysis.

The initial values of the nociceptive reflex threshold were identical in the three situations at about 10 mA (Table 1). As a function of repetition of the stress in time, this threshold increased progressively toward significantly higher values in the three groups (Fig. 1 and Table 1). However, injection of naloxone resulted in an immediate decrease (30 percent) in the threshold of the nociceptive reflex below its initial values at 7 mA ($P < .001$). This naloxone-induced facilitation in the nociceptive reflex lasted about 20 minutes. Then the threshold again increased progressively until the end of the session (Fig. 1 and Table 2). No significant change in this threshold was observed after injection of the placebo compared to the control situation (Fig. 1 and Table 2). No significant sex difference or cumulative influence from one session to the next was observed in the variations of the threshold.

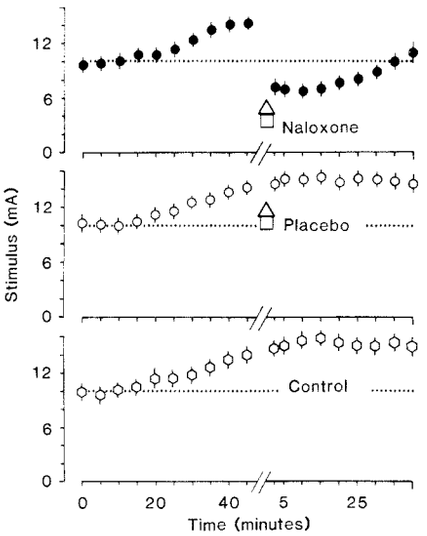

Fig. 1. Evolution of the threshold of the nociceptive flexion reflex from the biceps femoris muscle as a function of repetition of stress in time. Points represent mean values, and bars, 1 standard deviation.

The increase in the threshold of the nociceptive reflex from the biceps femoris muscle induced by the stress may be a sign of analgesia or hypoalgesia since this reflex is generally modulated in a parallel way to a pain sensation elicited by the same electrical stimulus (*5*). Thus, the phenomenon of stress-induced analgesia described in animal studies (*3*) may be applicable to humans during the specific stressing conditions described in this report. Further, the rapid and transient fall in the threshold below its initial values, induced by naloxone and corresponding to a facilitation of the nociceptive reflex, may be a sign of hyperalgesia in normal resting and relaxed people (*6*).

In conclusion, if a repetitive stress in human subjects can induce an antinociceptive effect involving endogenous opioids, one question at least remains unclear. How can the facilitation in the nociceptive reflex be explained when naloxone is given following a release of opiates? We have observed that low doses of naloxone (0.8 to 2 mg) do not have any effect in normal and relaxed subjects (*6*); others have reported very slight opiate-like activities such as slowing in the average of the alpha frequency on electroencephalogram recordings as well as lowering in the oral temperature when strong doses of naloxone (20 mg) were given to opiate-free subjects (*7*).

Table 1. Numerical values (means ± 1 standard deviation) of the threshold of the nociceptive reflex as a function of repetition of stress in time, from 0 to 45 minutes, in three situations: before injection of naloxone or a placebo and the control.

Minutes	Threshold (mA)		
	Naloxone	Placebo	Control
0	9.7 ± 0.5	10.3 ± 0.7	9.9 ± 0.9
5	9.9 ± 0.9	10.1 ± 0.9	9.5 ± 0.8
10	10.2 ± 0.9	9.8 ± 0.7	10.1 ± 1.1
15	10.9 ± 0.9	10.4 ± 1.0	10.4 ± 1.0
20	10.9 ± 1.1	11.1 ± 1.1	11.3 ± 1.2
25	11.4 ± 1.0	11.6 ± 1.2	11.3 ± 1.1
30	12.5 ± 1.2	12.5 ± 1.3	11.7 ± 1.1
35	13.7 ± 1.1	12.8 ± 1.2	12.5 ± 1.4
40	14.2 ± 1.2	13.9 ± 1.5	13.4 ± 1.3
45	14.2 ± 1.3	14.3 ± 1.3	13.9 ± 1.3

Table 2. Numerical values (means ± 1 standard deviation) of the threshold of the nociceptive reflex as a function of time after injection of naloxone, injection of a placebo, and no injection (control).

Minutes	Threshold (mA)		
	Naloxone	Placebo	Control
2	7.1 ± 0.2	14.7 ± 1.6	14.5 ± 1.2
5	7.0 ± 0.2	15.3 ± 1.9	14.9 ± 1.5
10	6.9 ± 0.2	15.2 ± 1.7	15.4 ± 1.4
15	7.1 ± 0.3	15.4 ± 1.5	15.7 ± 1.5
20	7.9 ± 0.4	14.9 ± 1.8	15.1 ± 1.5
25	8.2 ± 0.9	15.3 ± 1.8	14.9 ± 1.7
30	8.9 ± 1.0	15.1 ± 1.4	14.9 ± 1.4
35	10.0 ± 1.0	15.0 ± 1.5	15.2 ± 1.5
40	12.1 ± 1.1	14.8 ± 1.3	14.8 ± 1.4

In conclusion, if a repetitive stress in human subjects can induce an antinociceptive effect involving endogenous opioids, one question at least remains unclear. How can the facilitation in the nociceptive reflex be explained when naloxone is given following a release of opiates? We have observed that low doses of naloxone (0.8 to 2 mg) do not have any effect in normal and relaxed subjects (*6*); others have reported very slight opiate-like activities such as slowing in the average of the alpha frequency on electroencephalogram recordings as well as lowering in the oral temperature when strong doses of naloxone (20 mg) were given to opiate-free subjects (*7*).

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Visual and "Phonetic" Coding of Movement: Evidence from American Sign Language

Abstract. *Hearing subjects unfamiliar with American Sign Language and deaf native signers made triadic comparisons of movements of the hands and arms isolated from American Sign Language. Clustering and scaling of subjects' judgments revealed different psychological representations of movement form for deaf and hearing observers. Linguistically relevant dimensions acquired modified salience for users of a visual-gestural language. The data indicate that the modification of natural perceptual categories after language acquisition is not bound to a particular transmission modality, but rather can be a more general consequence of acquiring a formal linguistic system.*

American Sign Language (ASL) is the visual-gestural language used by deaf communities in the United States. The language is passed from one generation of deaf people to the next as a primary native language. Since the language has developed outside the auditory modality, its study can provide basic clues to the nature of language and to those psychological processes on which the comprehension and production of language rest. The principal aim of this experiment was to evaluate whether experience with a visual-gestural language could modify perception of the meaningless formational elements of the language.

Signs from ASL have at least three major formational attributes: configuration of the hands, location of the hands relative to the body, and movement of the hands and arms (*1*). Each attribute comprises a large inventory of discrete representatives, which are themselves essentially without meaning. Representatives are combined simultaneously but function separately to contrast minimally different signs, much as the phonemes of spoken languages minimally contrast words.

Experiments on the perception of speech indicate that a speaker's perception of phonemes can be determined either by natural nonlinearities of the auditory system or by the speaker's particular phonological experience (*2*). Human infants, for example, discriminate acoustic differences that cue the distinction between the phonemes /r/ and /l/ much as do English-speaking adults, in whose language the distinction is phonologically contrastive (*3*). Infants and adult English speakers are much better able to discriminate the same physical difference for stimuli across the English phoneme boundary than for stimuli within either phoneme category. The distinction between /r/ and /l/, however, is not contrastive in Japanese phonology, and unlike infants and English-speaking adults, Japanese-speaking adults fail to discriminate the acoustic differences (*4*). Linguistic experience has in this case modified innate auditory sensitivities. Is the modification of perception due to linguistic experience bound to the oral-auditory transmission modality? The differences between visual and auditory perception seem, after all, more striking than the similarities (*5*).

To evaluate effects of experience with

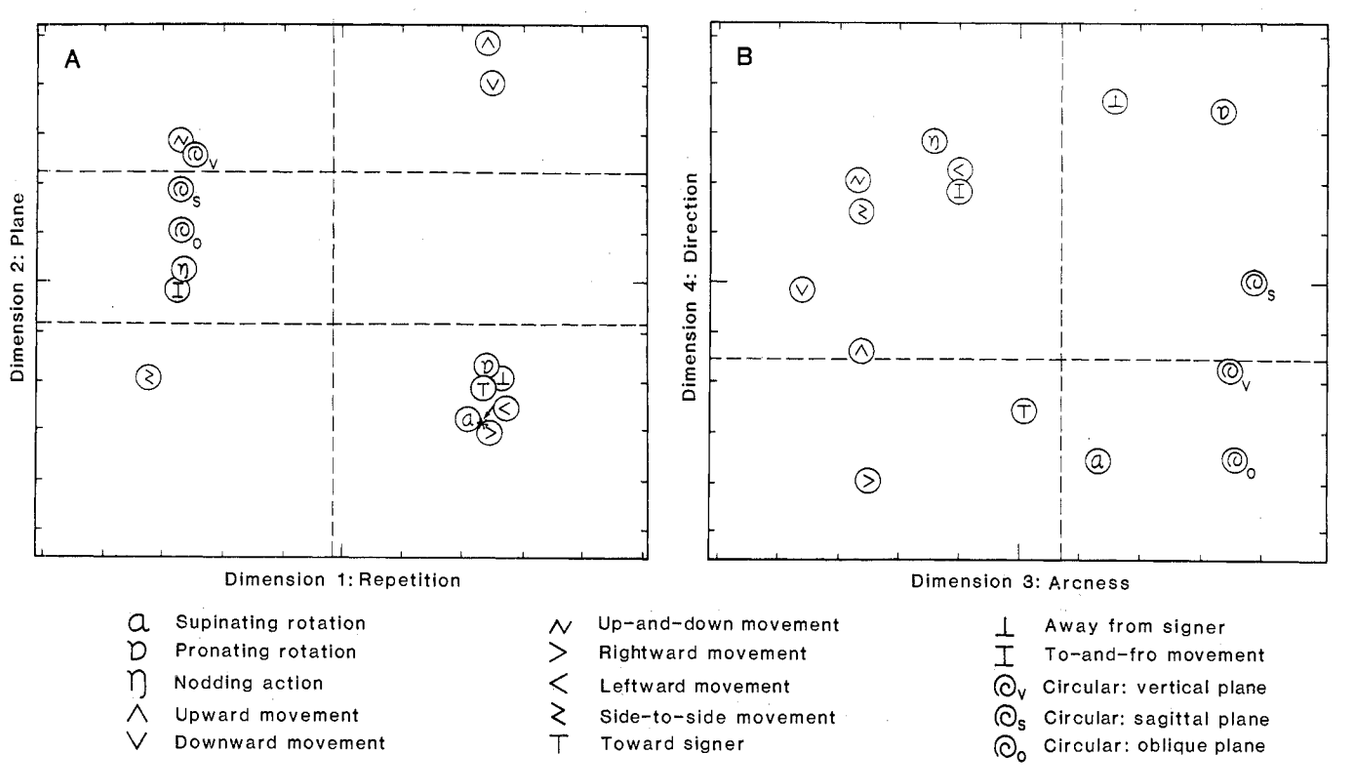

Fig. 1. Configurations of stimuli. Scaling was performed according to the individual differences scaling model (*10*) implemented with the SINDSCAL computer program (*11*). Fifteen one-handed movements were used as stimuli.

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