a vertical transmission of an acquired disease susceptibility. A single subdiabetic dose of alloxan, administered to either a male or female rat before mating, has been associated with abnormal glucose tolerance in their untreated progeny (*10*). The degree of glucose intolerance was found to increase in successive (untreated) generations, leading to elevated fasting blood glucose levels in the seventh generation. However, our experimental results may be the first example of transmission of susceptibility to a disease in which the trait was acquired in the parent generation by an environmental manipulation rather than by a drug treatment. We know of no satisfactory explanation of this phenomenon.

NEIL J. SKOLNICK
SIGURD H. ACKERMAN
MYRON A. HOFER
HERBERT WEINER

Department of Psychiatry, Albert Einstein College of Medicine at Montefiore Hospital and Medical Center, New York 10467

References and Notes

1. R. Erdösová, V. Flandera, J. Krěček, P. Wiener, *Physiol. Bohemoslov.* **16**, 400 (1967).
2. S. H. Ackerman, M. A. Hofer, H. Weiner, *Psychosom. Med.* **37**, 180 (1975); *Gastroenterology* **75**, 649 (1978).
3. By RGE susceptibility we mean the probability that food deprivation and restraint will produce gastric erosions under standardized experimental conditions. Statistically, we compare the RGE susceptibility of groups of rats by comparing the incidence of erosions following restraint.
4. H. Leigh and M. Hoffer, *Psychosom. Med.* **35**, 497 (1973).
5. S. Levine, G. C. Holtmeyer, G. G. Karas, V. H. Denenberg, *Physiol. Behav.* **2**, 55 (1967).
6. V. H. Denenberg and A. E. Whimbey, *Science* **142**, 1192 (1963).
7. S. Levine, *ibid.* **156**, 258 (1967).
8. E. F. Gauron and V. N. Rowly, *Psychopharmacologia* **30**, 269 (1973).
9. J. L. Bakke, N. L. Lawrence, S. Robinson, J. Bennett, *Biol. Neonate.* **31**, 71 (1977).
10. G. Spergel, L. J. Levy, M. G. Goldner, *Metabolism* **20**, 401 (1971); G. Spergel, F. Kahn, M. G. Goldner, *ibid.* **24**, 1311 (1975).
11. Supported by research scientists development award KI MH-00077 to S.H.A., research scientist award KO5 MH-38632 to M.A.H., and by grant RO1-AM-18804 from the National Institute of Arthritis, Metabolism, and Digestive Diseases. We thank R. Shindledecker and M. Pyka for laboratory assistance. Work was conducted in partial fulfillment of requirements for the Ph.D. degree by N.J.S. We thank Dr. George Cicala, University of Delaware, for help as dissertation sponsor.

18 December 1979

Saccades Are Spatially, Not Retinocentrically, Coded

Abstract. *Most models of the saccadic eye movement system imply that saccades are programmed for a certain distance and direction. Electrical stimulation of the brain was used to move the eyes of monkeys just before saccades to visual targets. Despite the stimulation-induced perturbation, saccades brought gaze to the target locations. This compensation indicates that saccades are coded to direct the eyes to a certain position in the orbit (or in space).*

When a target appears in the peripheral visual field, the eyes may make a rapid eye movement, or saccade, to bring its image onto the fovea. Most models (*1*) of the saccadic system assume that the oculomotor system attempts to minimize retinal error, the location of the image of the target on the retina relative to the fovea. The retinal coordinates of the target, computed by the visual system, could be used more or less directly by the oculomotor system to program a saccade with a particular amplitude and direction which will reduce retinal error. The saccade is thought to be ballistic, or programmed in advance for a certain direction and amplitude, since the movement cannot be modified or cancelled by visual information occurring later than about 50 msec before saccade onset (*2*). The superior colliculus, which has both retinocentrically organized visual and saccade-related neurons, has been suggested as a possible site for this sensorymotor interaction (*3*).

A number of deficiencies of the retinocentric models have been noted (*4*). Saccades can be made to the source of a sound in the dark or to a remembered target location in the dark (*5*). Clearly, a retinal error signal is not necessary to produce a saccade. Hallett and Lightstone (*6*) found that if a target is illuminated briefly during a saccade, the eyes will complete the saccade, and then look to the location of the target. Since eye movement occurred after target presentation, the correct localization of the target in space could not be due to a retinal error signal alone. They suggested that targets for saccades can be localized by combining eye position information with retinal error, although it does not follow that this is the usual means of defining the target location. Finally, the hypothesis that the amplitude and direction of the saccade is predetermined has also been challenged. Zee *et al.* (*7*) reported that patients with abnormally slow saccades can interrupt saccades in midflight in response to a new visual stimulus.

Robinson (*4*) and Zee *et al.* (*7*) have developed a spatial model of saccade generation based on these findings. In this model (i) targets for saccades are not localized relative to the fovea (that is, by retinal error) but rather by combining eye position with retinal error to form a representation of the target in space (*8*); (ii) the command to the saccadic generating system drives the eyes to a certain position in the orbit (*9*) and not just a certain direction and amplitude; and (iii) saccades are not programmed in advance but are directed to a final position by continuous feedback of eye position information.

We have attempted to test the retinocentric and spatial models by examining the interaction of visually elicited saccades and saccades produced by electrical stimulation of the monkey superior colliculus. Brief stimulation of the deeper layers of this structure produces an apparently normal saccade of short latency with an amplitude and direction largely independent of starting eye position or stimulation variables (*10*). The retinocentric and spatial models predict different outcomes if electrical stimulation drives the eyes away from the fixation point immediately before a saccade to a target. If, in preparation for a visually elicited saccade, the signal to the saccadic generator is a command to move the eyes in a certain direction for a certain distance, this movement should still be executed without modification just after the stimulation-induced saccade. In this case, the gaze will miss the target location by a distance and direction nearly equal to the stimulation-induced saccade. If the command to the saccadic system is a signal to move the eyes to a certain position in the orbit (or in space), the stimulation-induced saccade should produce an automatic readjustment of the vector of the visually elicited saccade so as to direct the gaze to the target location.

Two monkeys (a *Macaca mulatta* and a *Macaca nemestrina*) were trained to look at a visual target for a water reward. During training and stimulation sessions, the monkey's head was immobilized by a lightweight, permanently implanted head holder. The target was a small (0.1°) light spot on a short-persistence, large-screen oscilloscope (*11*) or a green light-emitting diode. Horizontal and vertical eye position was measured with a sensitivity of at least 0.25° through the use of an implanted electromagnetic search coil (*12*). A computer (PDP-8I) controlled the position of the target spot, triggered the electrical stimulator, monitored eye position, delivered reinforcement when tracking criteria were met, and produced on-line graphic displays of data and stimulus conditions. A description of the training procedures and apparatus has been published (*13*). The monkeys were

0036-8075/80/0606-1163$00.50/0

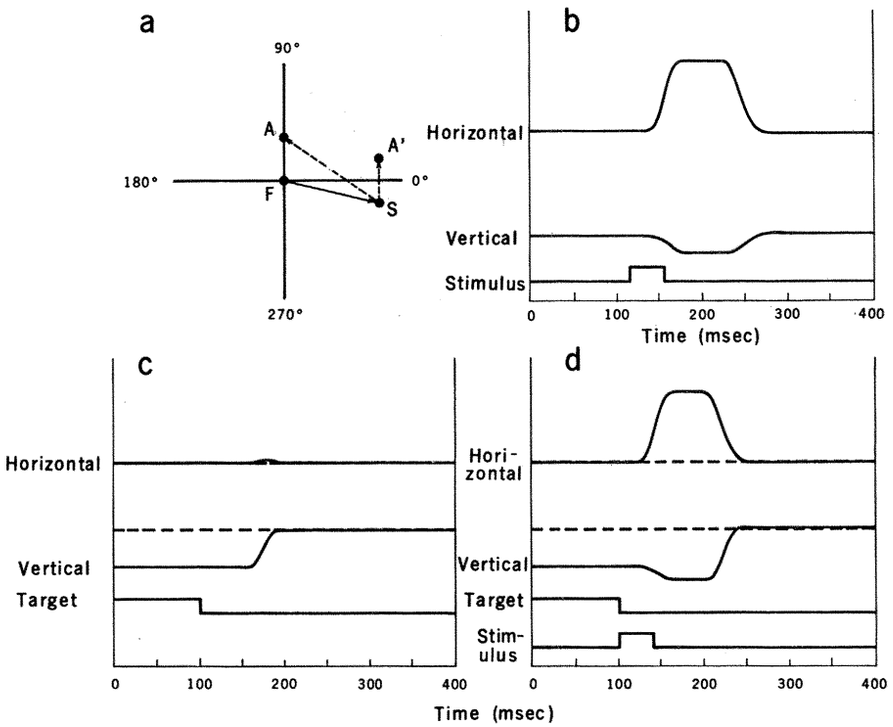
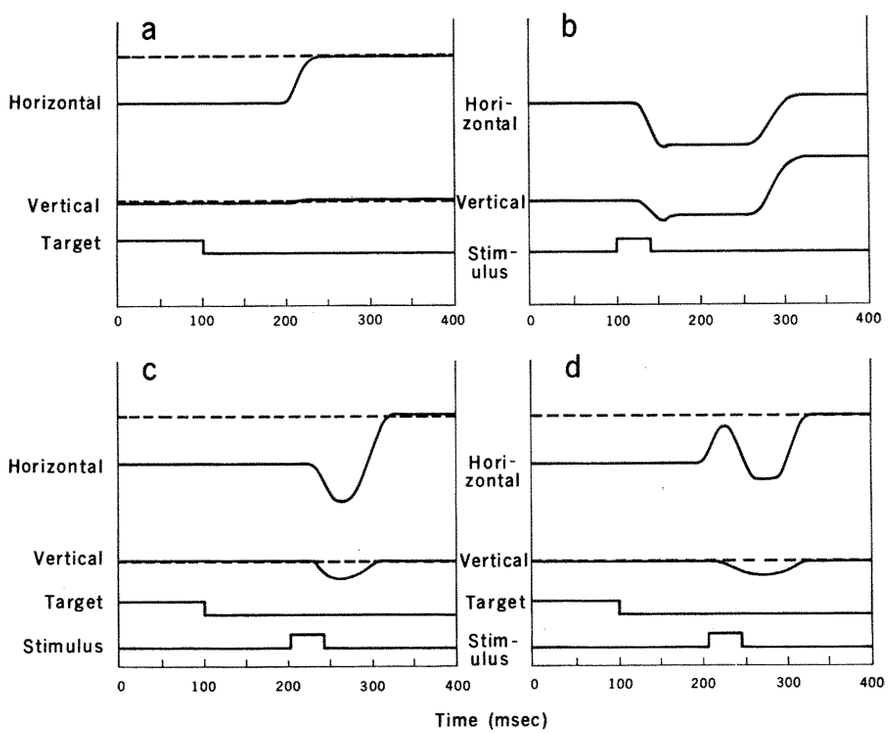


Fig. 1. The effect of a saccade induced by electrical stimulation upon a saccade to a visual target. (a) Orientations of the target and the saccades. While the monkey was fixating a target at point F, electrical stimulation of the left superior colliculus produced a saccade to point S. (b) A typical stimulation trial. Upward deflections of the horizontal trace represent rightward eye movements, and upward deflections of the vertical trace represent upward movements. Stimulation consisted of a 40-msec 50-μA pulse train. Since the trial required the monkey to maintain fixation of F to obtain a reward, a return saccade to F was made with a latency of about 60 msec. (c) A visually elicited saccade to a target flashed briefly (100 msec) at point A, 15° above point F. A saccade to A occurred with a latency of about 160 msec. The dashed lines represent the horizontal and vertical position of the visual target. (d) A trial in which electrical stimulation drove the eyes from F to S about 40 or 50 msec before the saccade to A would ordinarily have occurred. Less than 50 msec after the saccade to S, another saccade moved the gaze directly back to A. Since the target at A had been turned off before the electrical stimulation, there was no retinal error signal corresponding to this S and A saccade.



required to look at a center fixation target for a variable period (1 to 2 seconds) and then to make a saccade to fixate the target as it stepped to another location. Locations of the target step were randomly selected from a series specified by the experimenter. The superior colliculus was stimulated by a microelectrode hydraulically lowered through a stainless steel well. All stimulation sites yielded saccades with currents below 50 μA, although 50 μA was commonly used. A train of 200-μsec cathodal pulses was delivered at 500 Hz for 40 msec.

During each experimental session, a variety of trials was randomly intermixed. On some trials the monkey was required to make a saccade to a briefly presented (100-msec) target. The target was always turned off before the saccade started. On 20 to 50 percent of these trials, electrical stimulation was delivered after the target went off but before the saccade began. Other trials required fixation only (no saccade) with or without stimulation. In addition, electrical stimulation was occasionally delivered with no targets displayed. Trials were run either in dim light or in total darkness.

A saccade induced by electrical stimulation, a visually elicited saccade, and the interaction of stimulation and visually evoked saccades are shown in Fig. 1. The orientation of the visual target and the saccade vectors can be seen in Fig. 1a. Electrical stimulation of a point in the left superior colliculus during fixation of point F (Fig. 1, a and b) drives the eyes down and rightward to point S with a latency of 30 msec (Fig. 1b). Since continued fixation of F was required for reward, a saccade with a short latency re-

Fig. 2. The effect of stimulation-induced saccades that immediately precede or interrupt visually elicited saccades. (a) A visually elicited saccade to briefly flashed (100 msec) target 15° to the right of the fixation point. (b) Electrical stimulation of the right superior colliculus produced a saccade downward and to the left. (c) If electrical stimulation was delivered just before the time a visually elicited saccade would have occurred, the visually elicited saccade could follow or even interrupt the stimulation-evoked saccade. Even when the intersaccadic interval was 0, the second saccade brought the gaze accurately to the location of the target. (d) If electrical stimulation was applied just as the saccade to the target location began, the stimulation-induced saccade interrupted the visually elicited saccade. Nonetheless, the gaze was quickly brought to the location of the visual target. The adjustment of the saccades to bring the eyes to the appropriate target location could not be mediated by visual information; all saccades shown in Fig. 2 occurred in total darkness.

turned the gaze to F (Fig. 1b). A saccade to a visual target at location A (15° directly above F) is shown in Fig. 1c. If a saccade to S is induced by electrical stimulation just before the visually elicited saccade, a retinocentric model of the saccadic system would predict that the 15° upward saccade should still occur, causing a saccade from point S to A' (Fig. 1a). In the course of more than 10,000 trials at 29 stimulation sites, this result was never obtained. Instead, the stimulation-induced saccade was followed by a short-latency saccade from point S directly to location A (Fig. 1d).

Although there was often a period of 40 to 80 msec between the end of a stimulation-induced saccade and the beginning of the saccade to the location of the target, it was possible to time the stimulation so that the saccade to the target location immediately followed the stimulation-induced saccade. On other trials, the electrical stimulation interrupted the visually elicited saccade (Fig. 2). Except for the fixation and target spots, the room was in total darkness. For this series of trials, the visual target was 15° to the right of the initial fixation point. A visually elicited saccade to this target is seen in Fig. 2a. Electrical stimulation of a site in the right superior colliculus drives the eyes downward and to the left (Fig. 2b). Since fixation was not required during this stimulation trial, the eyes did not return to the original position.

Figure 2c shows a trial in which a saccade to the location of the visual target occurred immediately after a stimulation-induced saccade. Since the amplitude of the stimulation-induced saccade in Fig. 2c is smaller than that in Fig. 2b, the saccade to the visual target location may have interrupted the stimulation-induced saccade. Nonetheless, a saccade brought the gaze to the target location. Figure 2d shows a visually elicited saccade interrupted in midflight by a stimulation-induced saccade. Regardless of the point in space to which stimulation drove gaze, an accurate, short-latency saccade to the position of the target was made.

These results have implications for models of the saccadic system. Saccades to the actual target positions on stimulation trials (Figs. 1d and 2, c and d) could not have been directed by retinal error alone since all targets were turned off before any saccade. Since the occurrence of electrical stimulation on any trial was unpredictable, the compensation for the stimulation-induced saccade could not be determined in advance. Targets were not localized in space with respect to some visual frame of reference, since localization was about as accurate in the dark as in the light. It follows, then, that saccades directed to the positions of targets in space must have been localized by combining retinal error with an extraretinal eye position (*14*) signal. Since the compensation for eye position is precise even when visually elicited saccades are interrupted in midflight (*15*), the eye position signal must be derived from the accomplished rather than intended movement. That monkeys can localize targets accurately after saccades induced by stimulation of the superior colliculus indicates that the eye-position signal is derived from a point efferent from the colliculus.

Thus, our results are compatible with the spatial view of the saccadic system proposed by Hallett and Lightstone (*6*), Robinson (*4*), and Zee *et al.* (*7*). Saccades bring the eyes to a predetermined position in the orbit (or space) and do not drive the eyes a predetermined distance and direction.

LAWRENCE E. MAYS
Department of Physiological Optics, School of Optometry and *Neurosciences Program, University of Alabama in Birmingham, Birmingham 35294*
DAVID L. SPARKS
Department of Psychology and *Neurosciences Program, University of Alabama in Birmingham*

References and Notes

1. L. R. Young and L. Stark, *IEEE Trans. Hum. Factors Electron.* **4**, 38 (1963); D. A. Robinson, *Kybernetik* **14**, 71 (1973).
2. L. Wheeless, R. Boynton, G. Cohen, *J. Opt. Soc. Am.* **56**, 956 (1966).
3. P. H. Schiller and F. Koerner, *J. Neurophysiol.* **34**, 920 (1971); D. A. Robinson, *Vision Res.* **12**, 1795 (1972). A retinocentrically organized visual projection overlies a similarly arranged saccadic motor map in the superior colliculus. Retinal error could be directly translated into a saccadic eye movement if visually activated cells could drive the subjacent saccade-related cells. However, activation of visual cells is neither necessary nor sufficient to drive most underlying saccade-related cells or to produce a saccade [L. Mays and D. Sparks, *J. Neurophysiol.* **43**, 207 (1980)]. Thus, there can be no simple linkage between visual and motor layers of the superior colliculus.
4. D. A. Robinson, in *Basic Mechanisms of Ocular Motility and Their Clinical Implications*, P. Bach-y-Rita and G. Lernerstrand, Eds. (Pergamon, Oxford, 1975), p. 337.
5. J. R. Zahn, L. A. Abel, L. F. Dell'Osso, *Sens. Processes* **2**, 32 (1978); W. Becker and A. Fuchs, *Vision Res.* **9**, 1247 (1969); M. K. Komoda, L. Festinger, J. Sherry, *ibid.* **17**, 1231 (1977).
6. P. E. Hallett and A. D. Lightstone, *Vision Res.* **16**, 99 (1976); *ibid.*, p. 107.
7. D. S. Zee, L. M. Optican, J. D. Cook, D. A. Robinson, W. K. Engel, *Arch. Neurol.* **33**, 243 (1976).
8. S. Yasui and L. Young, [*Science* **190**, 906 (1975)] proposed a similar model for the pursuit eye movement system.
9. The question of whether a goal of a saccade is a position in the orbit or a point in space cannot be addressed by experiments in which the position of the head does not change.
10. D. A. Robinson, *Vision Res.* **12**, 1795 (1972).
11. We used an oscilloscope (Hewlett-Packard 1321A) with a special short persistence (P47) phosphor. This phosphor decays 90 percent in 83 nsec.
12. A. F. Fuchs and D. A. Robinson, *J. Appl. Physiol.* **21**, 1068 (1966).
13. D. L. Sparks and R. Holland, *Behav. Res. Methods Instrum.* **7**, 115 (1975).
14. Since the information about eye position does not depend upon visual information, it is of extraretinal origin. Zee's model (*7*) assumes that eye position is derived from an efference copy.
15. W. M. King, A. F. Fuchs, W. Becker, and G. Johanson [*Neurosci. Abstr.* **5**, 375 (1979)] and E. L. Keller [in *Control of Gaze by Brain Stem Neurons*, R. Baker and A. Berthoz, Eds. (Elsevier/North-Holland, Amsterdam, 1977), p. 327] reported similar data, which tend to confirm the spatial model. Saccades could be interrupted or truncated by stimulation of a region in the pons. When stimulation was terminated, a resumed or restarted saccade directed gaze to the desired position.
16. We thank S. Marcus and C. Horton for technical assistance and R. Sheetz for computer programs. Supported by NIH grants R01 EY01189, R01 EY02293, and P30 EY03039.

5 November 1979; revised 12 February 1980

Synthesis of the Contingent Negative Variation Brain Potential from Noncontingent Stimulus and Motor Elements

Abstract. *Slow shifts in brain potential (commonly called the contingent negative variation), obtained during a warned reaction-time task with a foreperiod of 1 second, were compared with waveforms synthesized by the addition of separately obtained potentials associated with individual (nonpaired) sensory stimuli and self-initiated motor movements. The synthesized waveforms match closely the actual contingent negative variation, suggesting that it is constituted largely of separate, noncontingent elements related to sensory and motor processes.*

The contingent negative variation (CNV) is a negative shift in brain potential that develops during the foreperiod between a warning stimulus (S1) and a subsequent imperative stimulus (S2) commanding a mental or motor response (*1*). It has usually been held to reflect expectation and preparation during the foreperiod, and as such has been considered to be a physiological index of mental activity. Recent findings suggest that the CNV may represent an admixture of two or more waves that are seen in combination when recorded at the traditional short foreperiod of 1 or 2 seconds. Some evidence for this may be adduced from variations in the appearance of the CNV brought about by changes in the task, motor response, or recording site (*2–4*). Additional evidence comes from situa-

0036-8075/80/0606-1165$00.50/0