Additional insight into the mechanism of action of fMet-Leu-Phe and C5a was obtained by consecutive addition of the two to the same sample of chlorotetracycline-loaded neutrophils (Fig. 3). The addition of even a large concentration of either of the chemotactic factors following a saturating concentration of the other has no further effect on the fluorescence of the cells, irrespective of which chemotactic factor is added first. These results strongly suggest that, although initiated by their binding to different receptors (*10*), the actions of fMet-Leu-Phe and C5a are mediated, at least in part, through the release of a common pool of membrane calcium.

The chemotactic factor-induced decrease of the fluorescence of chlorotetracycline-loaded neutrophils thus satisfies the following conditions for functional significance: (i) the two very different chemotactic factors tested induced a decrease in cell-associated chlorotetracycline fluorescence; (ii) the time course of the change in fluorescence is consistent with that of the biological effects of the chemotactic factors; (iii) the concentrations of chemotactic factors required to elicit biological responses and changes in chlorotetracycline fluorescence are similar; and (iv) the binding of fMet-Leu-Phe, the biological functions it induces, and the decrease in chlorotetracycline fluorescence can all be competitively inhibited by the same concentrations of Boc-Phe-Leu-Phe-Leu-Phe. To our knowledge these results represent the first direct experimental evidence for the postulated (*2*) involvement of membrane calcium in transmembrane signal transduction in the neutrophils. The factors modulating the chemotactic factor-induced decrease in the fluorescence of chlorotetracycline—or more specifically the underlying release of membrane calcium by chemotactic factors—remain to be elucidated. One attractive possibility is that this release of membrane calcium is related to the recently demonstrated chemotactic factor-induced protein carboxymethylation in neutrophils (*12*). Elucidation of these mechanisms should help in mapping the sequence of events that occur between the binding of the stimulus (chemotactic factor) to its specific receptors and the activation of the contractile apparatus of the neutrophils.

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Local Foveal Inhibitory Effects of Global Peripheral Excitation

Abstract. *Global excitation produced by oscillating a peripheral square-wave grating back and forth through one-half cycle inhibits the visibility of an incremental test flash only when the flash is presented in the foveal region of the visual field. This finding is discussed in the context of the neurophysiological periphery effect and shift-effect and their possible role in saccadic suppression.*

When a contour shifts or a grating consisting of black and white bars oscillates back and forth in the periphery of the visual field it can decrease the visibility of a central incremental light flash (*1-3*). This psychophysical effect is probably caused by an inhibition of the signal generated by the test flash (*3*) and therefore suggests that activity in one region of the visual field can be inhibited by excitation in another, remote region. We have found that the test flash inhibition produced by global peripheral excitation is obtained only locally at the fovea. Besides offering neurophysiological and functional interpretations of these results, we also suggest some implications for future neurophysiological and neuroanatomical studies.

The stimulus display (Fig. 1) was front projected from three projectors onto a white matte posterboard screen located about 230 cm from the subject. The display subtended an area of 24° by 19.5°. One projector supplied the outer surround consisting of either a vertical grating, as shown, or a uniform white field with a luminance equal to the space-averaged luminance of the black and white bars. From the grating, a disk-shaped central region 7.0° in diameter was deleted by an appropriate mask. In its place was projected from a second projector a uniformly illuminated background disk, onto which in turn was projected an incremental, 0.38° diameter test spot from a third projector.

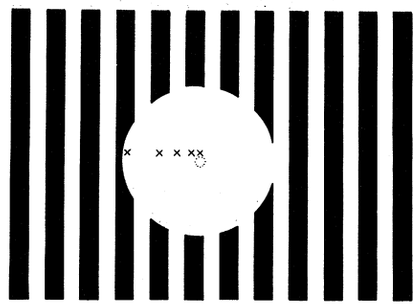

Fig. 1. The stimulus display. The central, incremental test flash is indicated by a stippled circle. The positions of the fixation point are indicated by x's.

The widths of the white and black bars of the grating were each 0.94°, corresponding to a spatial frequency of 0.53 cycle per degree; their respective luminances, L_{max} and L_{min}, were 11.10 cd/m^2 and 0.41 cd/m^2. The contrast of the grating, according to the formula $(L_{max} - L_{min})/(L_{max} + L_{min})$ was 0.93. The luminance of the uniform outer surround was $(L_{max} + L_{min})/2 = 5.75$ cd/m^2. The grating was oscillated at a previously determined optimal frequency of 4 Hz (*2*) by means of a mirror placed in the beam of the first projector and mounted on an electromagnet which, in turn, was driven by a function generator (Wavetek model 133). The grating was oscillated in a square-wave manner through one bar width producing a luminance modulation equivalent to pattern reversal. On the basis of an earlier study (*3*), the luminance of the background disk was set at optimal levels for each of

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the subjects: A.V., 8.22 cd/m^2; B.B., 20.55 cd/m^2.

All viewing was binocular. With his head resting on a chin and head brace, the subject focused on a fixation cross which, during a given experimental session, was located in one of several eccentric positions relative to the test spot (Fig. 1). For A.V., the test spot eccentricity varied from 0.19° to 1.75°; for B.B., it varied from 0.19° to 7.0°. A descending method of limits was used to determine increment thresholds. The test spot, preceded by a warning sound, was presented every 5 seconds for a duration of 100 msec. At the beginning of a determination it was presented slightly above threshold, and on subsequent trials its luminance, ΔL, was successively reduced by 0.02 to 0.04 log-unit steps until the subject reported not seeing the test spot on two successive trials. This luminance value was taken as threshold. Several such values ($n = 6$) were measured in the presence of the uniform white outer surround, and thereafter the same number were measured in the presence of the oscillating grating. Their respective averages, ΔL_W and ΔL_G, were taken as the increment thresholds. The log of the ratio $\Delta L_W/\Delta L_G$ was used to define the effect of an oscillating grating relative to a uniform outer surround on increment thresholds. Negative values indicate test flash inhibition.

The oscillating grating in the outer surround had an inhibitory effect only when the test spot was located at or near the fovea (Fig. 2). For both subjects the effect was strongest (0.4 to 0.8 log unit) when the eccentricity of the test spot was 0.19°, and it decreased rapidly, asymptoting to a value of 0.0 at an eccentricity of 1.75°. Thus the inhibitory effects of global peripheral excitation were restricted to the foveal and near-foveal region of the visual field.

A plausible interpretation of these results can be given in terms of two sets of neurophysiological findings. One set, McIlwain's periphery effect (*4*) and the shift effect investigated by Krüger, Fischer, and collaborators (*5*), indicates that the excitation of predominantly transient neurons (*6, 7*) can be markedly increased by remote stimulation falling outside their receptive fields as defined by classical spot-mapping techniques (*8*). The second set indicates that transient neurons inhibit neighboring sustained neurons (*9, 10*). With these two mechanisms, a decrease in sustained neuron activity can be produced by nearby transient neurons that, in turn, receive long-range excitation from remote stimulation. On the assumption that detection of

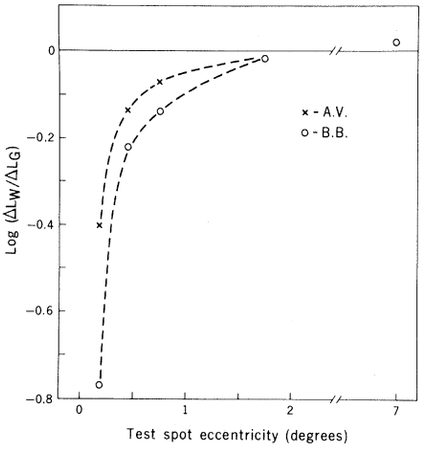

Fig. 2. The change in increment threshold, ΔL_G, produced by a peripheral oscillating grating relative to the threshold, ΔL_W, obtained in the presence of a uniform outer surround as a function of test spot eccentricity. Negative values indicate that the grating had an inhibitory effect, that is, increased threshold relative to the uniform surround. The standard error of the mean for each data point was approximately 0.05 log unit.

luminance increments is mediated by sustained neurons (*7*), our results can be explained in the framework of the above scheme.

The restriction of the test flash inhibition to the fovea is at first glance puzzling, since the periphery effect in transient neurons increases in strength with eccentricity, whereas the response of sustained neurons decreases in strength (*11*). On that basis alone, one might expect weakest inhibition at the fovea and progressively stronger inhibition in the periphery. Nonetheless, a broader functional interpretation based on saccadic suppression (*12*) adequately accounts for the current findings (*13, 14*).

Recent neural theories of metacontrast (masking of one stimulus by a succeeding, spatially adjacent stimulus) (*14, 15*) use the inhibition of sustained neurons by transient neurons as a basic explanatory mechanism. Moreover, this inhibition (*9*) and thus metacontrast (*15, 16*) have been implicated as mechanisms for saccadic suppresion. Metacontrast is weakest in the fovea and increases in strength with eccentricity (*17*). This is consistent with the findings that the ratio of transient to sustained neural activity is lowest in the fovea and increases with eccentricity (*18*). Since receptive fields are relatively small in the fovea, it is a relatively short-range effect there (*19*). Both of these findings indicate that short-range saccadic suppression is weakest in the fovea. This alone is a nonoptimal state of affairs from the standpoint of normal visual behavior in which visual inspection proceeds from one fixation to another. An additional mechanism would be required to optimize saccadic suppression of the foveal image.

Meyer and Maguire (*20*) recently showed that the visual icon or pattern persistence is dependent on spatial frequency and is most likely mediated by sustained neurons. Persistence increases with spatial frequency, reaching values as large as 400 msec at 15 cycles per degree. Now, because analysis of the higher spatial frequencies is performed in the fovea, one can see that sustained activity generated in a preceding fixation would persist into and thus mask sustained activity generated in the proceeding fixation. This type of forward masking would be detrimental to vision dependent on a sequential foveal analysis of pattern. We suggest that, to compensate, global peripheral excitation in transient channels converges on the retina and is converted there into inhibition in sustained channels. Thus, the periphery effects and shift effects may serve as global long-range mechanisms of saccadic suppression converging on and reinforcing a weak short-range (metacontrast) mechanism in the fovea.

We predict that whereas the periphery effects and shift effects are predominantly excitatory for transient neurons, they are predominantly inhibitory for sustained neurons. Recent neurophysiological findings on neurons in the lateral geniculate nucleus of the monkey (*21*) give weak but encouraging support to this prediction. We suggest that strong support for this prediction will be forthcoming when the effects of remote stimulation are investigated in sustained neurons representing the foveal region of visual space. Moreover, we predict that long-range lateral connections from the neural representation of the peripheral visual field to the neural respresentation of the foveal visual field exist at one or several levels of visual processing. Fairly long-range lateral connections that may be inhibitory have recently been identified at cortical levels (*22*).

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Electromagnetic Muscle Stretch Strongly Excites Sensorimotor Cortex Neurons in Behaving Primates

Abstract. *Responses of single units in primary motor and sensory cortex of behaving primates to electromagnetic streich of the muscle flexor carpi ulnaris are comparable in latency and intensity to responses to wrist extension. Thus, muscle stretch appears to be a major factor in cortical response to limb displacement during performance and probably has an important role in motor control at the cortical level.*

Single units in primary motor and sensory cortex respond quickly to limb displacement imposed during precisely controlled movements or postures (*1*). Such displacement rotates joints, stretches muscles, and moves other superficial and deep tissues. Knowledge of the part each form of stimulation plays in the cortical response to displacement is essential to understanding the role of peripheral feedback in motor control. Units which responded to abrupt displacement imposed during maintenance of a given hand position were studied for their responses to muscle stretch in the absence of joint rotation. Electromagnetic force, applied to an implanted iron slug, stretched a single muscle (*2*). The results support the hypothesis that muscle stretch is a powerful source of input to sensorimotor cortex in behaving primates and thus is probably a major factor in cortical control of performance.

Two monkeys (*Macaca mulatta*) were trained on a simple task. Each was seated in a primate chair, right elbow flexed to 90°, right arm restrained at elbow and wrist, and right hand held by a strap to a torque motor handle which moved in the plane of wrist flexion and extension. The monkey received liquid reward at 3- to 6-second intervals for maintaining the handle in a narrow middle zone of 10° with the wrist neither flexed nor extended. The presence of the handle in the correct zone was signaled by a light. The torque motor could apply flexion or extension steady-state torque to the handle, requiring exertion by wrist extensors or flexors, respectively, if the handle was to remain in the reward zone. One-half second before the reward was delivered, a 50-msec torque pulse, which produced an abrupt 10° to 20° displacement of the handle was superimposed on the steady-state torque. [In the arm of a cadaver that had not yet entered rigor mortis, extension of this magnitude stretched the muscle flexor carpi ulnaris (FCU) by 100 to 200 μm.] Both flexion and extension displacements were delivered in pseudorandom order. Reward was inevitable at the time of the torque pulse. Animals readily mastered the task.

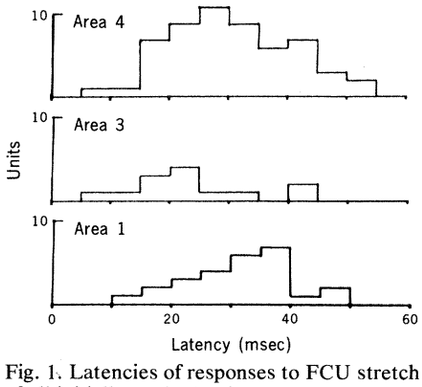

Fig. 1. Latencies of responses to FCU stretch of all initially excited units.

Under general anesthesia, a 2-g coated iron slug was embedded in the distal musculotendinous junction of the right FCU muscle (*2*), a head holder was bolted to the skull to allow the head to be immobilized, a recording cylinder was bolted over the arm region of motor and sensory cortex on the left side (*3*), and a pyramidal-tract stimulating electrode was positioned in the left pyramid.

Several days after surgery, animals resumed the task. The design was identical to that during the training period, except that 1 to 2 seconds before displacement a 100-msec (7-msec rise time) d-c current pulse was delivered to a solenoidal coil encircling the monkey's wrist. The pulse exerted a 70-g force, directed distally along the axis of the forearm, on the embedded slug, and thus stretched the FCU. This stimulus produced no detectable change in handle position, and the animals appeared to ignore it totally. (Pulse-induced movement of the muscle, measured in the cadaver arm at a point 5 mm proximal to the proximal end of the slug, was 75 μm, with a rise time of 50 to 70 msec. In the cadaver arm, at least half of this movement was due to movement of the entire forearm and thus did not represent FCU stretch.) Single-unit recordings were made from each animal over a period of 2 to 3 months. For each well-isolated unit that appeared to respond to flexion or extension displacements, unit activity and handle position were recorded for a full stimulation cycle (5 steady-state torque levels with 16 displacements and 8 or 16 FCU stretch pulses at each level). Selected

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