ripheral auditory system of anurans is roughly "tuned" to the energy in the mating call [R. R. Capranica, in *Frog Neurobiology*, R. Llinas and W. Precht, Eds. (Springer-Verlag, New York, 1976), p. 551], and we wanted to be confident that any response specificity we might find in hybrids would be based mainly on temporal properties of vocalizations and not strongly biased by "peripheral filtering." Behavioral coupling might occur in hybrids between species of different size for the trivial reason that both call frequency and frequency sensitivity could be correlated with size, and hybrids would be intermediate in this respect.
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Erectile Mechanisms in Man

Abstract. *Increases in penile circumference during sleep-related erections in human subjects closely reflected increases in penile blood flow, and bursts of activity in the bulbocavernosus and ischiocavernosus muscles were temporally related to these increases. The penile arterial system and the perineal muscles appear to have important coordinated roles in human penile erection. Monitoring sleep-related erections and penile blood flow holds promise for the study of erectile mechanisms and dysfunction and for screening of drugs.*

Human penile erection is a complex psychophysiological phenomenon dependent on multiple systems, but hemodynamic processes produce the major proximal changes necessary for the initiation and maintenance of erection. The nature of these changes has been postulated to involve restricted venous outflow, both increased arterial inflow and restricted venous outflow, or increased arterial inflow (*1*). Early research on this problem relied on anatomical examinations (*2*). In more recent studies cavernosography and phalloarteriography have been used as attention was directed to the dynamics of the process (*3*). The controversy over the relative contributions of the arterial and venous systems nevertheless remains unresolved.

Few investigators in this area ascribe any role in human erection to the perineal muscles. The studies of Bors and Comarr (*4*) and Kollberg *et al.* (*5*) are typically cited as evidence negating such a role. In the former study, patients were diagnosed as having lower motor neuron lesions of sacral segments on the basis of an absent bulbocavernosus reflex and abnormal detrusor muscle function. None of these patients experienced reflex erections, but some had psychogenic erections. Absence of the bulbocavernosus reflex was determined by manual examination (*6*), not by electrophysiological evaluation, and data on erectile function came from patient interviews, not from direct observation. Kollberg *et al.* did an electromyographic study of ejaculation achieved by masturbation. They did not monitor degree of erection. In summarizing some observations made from the start of erection, the authors stated that activity in the striated muscles of the pelvic floor sometimes increased before and during erection. They concluded that this activity is not necessary for the occurrence of erection, but noted that its importance in erection remains unclear.

Our previous observations suggest that the bulbocavernosus and ischiocavernosus muscles do play a role in human erection (*7*). Bursts of activity in the muscles were seen to precede slightly and accompany the penile pulsations characteristic of early phases of sleep-related erections. Penile circumference was usually greater after a pulsation than before. We speculated that contraction of the muscles may sporadically pump blood into the penis to assist in the initiation and maintenance of erection.

Failure to achieve erection is a common complaint, especially among older men. As the U.S. population grows older, the complaint will become even more widespread. The more we learn about the mechanisms of erection, the better will be the medical care available to new victims. Several methodological improvements may pave the way for a clearer understanding of both the hemodynamic and neuromuscular mechanisms. To our knowledge, in all studies to date erections have been induced by purely artificial means (saline infusion into the corpora cavernosa) or by presentation of erotic pictures. In no study has detailed simultaneous examination of penile erection and penile hemodynamics been made by noninvasive measurement of segmental pulsative blood flow. Finally, no study has combined examination of penile blood flow with monitoring of perineal muscle activity.

We examined penile blood flow and its relation to bulbocavernosus and ischiocavernosus muscle activity (BCA) during nocturnal penile tumescence (NPT) episodes in seven healthy, potent men 22 to 30 years of age. NPT occurs naturally and regularly during sleep in all healthy boys and men; most of the time it is temporally related to rapid-eye-move-

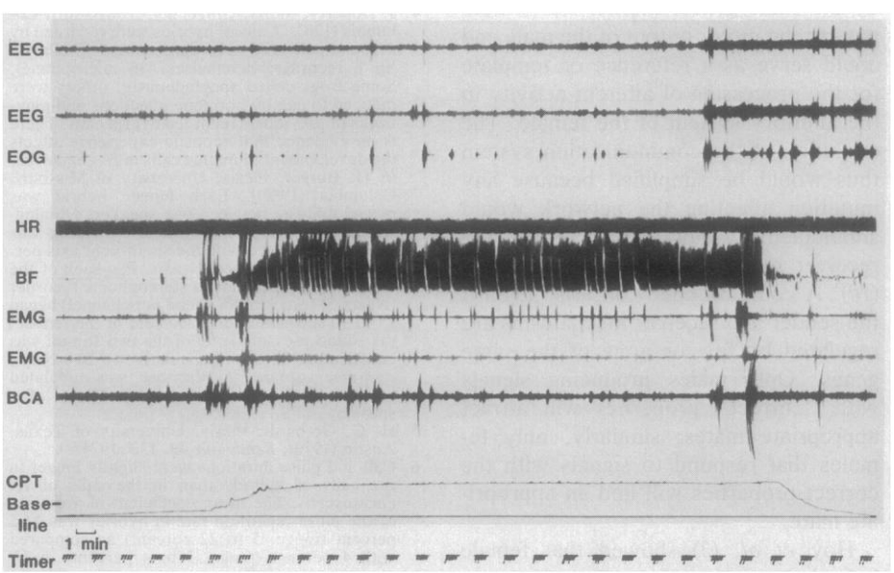

Fig. 1. Polygraph tracing (0.25 mm/sec) for a representative NPT episode. Channels are electroencephalograph (*EEG*), electrooculograph (*EOG*), heart rate (*HR*), blood flow (*BF*), left- and right-leg electromyograph (*EMG*), bulbocavernosus and ischiocavernosus muscle activity (*BCA*), circumference change at the penile tip (*CPT*), penile tip circumference baseline, and timer.

ment sleep (*8*). All subjects had participated in previous studies, so they were familiar with the laboratory procedure, and we had detailed knowledge of their NPT patterns. Both previous NPT data and subjects' reports of sexual performance established their potency; a physical examination, a screening interview, and routine psychological testing established their good physical and mental health.

Each subject spent two nights in the sleep laboratory. Throughout each night continuous polygraphic and magnetic tape recordings were made of (i) electroencephalographic, electrooculographic, and chin electromyographic activity (*9*) to determine quality and type of sleep; (ii) changes in penile circumference at the coronal sulcus (called the tip channel) and the base (*10*) to identify erectile episodes; (iii) segmental pulsative blood flow; (iv) BCA; (v) electromyographic activity of one or both legs to detect movement artifact; and (vi) heart rate to detect vascular artifact. The blood flow recorder, consisting of a monitoring cuff and an electronic package, has been tested for reliability and validity (*11*). We monitored blood flow continuously during each NPT episode. BCA was monitored continuously with two surface electrodes placed 2 cm apart on either side of the midline, about halfway between the base of the scrotum and the anus.

Polygraphic recordings were independently examined by two scorers to identify all full erectile episodes (tip channel) free of gross artifacts in both the NPT and blood flow tracings. A total of 21 episodes from nine all-night recordings met this criterion. The scorers next independently scored (*10*) the tip-channel tracings for the onsets of the distinguishable NPT phases—ascending erection (T_{up}), maximum erection (T_{max}), descending erection (T_{down}), and subsequent flaccidity (T_0)—and identified transient artifacts in the NPT and blood flow tracings. Agreement between the scorers was virtually perfect.

The magnetic tape data for the NPT tip channel and for the blood flow channel were digitized in real time. An 8080-based microprocessor system analyzed the data to detect, for each 2-second epoch, the largest voltage for the NPT channel and the absolute peak-to-trough voltage for the blood flow channel (*12*). For this analysis the blood flow data were initially sorted on the basis of the scorers' NPT phase determinations. Each NPT phase was then divided into six equally spaced intervals, with sampling times set at the onset of each interval. For each sampling time we calculated, for both penile circumference change and blood flow, the mean of the two values nearest the sampling time. The mean of readings from the roughly 1-minute period before T_{up} was used as the baseline value. Changes from baseline for each parameter at each sampling time were evaluated with *t*-tests for dependent measures, while inter- and intrasubject variations were assessed with *F*-tests.

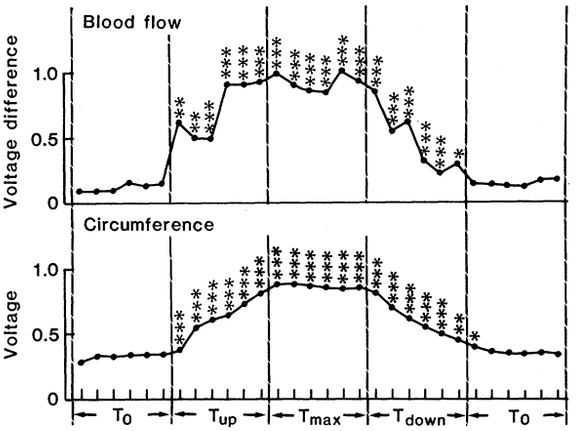

Fig. 2. Average changes in penile pulsative blood flow and penile circumference at the tip. Each point represents the mean for 21 NPT episodes in seven subjects. Asterisks indicate values that differ significantly from the T_0 level before erection at $P < .05$ (*), $P < .01$ (**), or $P < .001$ (***) (*t*-test for dependent measures).

Penile blood flow was related in a consistent fashion to both changes in penile circumference and bursts of BCA. Circumference changes were always preceded by blood flow changes, but smaller, phasic changes in blood flow were not always followed by measurable changes in circumference. At the onset of an NPT episode (Fig. 1), blood flow began increasing somewhat before the first change in circumference of the penile tip. Coincident with the initial bursts of blood flow pulses were relatively large and extended bursts of BCA. Blood flow rose rapidly during T_{up} and sustained one or more additional large bursts, which were accompanied by BCA bursts. At or near the onset of T_{max} it attained its maximum level. It oscillated around this level throughout T_{max}. Bursts of BCA continued to occur during this time; they were largest and longest during the initial part of the phase. Just before the onset of T_{down}, blood flow abruptly dropped and the BCA bursts disappeared.

Figure 2 shows the results of the statistical analyses of blood flow and circumference change for the 21 episodes. All values during the T_{up}, T_{max}, and T_{down} phases were significantly elevated relative to baseline. During posterection T_0 only the first circumference value and none of the blood flow values were significantly elevated. For both circumference change and blood flow, over half the intersubject variances were, relative to intrasubject variances, significant. Significance levels for blood flow were generally greater than those for circumference change. With respect to circumference change, increases in intrasubject variability coincided with increases in mean levels; with respect to blood flow, changes in intrasubject variability were not consistently related to mean levels. These results, especially since they come from normal subjects, indicate that both parameters are sufficiently stable within subjects to allow detection of between-subject differences, and suggest that blood flow may be an even more sensitive predictor of between-subject differences than circumference change.

Our results demonstrate the intimate relation during erection between increases in penile circumference and increases in penile blood flow and between phasic changes in blood flow and BCA bursts. We did not examine the venous drainage system, but the close relation between blood flow, a function of the arterial system, and erectile expansion indicates that the arterial system is a significant factor in erection. The venous system, if it has a role, must be supportive of the arterial system. These results also constitute further evidence that the bulbocavernosus and ischiocavernosus muscles actively participate in the initiation and maintenance of penile erection in humans.

The picture suggested by our data is this: Changes in penile blood flow always precede changes in penile circumference. Continuous increased blood flow is the primary determinant of penile expansion and rigidity during erection. Delicate fine-tuning mechanisms, signaled by the oscillations in blood flow during full erection, modulate blood flow to keep the cavernous bodies maximally filled. The mechanisms sometimes involve the bulbocavernosus and ischiocavernosus muscles, which are called into action, under supraspinal control, when pumping of the blood is needed to sup-

plement the flow mechanisms. Both the vascular system and the perineal muscle system may have feedback connections with cavernosal smooth muscle, and contraction of smooth muscle may be the final necessary condition for achievement and maintenance of maximum penile rigidity.

Sleep-related erections are entirely natural events, and because they occur predictably and reliably in all healthy men, they are always available for study. Their duration (an average of 30 minutes per episode in young adults) is comparable to that of sexual erections and allows ample time for dynamic studies of the erectile process. The subject, being asleep, is presumably less conscious of the social and psychological factors that may inhibit erections elicited with erotic stimuli in a laboratory setting. This methodology, including particularly blood flow measurement, holds promise not only for studies of the phylogeny (in some species) and ontogeny of the mechanisms of erection, but also for explorations of erectile pathophysiology and for screening of drugs. Numerous drugs commonly used by psychiatrists and general practitioners are claimed to have stimulating or inhibiting effects on erection (*13*). Since our analyses of inter- and intrasubject variability in circumference change and blood flow showed the sensitivity of the parameters as dependent variables, this new methodology offers a means of systematically examining such claims.

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12. Data for each run (data for about 40 minutes) were initially scanned for the largest values of circumference change and peak-to-trough blood flow. The system was then calibrated as follows: baseline, ground; largest circumference change, 1 V; largest peak-to-trough blood flow pulse, within ±1 V. The basic sampling epoch was 2 seconds for both channels. For the blood flow channel, initial sampling was at a minimum rate of 500 μsec; for each 2-second epoch, the absolute minimum and the absolute maximum voltages were detected and the peak-to-trough voltage was calculated. Finally, the scorers' detections of transient artifacts were used to delete from the data file all 2-second epochs containing such artifacts.
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Light and Agonists Alter Pineal *N*-Acetyltransferase Induction by Vasoactive Intestinal Polypeptide

Abstract. *Vasoactive intestinal polypeptide stimulated serotonin* N-*acetyltransferase activity in rat pineal glands in organ culture by a postsynaptic action that was independent of the beta-receptor. The magnitude of stimulation could be altered by environmental lighting conditions and by prior exposure to the agonist. Such up- and down-regulation, well known for catecholaminergic stimulation of this system, is compatible with a possible control of the pineal by vasoactive intestinal polypeptide as well as by catecholamines.*

Many peptide hormones discovered in peripheral organs also occur in neurons (*1*), are released during neural stimulation (*2*), and affect postsynaptic receptors (*3*). Some appear to exist in the nerve terminal with "classical" neurotransmitters and are released concurrently with them (*4*). Such corelease might modulate the time course or magnitude of the postsynaptic response to the transmitters.

The pineal gland may be useful in examining peptide-transmitter interactions. It is well established that norepinephrine released from sympathetic nerve terminals innervating the gland activates a β_1-adrenergic receptor, elevating adenylate cyclase activity, the concentration of adenosine 3′,5′-monophosphate, and the activity of serotonin *N*-acetyltransferase (NAT) (E.C.2.3.1.5) (*5*). The magnitude of this enzymatic response can be modulated by prior stimulation history: glands deprived of stimulation become supersensitive to agonists while those stimulated for long periods become subsensitive. This homeostatic mechanism of "up- and down-regulation" is common to many physiologically functioning systems and, in the case of catecholaminergic stimulation of the pineal gland, has been shown to be related to the number of titratable receptors (*6*).

Vasoactive intestinal polypeptide (VIP) can also elicit an increase in NAT activity (*7, 8*) by a postsynaptic action, and the pineal contains nerve fibers with immunologically detectable VIP (*9*). The action of VIP on NAT activity seems independent of the beta-receptor, but may involve a peptide receptor. Response to VIP can be blocked by the polypeptide secretin, which shares some peptide sequences with VIP, but not by somatostatin, which does not (*8*). It was of interest to determine whether stimula-

Table 1. Effects of lighting on the pineal response to VIP. Young (120-g) male rats were maintained under a light-dark cycle or exposed to constant light for 4 days. All animals were killed 3 hours after the end of the final dark interval, and their pineals were removed and placed in organ culture (*10*). After 30 minutes 10 μl of water alone, water containing VIP (to a final concentration of 0.01 μ*M*), or isoproterenol (ISO) (to a final concentration of 0.1 μ*M*) was added. Incubation continued for 5 hours. Pineals were then frozen in solid CO_2 and assayed for NAT activity the next day (*10*). Values are means ± standard errors for pineals from six animals. All the values for the "light-dark" group differ significantly from the corresponding values for constant light ($P < .02$, Student's *t*-test).

Additions	NAT activity (nanomoles of product per hour per gland)	
	Constant light	Light-dark
Water	3.00 ± 0.74	0.13 ± 0.01
VIP (0.01 μ*M*)	7.14 ± 0.92	1.74 ± 0.23
ISO (0.1 μ*M*)	25.49 ± 2.77	9.22 ± 0.99
VIP − water*	4.13 ± 0.92	1.61 ± 0.23

*Mean value for water only subtracted from individual values for VIP exposure.