ducing phase shifts and behavioral changes during stimulation.

The large stimulation field presumably generated by the electrodes used in the hamster study do not permit localization of the effects of stimulation to the SCN. However, the similar effects produced by stimulation within the SCN of rats strengthens the conclusion that changes in neural activity within the SCN mediate the observed effects of stimulation in both species.

These findings are consistent with the hypothesis that neural activity in the SCN regulates phase and period of rodent circadian rhythms. There is, however, substantial evidence for the existence of circadian oscillators outside the SCN (*15*). Therefore, the SCN may function as a pacemaker by generating a circadian rhythm of neural activity that is entrained by photic input and which regulates the activity of other oscillators in the circadian system.

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6. Adult male albino rats (Wistar) were housed in an open vivarium under a light-dark cycle, but their rhythms did not entrain after they were blinded by bilateral enucleation. Surgery was performed under Hypnorm anesthesia (Philips-Duphar; 1 ml/kg). Blinding was necessary to ensure that stimulation did not affect visual afferents to the SCN. Feeding was recorded as described [W. J. Rietveld, F. Ten Hoor, M. Kooij, W. Flory, *Physiol. Behav.* **21**, 615 (1978)].
7. Nine rats were stimulated in the SCN, two were stimulated lateral or caudal to the SCN, two were sham-stimulated (no current), and two were anesthetized controls. Stimulation consisted of 0.5-msec constant current pulses (300 μA) at 25 pulses per second; electrode tip diameters were 10 to 30 μm. Small lesions were placed near the last stimulation site to permit histological localization of the stimulated area. No visible necrosis was detected at the stimulation sites in the SCN.
8. The first daily burst of eating at the beginning of the subjective night was determined by visual inspection of the records. Linear regressions through these points before and after stimulation were used to assess changes in phase and period.
9. Adult male hamsters (Charles River–Lakeview; LVG:lak) were enucleated several weeks before the electrodes were implanted; all surgery was performed under Nembutal anesthesia (Abbott; 80 mg/kg). At the time of enucleation, hamsters were implanted subcutaneously with two 50-mm lengths of melatonin-filled (Sigma) Silastic tubing (Dow-Corning) to prevent testicular regression [F. W. Turek, C. Desjardins, M. Menaker, *Science* **190**, 280 (1975)] which can disrupt hamster activity rhythms [G. A. Eskes and I. Zucker, *Proc. Natl. Acad. Sci. U.S.A.* **75**, 1934 (1978); G. B. Ellis and F. W. Turek, *J. Comp. Physiol.* **132**, 277 (1979)].
10. The electrodes (MS 303/3; Plastic Products) were oriented with the tips in the anterior-posterior plane separated by 0.1 to 0.4 mm. They were implanted in the midline, 0.0 to 0.3 mm anterior to bregma and 8.0 mm below the top surface of the skull, with the upper incisor bar at 2 mm below the interaural line.
11. Bipolar stimulation was delivered as either 0.2-msec square wave pulses, 200 pulses per second at 150 V or 10 msec pulses, 20 pulses per second at 50 V with the use of a Grass S44 stimulator. A 0.5-megohm resistor in series with the stimulator provided essentially constant current stimulation of 100 to 300 μA.
12. Of three hamsters (Fig. 1) two had electrode tips at the dorsal anterior border of the SCN; necrosis around the tips in one hamster did not permit electrode localization. Rhythms of hamsters with electrode placements anterior or lateral to the SCN were not phase-shifted by stimulation.
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Accommodative Defocus Does Not Limit Development of Acuity in Infant *Macaca nemestrina* Monkeys

Abstract. *In an experiment with ten macaque monkeys (*Macaca nemestrina*), a combination of photorefraction and corneal reflex photography was used to measure simultaneously the plane of focus and direction of gaze while they were presented with fixation targets. The monkeys ranged in age from 2 days to 10 weeks. Some of the infants that were less than 1 month old failed to change accommodation to targets at any distance, whereas others showed limited accommodative abilities. The magnitude of the accommodative response of infants older than 4 weeks appeared to be adultlike. Infant monkey's visual acuity improves dramatically after 4 weeks. These results, which show that the improvement in spatial resolution cannot be accounted for by increased accommodative accuracy, parallel those obtained from human infants where accommodative competence is attained by about 4 months of age.*

Visual resolution, or acuity, is poorer in infants than in adults (*1*), but it is not known to what extent the improvements in acuity with age are due to changes in the optics or in neural processing. Experiments to determine this issue are often potentially invasive and not feasible with humans. Infant macaque monkeys (*Macaca nemestrina*) are useful for studying mechanisms of human visual development (*2*), and we now present results obtained from this animal model.

Previous work has shown that the optical quality of the infant monkey eye, as assessed by the line spread function for well-focused images, is not responsible for its poor resolution (*3*). However, if infants are unable to accommodate properly to bring targets into sharp focus at the retina, the poor resolution might be due to optical defocus. We have measured accommodative defocus and our results demonstrate that infants over 4 weeks of age accommodate similarly to adults. Therefore, the improvements in spatial resolution after 4 weeks of age cannot be accounted for on the basis of improvements in accommodative accu-

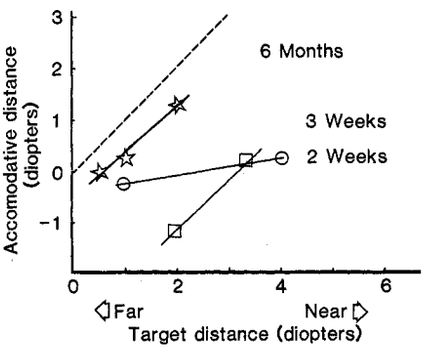

Fig. 1. Accommodation in infant monkeys. The abscissa shows the fixation target plane specified in diopters (1/target distance in meters). The ordinate is the fixation plane of the monkey, also specified in diopters. Zero on the ordinate indicates that the animal is fixated at optical infinity. Positive values indicate that fixation is closer than optical infinity; negative values indicate fixation beyond optical infinity. The dotted line indicates the performance we would expect from an animal with perfect accommodation. Data points falling above this line indicate that the animal is fixating in front of the target, whereas data points below this line indicate fixation beyond the target. Data are shown for three separate animals aged 6 months (stars), 3 weeks (squares), and 2 weeks (circles). Solid lines through the symbols are least-squares linear regression lines.

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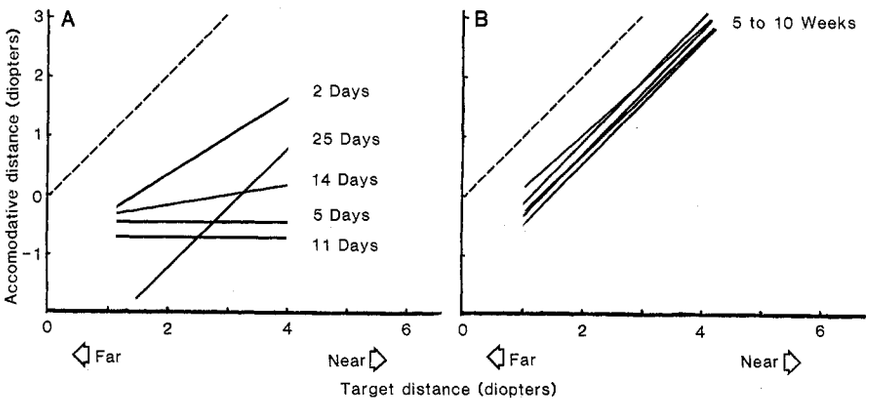

Fig. 2. Summary of the accommodative functions from all the infants. For clarity the data points have been omitted and only the regression lines are shown. (A) Five infants less than 4 weeks old. (B) Results for five infants more than 4 weeks old.

racy (*4*). Thereafter the development of spatial resolution must reflect improvements in neural processing rather than in the optics of the eye.

We used photographic methods to assess accommodative abilities in awake infant monkeys while they fixated visual targets. We chose these methods because the standard techniques of measuring refractive error in a cycloplegic eye do not answer the question of whether the infants are capable of changing focus appropriately for visual targets at various distances. Dynamic retinoscopy is also not an adequate technique because infant monkeys switch their gaze and accommodation very rapidly from position to position when viewing visual targets, and generally do not hold fixation long enough to obtain an accurate retinoscopic reading.

We used two 35-mm cameras with 55-mm f/2 lenses to obtain simultaneous measurements of refractive error and direction of gaze. The cameras were mounted on a single tripod with their lens centers separated by 7 cm. One camera was used with a photorefractor attachment to photograph the fundal reflection (*5*); the second camera was used to photograph the corneal reflex of the flash. The cameras were placed 1 m from the subject.

The monkey was held on the lap of a holder and faced the camera. The photographer or a third person attempted to get the animal to fixate the accommodative target using the face of the photographer, pieces of apple or other fruit, or a small rubber squeaking toy. Both cameras were triggered simultaneously when the photographer judged that the monkey was fixating the target.

From the corneal reflex photographs we determined the angle of gaze relative to the camera. We only scored refractive error on trials in which the animal was fixating within 5 degrees of the cameras (*6, 7*).

For trials in which the monkey was fixating on-axis, we determined the plane of focus by projecting the photorefractive pictures, measuring the lengths of the star arms, and converting the lengths to diopters of defocus (*6*). Net spherical defocus was computed from measurements of orthogonal meridia. We obtained sign of the defocus (myopic or hyperopic) by examining the color of the fringes of the photorefractive pictures (*8*).

To summarize our data for each monkey we plotted accommodative state as a function of target distance (Fig. 1). If an animal is accommodating at the same plane as the visual target, we expect the accommodative function to have a slope of 1.0 and to fall along the dashed line shown in Fig. 1. Representative data are shown in this figure for two infants and a 6-month-old animal. The straight lines drawn through the data points were derived by least-squares linear regression (*7*). The accommodative function for the 6-month-old monkey has a slope of approximately 1.0, which indicates that this animal was accommodating appropriately to the various target distances. The fact that this older monkey's regression line falls somewhat below, but parallel to, the theoretical prediction for perfect accommodation (the dashed line) may be accounted for by either the small eye artifact (*9*) or a large depth of focus (*10*).

The data for the two infants shown in Fig. 1 are representative of the results we obtained from infants less than 4 weeks of age. Some infants failed to change accommodation for any visual targets, thus producing accommodative functions with slopes near zero. Other infants had functions with positive slopes, but their regression lines were shifted several diopters further away from the theoretical prediction (dashed line) than the accommodative functions for older animals. The data in Fig. 2 indicate that none of the younger infants accommodated accurately whereas all of the older group consistently showed appropriate accommodation.

From these results we conclude that accommodative accuracy does not improve appreciably between the ages of 1 and 6 months. During this same age range, spatial resolution as measured behaviorally improves by nearly three octaves (*1, 2*). Therefore the improvements in spatial resolution cannot be due to improved accommodative accuracy.

On the basis of comparisons between human and monkey infants on behavioral measurements of acuity and contrast sensitivity development, it has been suggested that visual development in the two species follows a similar time course, with 1 week of monkey development corresponding to 1 month of human development (*2*). The present results are consistent with this general notion of a weeks-to-months relation between human and monkey visual development. Previous work has shown that accurate accommodative responses develop at approximately 4 months of age in humans (*11*) compared to 4 weeks in the monkeys as found in in the present study.

Now that optics have been ruled out as a major factor, it should be possible to determine in this monkey the locus of the specific neural mechanisms responsible for the development of spatial resolution (*12*).

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7. The fact that we scored only photographs that were on-axis sometimes resulted in missing data points. We always photographed with at least three target distances for each infant (typically 0.25, 0.5, and 1.0 m or 0.5, 1.0, and 2.0 m). However, missing data points sometimes resulted in accommodative functions being derived from only two target distances (see Fig. 1). For some animals at some target distances, we obtained more than one photograph that could be scored. These repeated measures provide an estimate of the reliability of our method. Standard deviations calculated from these repeated measures were typically about 0.25 diopter and ranged from 0.10 to 0.67 diopter.
8. When the animal is focused hyperopically relative to the camera, the distal tips of the orthogonal star arms are reddish in hue; when myopically focused, the tips are blue. The effect is due to the longitudinal chromatic aberration of the eye, and is particularly apparent in simian eyes.
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Long-Term Synaptic Potentiation in the Superior Cervical Ganglion

Abstract. *Brief tetanic stimulation of the preganglionic nerves to the superior cervical ganglion enhances the postganglionic response to single preganglionic stimuli for 1 to 3 hours. This long-term potentiation of transmission through the ganglion is apparently not attributable to a persistent muscarinic action of the preganglionic neurotransmitter, acetylcholine, since neither the magnitude nor the time course of the phenomenon is reduced by atropine. The decay of long-term potentiation can be described by a first-order kinetic process with a mean time constant of 80 minutes. We conclude that long-term potentiation, once considered a unique property of the hippocampus, is in fact a more general feature of synaptic function. This form of synaptic memory may significantly influence information processing and control in other regions of the nervous system, including autonomic ganglia.*

Long-term potentiation (LTP), a use-dependent form of enhanced synaptic efficacy, can last for hours, days, or even weeks (*1, 2*). It can be induced by tetanic activation of the synapses for only a few seconds. Partly for these reasons, LTP has been considered by many to provide a possible neuronal substrate for certain aspects of learning and memory (*1, 3, 4*). The only published reports of LTP have been in studies of the hippocampus, a brain region long implicated in learning and memory functions (*4, 5*). It is therefore natural to ask whether LTP is an exclusive property of hippocampal synapses or a more general feature of neuronal function. We have investigated the superior cervical sympathetic ganglion, a peripheral nervous system structure not traditionally associated with learning and memory (*6–8*). We have found LTP in the sympathetic ganglion and describe it by a first-order kinetic process.

The ganglion was removed (from decapitated Sprague-Dawley rats), decapsulated, and maintained at room temperature in oxygenated Locke solution (*9*). Supramaximal stimuli were applied to the preganglionic (cervical sympathetic) nerve via a suction electrode coupled to an isolated stimulator (Fig. 1A) (*10*). Records of compound action and synaptic potentials were recorded by a suction electrode applied to the internal carotid (postganglionic) pole of the ganglion, the signal from which was differentially amplified (2 Hz to 10 kHz) and displayed for photography on a storage oscilloscope. In some experiments, the responses were digitized and stored by computer for later analysis. Sometimes a loop of the preganglionic nerve was sucked into a second recording electrode, and the response from this electrode was similarly amplified and displayed on a second trace of the oscilloscope (Fig. 1A). Thus, preganglionic stimulation set up a volley of action potentials conducted past one recording electrode into the body of the ganglion to excite synaptically postganglionic neurons whose response was recorded with a second suction electrode. Normally, supramaximal stimulation of the preganglionic nerve was sufficient to initiate action potentials in nearly all of the postganglionic neurons. In order to spare postganglionic neurons for recruitment during an increase in synaptic efficacy, we reduced synaptic excitation either by adding curare (100 to 150 μM) or by suitable changes in the Ca^{2+} and Mg^{2+} concentrations (*11*) in the bathing medium. In most of the experiments reported here, atropine (2 μM) was added to the Locke solution to block muscarinic responses (*7, 12*). The amplitudes of postganglionic responses to single preganglionic stimuli were measured at 1-minute intervals for 5 to 60 minutes before and 1 to 3 hours after tetanic preganglionic stimulation (20 Hz for 10 to 20 seconds).

During the tetanic preganglionic stimulation, the amplitude of the postganglionic response rapidly decreased because of synaptic depression. However, a single preganglionic stimulus delivered 1 minute after the tetanus produced a postganglionic response that was more than twice as large as control responses measured before the tetanus. Subsequently, the postganglionic response progressively decreased in amplitude, but it remained elevated above control (pretetanic) levels for more than an hour after the tetanus (Fig. 1B, inset). This was a highly reproducible observation in the more than 20 ganglia studied.

To evaluate the decay kinetics of the enhanced synaptic transmission, we transformed the voltage-amplitude data into a dimensionless incremental response $I(t)$ that normalized the posttetanic response amplitude to a fractional increase over the pretetanic control response amplitude

$$I(t) = [V(t) - V_C]/V_C \quad (1)$$

where V_C is the mean control value and $V(t)$ is the posttetanic value as a function of time t (*8, 13*). A semilogarithmic plot of the time course of $I(t)$ showed that there was always an early rapid decay phase followed by a much more slowly decaying phase (Fig. 1B). The simplest expression that we found to describe accurately the overall posttetanic time course of the enhanced response consisted of the sum of two exponential terms

$$I(t) = P\exp(-t/\tau_P) + L\exp(-t/\tau_L) \quad (2)$$

where P is the early, rapidly decaying component and L is the slowly decaying, long-term component. The magnitudes (P and L) and time constants (τ_P and τ_L) of these components were determined by standard exponential fitting and peeling (*14*). That we could accurately describe the entire posttetanic time course in terms of Eq. 2 (Fig. 1B) suggests the possibility of two first-order kinetic processes. For convenience, and by analogy to similar phenomena observed by other investigators, we refer to the more rapidly decaying component as posttetanic potentiation (PTP) and the slowly decaying component as LTP (*15*).

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