## Neural Symbolic Activity

Visual inspection of a grating has a number of effects on subsequently seen test gratings of similar orientation. These effects include a change in the apparent spatial frequency of that test grating (*1*) and a decrease in its visibility (*2*). Such findings have been attributed to adaptation in specific classes of human sensory mechanisms. Recently, Weisstein claimed to have measured, in a similar experiment, the "neural representation in the visual system of the concept 'in back of'" (*3*). We have serious doubts about her claim and question that her findings support it.

In the condition of Weisstein's experiment most critical to her interpretation, a subject viewed a grating for 10 seconds. The center section of that grating was obscured by a perspective drawing of a cube (*4*). After the grating and cube were removed from view a small test disk was flashed in the region of the visual field previously occupied by one face of the cube drawing and which, as a result, was free of grating contours. The test disk contained several cycles of a grating similar in orientation and spatial frequency to that which had surrounded the cube in the adaptation field. Using a method resembling "magnitude estimation" (*5*), the subject made a numerical judgment of the apparent contrast of the grating within the test disk. This condition produced a reduction in judged test contrast.

As Weisstein admits, the fact that the judged contrast of the test grating is reduced, in the condition we have described, may actually have nothing whatever to do with the fact that it is presented in an area of the visual field which had contained an object in apparent depth. There is a critical control condition that she neglected to test. In that condition the cube drawing would have been replaced by a gap in the grating, a gap which would not appear to lie in front of the grating plane. Weisstein acknowledges that "in order to test that activity in response to nongrating portions of the stimuli used in this experiment actually symbolizes 'in front of,' it must be shown that, with scenes in which gratings are simply interrupted, such as a picture of a grating with a hole in its middle, there is no adaptation effect." Such a control should have been tested before publication of her report, because already available data make it unlikely that her findings are at all relevant to her interesting and provocative speculations about "neural symbolic activity."

We will consider two possible mechanisms, either one of which could have mediated Weisstein's findings and neither one of which is related to "neural symbolic activity." The first involves the effects of eye movements during the adaptation period; the second mechanism does not involve eye movements, but would predict Weisstein's data on the basis of a simple spread of effect from one area of the visual field to a neighboring one.

How can we assess the likelihood that, during the 10-second period of adaptation, the subject's eye would wander sufficiently to bring the area of his retina upon which the test target would later be imaged onto the grating portion of the adaptation field? Had the test and adaptation fields been presented simultaneously, the minimum distance from the edge of the test disk to the surrounding grating would have been 25.8 minutes of arc. Citing the data of Steinman (*6*), Weisstein assumed that the standard deviation of eye movements in her experiment would be about 5 minutes of arc and, therefore, that the probability of an eye movement as large or larger than the distance from the test disk to the edge of the adaptation grating was less than .00009. However, Weisstein makes no mention of either a fixation point or of a biting board to steady her subject's head. If no fixation point were present during the adaptation period we would expect far larger motions of the eye than those obtained by Steinman.

The absence of a biting board would amplify the drift of the adaptation pattern across the retina by introducing significant movement of the subject's head (*7*). The tachistoscope that Weisstein used comes equipped with forehead rests, but these are no substitutes for a biting board. Any combination of the above factors increases the likelihood that an area of the retina hit by the test disk would have been stimulated by the grating during some fraction of the adaptation period.

There is also the possibility that at a distance of 25 minutes of arc and more, one contour could affect the visibility of another. A number of studies (*8, 9*) would seem to bear on the possibility of a spatial spread of effect in Weisstein's experiment. Such a spread of effect does not mandate the invocation of "neural symbolic activity." Alpern found interactions between visual contours separated by as much as a degree (*8*). Parlee (*10*) found that with separations of 26 minutes between adaptation and test contours there was a very substantial effect on the visibility of the test line. The next largest separation she examined was 1 degree, where there still seemed to be some interaction between test and adaptation contours. It is difficult to know, in the absence of the appropriate control condition, whether 1 degree was in fact the limit of the spatial interaction. Parlee's stimulus flashes were brief enough so that we may consider them to have been essentially fixed on a motionless retina (*11*).

We must consider whether procedural differences between the experiments of Parlee and Weisstein might render our extrapolation invalid. Parlee presented her test target temporally before the adaptation target, whereas Weisstein did the reverse. However, other experiments on orientation-specific interactions of contours (*12*) confirm the equivalence of orientation effects in the two temporal orders.

In summary, we believe that the effect which Weisstein attributed to "neural symbolic activity" is more likely mediated by a combination of eye movements, during the prolonged adaptation period, and a simple spatial spread of the orientation-specific adaptation, of the kind that Parlee described.

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### References and Notes

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2. A. Pantle and R. Sekuler, *ibid.* **162**, 1146 (1968).
3. N. Weisstein, *ibid.* **168**, 1489 (1970).
4. Although the cube shown in figure 1 of Weisstein's report exhibits considerable fluctuations and reversals in its apparent depth, we will accept Weisstein's assumption that the cube consistently appeared to lie in front of the surrounding grating.
5. It is somewhat difficult to interpret the meaning of Weisstein's dependent variable, because she neglected to provide a physical scale against which to calibrate the reported numerical estimates of contrast. To remedy this problem she might have presented subjects

with gratings of various contrasts and asked them to judge the contrast.
6. R. M. Steinman, *J. Opt. Soc. Amer.* **55**, 1158 (1965).
7. R. M. Boynton, in *Experimental Methods and Instrumentation in Psychology*, J. B. Sidowski, Ed. (McGraw-Hill, New York, 1967), pp. 273–330.
8. M. Alpern, *J. Opt. Soc. Amer.* **43**, 648 (1953).
9. J. L. Brown and C. G. Mueller, in *Vision and Visual Perception*, C. H. Graham *et al.*, Eds. (Wiley, New York, 1965), pp. 208–250.
10. M. Parlee, *Vision Res.* **9**, 199 (1969).
11. L. A. Riggs, J. C. Armington, F. Ratliff, *J. Opt. Soc. Amer.* **44**, 315 (1954).
→ R. Sekuler, *J. Exp. Psychol.* **70**, 401 (1965); K. Houlihan and R. Sekuler, *ibid.* **77**, 281 (1968).

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It is highly unlikely that my results were due to eye movements. Subjects fixated on a continuously present figure measuring 4 minutes by 2 minutes of visual arc and having a luminance of 4.32 millilamberts; head movements were restrained by a head and chin rest (Bausch & Lomb). Adaptation stimuli were only 10 seconds long. Under these conditions, the estimate of 5 minutes as the standard deviation ($\sigma$) of a fixating eye about its mean position is an upper bound. In Steinman's report, the $\sigma$ along a single average meridian for a fixation target larger than my own, for fixation periods 20 seconds longer than my own, for the most variable subject is only 3.8 minutes of visual arc (*1*).

I calculated the probability of joint stimulation by measuring the minimum distance from the target circumference to the nearest grating area (*2*), and by assuming that the position of the eye is normally distributed on any meridian. Suppose this assumption does not hold, and assume an extreme case—that all eye movements outside the calculated distribution fell on grating areas. Assume that a very unlikely 2.5 percent did so. Would this lead to a reduction in apparent contrast? Since one would assume, in the case of eye movements that stimulation by the grating would be intermittent, a direct comparison cannot be made; however, Gilinsky (*3*) reports that perception of a test grating is facilitated in inverse proportion to the duration of a prior presentation of an adaptation grating in the same orientation for durations of at least 250 msec or less. Thus, even if eye movements large enough to produce joint stimulation cannot be entirely ruled out, it would still be extremely unlikely that these would lead to a reduction in apparent contrast (*4*).

Sekuler and Armstrong's second explanation for my findings, "a simple spatial spread of the orientation-specific adaptation," is a very ambiguous explanation. Their contention that the effect is "simple" may mean that it is simply an instance of a broad class of masking effects in which one need not assume prior neural activity. The studies that they cite indicate that this is what they have in mind. But they contradict this when they propose a "spread of . . . adaptation." This implies prior neural activity in areas not directly stimulated. With the latter explanation I have little disagreement. I suggested that this prior neural activity was connected with modeling ("in back of"); others have suggested, for instance, that if the effect were also obtained under the control condition, this could be due to frequency coding (*5*). Neither case is "simple." With their former contention, I disagree. It is highly unlikely that the effect I obtained is due to the same mechanism as that causing the effects obtained in the studies they cite. Moreover, if it were, it would be even less "simple" (*6*).

The studies they cite (*7*, *8*) which are relevant (*9*) found backward masking for single rectangular stimuli at separations between target and mask greater than 26 minutes or 1 degree (or both). My study found forward masking for a disk containing a grating. In contrast to the other studies, target and mask were neither identical in form nor size. Moreover, the appropriate distance comparison is neither 26 minutes nor 1 degree but 1 degree 30 minutes. These differences are not simply procedural; what they imply is that one would not have expected an effect in my study on the basis of general masking effects, and therefore, the hypothesis of prior neural activity is reasonable.

In particular (i) Sekuler and Armstrong claim that it makes no difference for their arguments whether one measures forward or backward masking: "orientation effects in the two temporal orders [are] equivalent." It is not clear what "orientation effects" means in this context; in any case, forward and backward masking are certainly not equivalent. Especially when target and mask do not superimpose on the same retinal area, forward masking is generally very small compared to backward masking (*8*). (ii) Masking results for gratings cannot be predicted from the results for single stimuli. Gilinsky (*3*) found enhancement of target thresholds when preceded by gratings presented for short periods; the reverse is found for single stimuli. Gratings mask and are masked over a much more restricted angular range of orientations, given a fixed target orientation, than single rectangles (*10*). Hence, one would also expect that contours of a target grating would have to be much nearer masks, especially grating masks, in order for their visibility to be affected. (iii) In general, contour masking is negligible for adjacent stimuli unless they are the same form and the same size (*11*). Thus, Buchsbaum and Mayzner found that as target lines became shorter than successive flanking lines, target detection increased rapidly. Even with superimposed stimuli, Parlee (*7*) found a similar nonlinearity; when a mask which completely overlapped a target became longer than the target, detection improved. The grating portions of my target and mask were of the same frequency, but they were dissimilar lengths enclosed in dissimilar forms. (iv) The 25.8-minute separation between target and mask refers in my study, not to targets and masks on the same horizontal axis, but to a distance from target circumference to inner mask perimeter at a 33-degree angle. The distance from circumference to nearest full flank is 1 degree 30 minutes (*12*). Even if masking of targets were not negligible when the mask is dissimilar in form and size, it is probably negligible at that distance (*8*), especially if both target and mask are gratings.

Hence, previous results with masking would not have led me to predict an effect on the target for the conditions in my study. But just suppose, for the sake of speculation, that the effect were caused, in all three studies, by the same mechanism. What would it mean in this case to say that this is simple spatial spread? "Spread" is neither simple nor linear: it goes away when the stimuli differ in size or form. If there is "spread" in the case of identical stimuli, but little, if any, when the stimuli differ in size and shape, then the effect is, in fact, quite selective and sophisticated. Neural symbolic activity at least as complicated as that suggested by my hypothesis must be assumed.

Underlying Sekuler and Armstrong's comment is their objection to the use

of the idea of symbolic activity when there exist "simpler" explanations. But these explanations hold only if one restricts one's attention to special cases on an ad hoc basis. If the entire range of cases is considered, then it is clear that there will be no possibility of a unifying (simplifying) explanation of "spreads of effect" unless we begin to consider their functional meaning for perception; that is, their symbolic function.

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### References and Notes

1. R. M. Steinman, *J. Opt. Soc. Amer.* **55**, 1158 (1965); recalculated 1970 (personal communication).
2. There was an inadvertant deletion in the original report which stated that the 25.8 minutes was the measurement from circumference to grating.
3. A. Gilinsky, *Psychonom. Sci.* **8**, 395 (1967).
4. Use of $\sigma$ permits calculation of the probability of extreme excursions. It is also of interest to examine average saccade amplitudes. R. W. Ditchburn and J. A. Foley-Fisher [*Opt. Acta* **14**, 113 (1967)] summarized data for 30 subjects in 14 studies; they found a 4.5-minute median and 6.5-minute mean. Suppose finally, then, that there are one or two subjects with extreme eye movements; since all subjects in my study showed the effect, eye movements could not explain it.
5. H. Barlow, personal communication.
6. It should be noted, in addition, that the control that both I and Sekuler and Armstrong suggested would not test this former contention. For such a test, one would need grating fields of short duration as masks.
7. M. Parlee, *Vis. Res.* **9**, 199 (1969).
8. M. Alpern, *J. Opt. Soc. Amer.* **43**, 648 (1953).
9. Studies other than Alpern's (*8*) in the Brown and Mueller chapter [J. L. Brown and C. G. Mueller, in *Vision and Visual Perception*, C. H. Graham *et al.*, Eds. (Wiley, New York, 1965), pp. 208–250] cited by Sekuler and Armstrong are not directly relevant.
10. In order of decreasing angular range of effect: Parlee (*7*), single target and mask, 90 degr[illegible] R. Sekuler [*J. Exp. Psychol.* **70**, 401 (1965)], single target, grating mask, 60 degrees; F. W. Campbell and J. J. Kulikowski [*J. Physiol* **187**, 437 (1966)], grating target and mask, 20 degrees.
11. H. Werner, *Amer. J. Psychol.* **47**, 40 (1935); W. H. Buchsbaum and M. S. Mayzner, *Psychonom. Sci.* **15**, 111 (1969). Also see W. R. Uttal, *Percept. Psychophys.* **7**, 321 (1970); flanking rectangles do not mask a triangle, flanking triangles do.
12. Before this distance, if the target were translated until it overlapped the mask, the overlap would be less than 50 percent. Hence, either bars in the grating are mainly above the target, or they flank it but are much longer. When they flank it, they are also at a much greater separation.

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## Proteins in Excitable Membranes

The article by Nachmansohn (*1*) will probably do more to stimulate discussion than to provide definitive answers, as the closing sentence implies. Although it is pleasing to see reference to one's own work or to work in which one has shared (*2*), in this instance perhaps more is being imputed to the findings than is, as yet, warranted. It is true that the squid giant axon contains a high concentration of an enzyme which hydrolyzes and thereby detoxifies the powerful cholinesterase inhibitor, diisopropylphosphorofluoridate (DFP). The squid head ganglion is an even richer source of this enzyme, trivially called diisopropylphosphorofluoridase (*3*). However, the fact that (i) this enzyme is found predominantly in the axoplasm (*2*), (ii) the diisopropylphosphorofluoridase that appears to be associated with the axonal envelope may really have been due to residual axoplasm, and (iii) on ultracentrifugation the diisopropylphosphorofluoridase remains in the soluble fraction, raises the question of whether DFP applied to an intact squid axon at external concentrations which do not block conduction, for example, at less than $5 \times 10^{-3}M$, crosses the excitable membrane as DFP or as the hydrolysis product. Furthermore, DFP blocks conduction at about $5 \times 10^{-3}$ to $10^{-2}M$ in axons of squid, lobster, and spider crab and in the electroplax of the electric eel, although the approximate relative concentrations of diisopropylphosphorofluoridase in these four preparations are 100, 10, 1, and undetectable, respectively. Other organophosphates, even more potent cholinesterase inhibitors than DFP, are not detoxified, do penetrate into the squid axon in their inhibitory form, and block conduction *if at all* only at external (and now internal) concentrations of $10^{-3}M$ or higher (*4*, *5*).

Nachmansohn points out the difficulty of attempting to extrapolate from the concentrations of compounds in solution to their behavior in intact cells; one might even extend this to include their behavior in subcellular organelles. However, in the present instance there is some indication that the organophosphates have indeed reached one such "organelle" in a sense, namely, the postulated receptor (*6*). If this is so, it becomes increasingly difficult, but of course not impossible (*7*), to explain how a variety of cholinesterase inhibitors, some predominantly water-soluble, others more lipid-soluble, can reach the receptor but cannot reach the reputedly essential acetylcholinesterase, whereas acetylcholine is required to reach both.

It has been implied that the fact that "block of conduction is sometimes effected under conditions different from those expected from reactions in vitro" (*1*) is not an impediment to an essential role for acetylcholinesterase in conduction. Rather than a "sometimes" condition, it appears that almost all of the cholinesterase inhibitors which finally do block conduction do so between $10^{-3}$ and $10^{-2}M$, whether reversible or irreversible, penetrating or not penetrating, water-soluble or lipid-soluble, or detoxified or not. The effect of physostigmine (eserine) on the node of Ranvier of the frog sciatic nerve has been cited as an exception (*1*). It does not appear to be much of an exception; the pertinent words are these (*8*): "At . . . $10^{-3}M$ conduction was blocked within 25 sec. . . . At . . . $2 \times 10^{-4}M$, block . . . occurs, *if at all* only after 15–20 min. . . ." The italics are mine. Further, the legend under figure 3 of (*8*) implies that block may not always have occured even at $5 \times 10^{-4}M$. It should be noted that I refer only to block of action potential rather than partial reduction, prolongation, change of shape, and so on.

Finally, while it is true that "a successful dissociation of electrical and enzyme activity after exposure to organophosphates" (*1*) has not been accomplished, it seems premature to conclude that the failure to demonstrate such a dissociation of electrical and cholinesterase activities, especially for reasons of technical inadequacy, is proof that the two activities are directly associated. This is not to say that, in the second half of the 20th century, it will not be accepted a priori that bioelectric activity is controlled by macromolecules whose properties are expressed in terms of enzyme kinetics.

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### References and Notes

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3. F. C. G. Hoskin, *Biol. Bull.* **137**, 389 (1969).
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5. F. C. G. Hoskin, L. T. Kremzner, P. Rosenberg, *Biochem. Pharmacol.* **18**, 1727 (1969).
6. E. Bartels and D. Nachmansohn, *Arch. Biochem. Biophys.* **133**, 1 (1969); see also figure 2 of (*5*).
7. See, for example, evidence and speculation that regulatory sites on the acetylcholinesterase molecule may serve as receptor sites [J.-P. Changeux, T. R. Podleski, J.-C. Meunier, *J. Gen. Physiol.* **54**, No. 1, part 2 (supplement), 225 (1969)].
8. W.-D. Dettbarn, *Biochim. Biophys. Acta* **41**, 377 (1960).

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