in man. The retinal lesions produce acuity reductions slightly smaller than that predicted from the human eccentricity curve, although it should be noted that the subsequent acuity of unoperated control animals shows a slight improvement over original preoperative values: relative acuity in these controls has a mean of 104 percent, as shown by the large circle displayed at 0° on the abscissa of Fig. 1. This would tend, in effect, to displace the entire human eccentricity curve slightly upward. Our results are to a degree consistent with that of Yarczower *et al.* (*6*), who report a drop in acuity after a "foveal" lesion in a single stump-tailed monkey. No reconstruction of the lesion, however, was provided by them, and the relative acuity (16 percent) was so low as to suggest either that their lesion functionally affected much more than the fovea or that the stump-tailed macaque is very different from the rhesus macaque. Or, possibly, the animals were incompletely trained, as suggested by their relatively high value of preoperative acuity (1.4 minutes).

It should be stressed that the discrepancy between the retinal and cortical results is conservatively based: at each doubtful juncture we made assumptions which increased the retinal lesions and decreased the cortical lesions. Therefore, if the present results are mistaken they are probably an underestimate of the discrepancy.

The failure of the electrophysiological map to predict the acuity results following striate cortical lesions has several possible explanations. It could be that the map displayed in Fig. 2 itself is wrong. The only other data for the monkey on which a map could be based are those of Daniel and Whitteridge (*7*). By integrating their curve relating "magnification factor" to degrees of eccentricity one can obtain an estimate of linear distance on the cortex for degrees of eccentricity in the field. When this is done the resulting cortical lesion would be expected to affect even larger regions of visual space, and the results (squares in Fig. 1) depart even further from the retinal results. But it is worth mentioning that other internal evidence provided by Daniel and Whitteridge indicates that their map should more closely approximate Talbot and Marshall's (*8*) map than in fact is achieved by using their magnification factor data, and they themselves strongly imply in their discussion an endorsement of these features of Talbot and Marshall's map which are relevant to the present point.

An attractive explanation of the results which would preserve the "point-to-point" concept would be the development of partial "denervation supersensitivity" at the edges of the cortical lesions, thereby making them able to respond to smaller differences between signals (*9*). But this explanation seems unlikely, since, in a further experiment, we found that the effects of combined retinal and striate lesions on acuity (involving the same regions of visual space) were equivalent to a retinal lesion alone. The supersensitivity argument should predict that the combined lesion be less deleterious than the retinal lesion alone. Projections from the retina to the midbrain or nonstriate cortex might also be able to carry the appropriate information so as to compensate for a striate cortical lesion. But, if so, the results clearly do not fit the hypothesis that such a projection has a fixed capacity so far as acuity is concerned, and one is inclined to examine simpler hypotheses. One hypothesis which neatly fits the facts stems from the definite knowledge that at various stages of the visual system, including the retina, ample opportunity exists for the interaction of neighboring regions, as manifested, for example, in "lateral inhibition." If information transmitted along such pathways of interaction (at a stage prior to the cell bodies of the lateral geniculate body) could be exploited by an animal with a cortical lesion, the obtained acuity results could easily be explained. The actual size of the difference between the retinal and striate cortical reduction results would give an indication of how far laterally information could have an influence. Another prediction which stems from this hypothesis is that the size of the field defect following a cortical lesion ought to be smaller than that predicted by the electrophysiological map. Exactly this result has been found by one of us (A.C.): the field defect measured perimetrically was found gradually to have shrunk over the course of the first few postoperative years, even though it originally was of a size corresponding closely to the one predicted by the map.

L. WEISKRANTZ
A. COWEY
Psychological Laboratory, University of Cambridge, Cambridge, England

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Evoked Pressure Responses in the Rabbit Eye

Abstract. *In the rabbit, a sensory stimulus of low intensity evokes a characteristic transient intraocular rise in pressure with an amplitude as great as 10 millimeters of mercury. This α-adrenergically mediated phenomenon occurs concomitantly with a general arousal response and appears to be caused by contraction of the orbital smooth muscle of Müller.*

Characteristic intraocular pressure responses as great as 10 mm-Hg in amplitude have been recorded in the eyes of conscious rabbits following low-intensity sensory stimulation. Electroencephalographic (EEG) changes indicate that this evoked rise in pressure occurs concurrently with a general arousal response. Thus, intraocular pressure parallels other physiological changes accompanying arousal in almost every system of the body (*1*). The latency, rate of rise, and rate of decay of evoked intraocular pressure transients are practically independent of stimulus parameters. However, habituation to a constant, periodically repeated sensory stimulus can often be observed, as with any stimulus which loses its novelty. Smaller replicas of the characteristic pressure wave sometimes appear spontaneously. These "internally" triggered events are accompanied by a K complex in the EEG. The evoked intraocular response was observed in each of the 32 New Zealand albino rabbit eyes that were tested.

In these unanesthetized and be-

haviorally responsive animals, intraocular pressure was continuously monitored with a passive radio transensor 2 mm thick and 6 mm in diameter. This device is small enough to be implanted in a rabbit eye and has no tubes or wires to pierce or even touch the globe (*2*). Implanted transensors have functioned satisfactorily for over 6 months without visible disturbance to the eye in 15 out of 17 animals living under normal laboratory conditions.

Intraocular pressure response has been evoked by the following types of physiological stimulation: (i) clicks or short (0.1 to 1 second) pulses of sound at intensity levels down to approximately 0.0002 μbar (the threshold of human hearing) and between the frequencies of 100 to 10,000 cycle/sec; (ii) brief (0.25 to 1 second) flashes of reflected incandescent light at a luminance of 10 mlam and below; (iii) movement of the experimenter's finger at a distance of 1 m; (iv) raising the temperature of a wire in contact with the surface of the skin by approximately 10°C; (v) lightly touching the fur or a whisker; and (vi) the odor of an air mixture of amyl acetate or ammonia, judged by the experimenter to be of moderate intensity. Intraocular pressure response was also elicited by direct electrical stimulation of the cervical sympathetic nerve in unanesthetized rabbits. Change of intraocular pressure occurred homolaterally with the nerve stimulated, but not contralaterally. Similar responses in anesthetized cats and dogs have been documented by others (*3*).

Mean latency of onset of the rise in pressure following 740 audible stimuli repeated at 10-second intervals was 0.4 second (standard deviation of 0.1 second). Mean latency to the peak of the pressure wave was 2.0 seconds (standard deviation of 0.2 second).

The 0.4-second latency is too short for humoral regulation, which generally involves delays at least ten times longer. The rate of rise (5 mm-Hg per second) is also too fast to be produced by aqueous secretion or outflow resistance changes from the eye, because one can expect a maximum rate of change of intraocular pressure, due to complete stoppage of outflow, of only 0.2 mm-Hg per second. Thus, only muscular or vascular phenomena remain as possible mechanisms.

Venous pressure measured at the level of the vena cava did not increase with the evoked response. However, a general arterial blood-pressure wave,

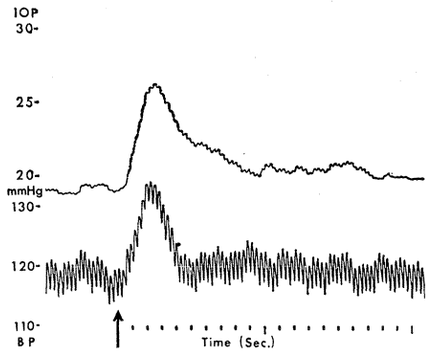

Fig. 1. (Top) Intraocular pressure (*IOP*) response evoked in a rabbit by a tactile stimulus (touching whisker) at arrow. (Bottom) Blood pressure (*BP*) measured simultaneously in the abdominal aorta. Pulsatile variations in both curves were reduced by 0.5-cycle/sec low-pass filters.

with a similar characteristic shape and amplitude, occurred simultaneously with the evoked intraocular pressure response (Fig. 1). Sectioning a cervical sympathetic nerve on one side completely eliminated the sensory-evoked intraocular pressure response on that side. Yet, in this preparation the large evoked arterial blood-pressure wave persisted. This shows that the intraocular pressure response is not a passive reflection of changes in blood pressure.

General, surgical-plane pentobarbital anesthesia eliminated both the blood-pressure wave and the intraocular pressure response. However, characteristic intraocular pressure responses, resembling those evoked by sensory stimulation, could be elicited by stimulating the homolateral cervical sympathetic nerve immediately after exsanguination, when all blood flow had stopped. Therefore, the evoked intraocular pressure response is not due to active vascular mechanisms.

If this pressure response were caused by retraction of the bulb, one should be able to measure the retraction and a resultant increase in retrobulbar pressure. Axial eye movements were recorded by means of a precalibrated, head-mounted strain gauge with a fiber lever bearing on a scleral contact lens. Changes in retrobulbar pressure were measured with a hypodermic needle inserted behind the eye; 0.5 ml of injected saline was used as a pressure-measuring reservoir. No enophthalmos (retraction of the eye) or rise in retrobulbar pressure occurred during evoked intraocular pressure responses; however an insignificant proptosis (approximately 50 μ of protrusion) was noted. From these measurements, it appears that action of the retractor bulbi or orbicularis muscles does not contribute to intraocular pressure response.

The evoked pressure response is not caused by contraction of any of the striated ocular muscles, since normal eye movements and blinking were still observed while both intraocular and blood-pressure responses due to sensory and direct nerve stimulation were eliminated by the α-adrenergic receptor blocking agent phenoxybenzamine (Regitine). Moreover, evoked responses were transiently reduced by the α-adrenergic stimulant methoxamine (Vasoxyl). Cholinergic and β-adrenergic receptor blocking agents (*4*), in doses sufficient to block appropriate receptors, had negligible effect on the response. Similarly, cholinergic and β-adrenergic stimulants did not visibly alter the response. These results indicate that the evoked intraocular pressure response appears to be α-adrenergically mediated.

This is consistent with the hypothesis that the evoked pressure response is produced by smooth muscle contraction. Furthermore, the long latency, slow rise, and long duration of the evoked intraocular pressure response are not characteristic of striated but of smooth muscle activity. The most prominent smooth muscle of the orbit, as described by Müller, radiates fan-like in a thin layer over the orbital floor and is innervated by the cervical sympathetic nerve (*5*).

Direct electrical stimulation with single 20-volt, 10-msec pulses delivered from the flush tip of a No. 22 coaxial needle electrode in the region of Müller's muscle produced small intraocular pressure waves resembling the evoked pressure response. The attenuation of this electrically induced response was probably due to the small volume of muscle stimulated. The response was not due to striated muscle. This was evident when the stimulating electrode mistakenly contacted striated muscle, since the latency, rise time, and duration of the sharp pressure transients then produced were an order of magnitude shorter than sensory-evoked intraocular pressure responses. In addition, it was shown experimentally with a thread creasing the cornea that less than 5 g of force, well within the capabilities of Müller's orbital smooth muscle, need be exerted by a small-diameter smooth muscle slip bearing on the globe to produce intraocular pressure changes of the same magnitude as the evoked pres-

sure response. A few widely separated muscle slips would require even less tension in each.

The evidence presented suggests that the evoked intraocular pressure response is produced by contraction of the orbital smooth muscle of Müller. This muscle contraction appears to be α-adrenergically mediated through the sympathetic nervous system which, in turn, is activated during a general arousal response to a sensory stimulus.

CARTER COMPTON COLLINS
Institute of Visual Sciences,
Institute of Medical Sciences,
Presbyterian Medical Center,
San Francisco, California

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Temporary Abolition of Pain in Man

Abstract. *In eight patients with intense chronic cutaneous pain, sensory nerves or roots supplying the painful area were stimulated. Square-wave 0.1-millisecond pulses at 100 cycles per second were applied, and the voltage was raised until the patient reported tingling in the area. During this stimulation, pressure on previously sensitive areas failed to evoke pain. Four patients, who had diseases of their peripheral nerves, experienced relief of their pain for more than half an hour after stimulation for 2 minutes.*

One of the predictions of the "gate control" theory of pain is that stimulation of large diameter cutaneous afferent nerve fibers might reduce pain (*1*). The prediction was based on the observation, made in cats, that volleys of impulses in afferents set off a depolarization of terminal arborizations of cutaneous fibers (*2*). This presynaptic depolarization is believed to be the result of activity in the small cells of substantia gelatinosa (*3*). Presynaptic depolarization reduces the excitatory effectiveness of afferent impulses on cells in the dorsal horn (*4*). Eight patients with severe cutaneous pain were stimulated and the results were divided into two groups. In one group (patients No. 1 through 4) the effects lasted more than 30 minutes after 2 minutes of stimulation. In group two (patients No. 5 through 8) the effects lasted from a few seconds to a few minutes after the stimulus ended. The type of stimulation used (0.1-msec square-waves at 100 cycle/sec) was tested on ourselves before it was used in the experiment. Needle electrodes insulated except for the tip were applied to our infraorbital nerves; a tingling or buzzing sensation was evoked near threshold in the sensory region of the nerve. It was not unpleasant and always tolerable for an indefinite period. During stimulation and for a few minutes thereafter, pin prick in the tingling area did not feel sharp to either of us. In all eight patients, the sensations produced by stimulation were not painful and were acceptable for an indefinitely long time.

Patient No. 1 was a 26-year-old female suffering from the consequences of a fractured elbow; she experienced a burning and stabbing pain and extreme tenderness in the skin area supplied by the ulnar and median nerves. The disease became progressively worse over a period of 2½ years and had been treated by transplantation of the ulnar nerve and by severance of the dorsal roots C7 through T2. The medial side of her arm and hand lost feeling, but she reported a steady burning pain in the anesthetic region of the hand and extreme tenderness of the middle finger and the mid-palm. Silastic split-ring platinum electrodes were implanted around the median nerve above the elbow with the leads being run through the skin of the antero-medial forearm. Threshold stimulation of the median nerve at 100 cycle/sec with 0.1-msec square-waves induced a sensation of tingling and buzzing in the lateral palm, thumb, and first and second fingers. During the stimulation, pressure on the tender areas failed to cause any discomfort to the patient. For a period of more than half an hour after the stimulation, the patient reported that the hand felt numb and free of pain, and it could be moved freely. Light pressure on the previously tender areas was reported by the patient as touch.

Patient No. 2 was a 40-year-old man who had been shot 2 months prior to the study. The .32-caliber bullet had entered behind the right shoulder and emerged above the medial end of the left clavicle. There were no immediate neurological signs but, after 3 days, severe burning pain developed in the third and fourth fingers of the right hand. The patient said that the pain felt as though a blowtorch was being passed over his fingers. Lancinating pains radiated proximally from the fingers. The brachial plexus was explored and the sympathetics were blocked without effect. A 20-gauge concentric bipolar stimulating hypodermic needle was placed close to the ulnar nerve in the wrist. Electrical stimulation of the type used in patient No. 1 produced tingling in the medial side of the hand and in the third and fourth fingers. The results during 2 minutes of stimulation and for more than half an hour after stimulation were the same as in patient No. 1.

Patient No. 3 was a 50-year-old man with severe burning and stabbing pain of unknown origin in the area supplied by the ulnar nerve. The pain had been treated unsuccessfully for 3 years by removal of the C6 disc, exploration of the ulnar nerve at the wrist and elbow, exploration of the brachial plexus, and partial section of the dorsal roots C7 through T2. Stimulation of the ulnar nerve at the wrist through electrodes on the skin surface produced a buzzing and tingling sensation in the medial side of the hand and in the third and fourth fingers; the general results were the same as in the previous patients.

Patient No. 4 was a 55-year-old woman who had severe burning and stabbing pain in her right big toe and in the medial arch of her foot. The pain had lasted for 6 months and was accompanied by tenderness on the back of the leg and wasting of the calf. The diagnosis was diabetic neuropathy. Surface stimulation of the saphenous nerve with the standard intensities and frequencies produced a tingling sensation in the middle of the leg down to the ankle, but the stimulation had no effect on the pain. Surface stimulation of the superficial peroneal produced what the patient termed "an electric feeling" in the toes and in the top of the foot. After 2 minutes of stimula-