and the oppositely sloping portions of the curves in each panel. Within these limits the color of the CAE is determined not by line orientation but by direction of curvature. So what is curvature? It is rate of change of slope or orientation of line. That feature, present all along the test curves, seems to govern their color. Lines that are concave up have a constantly increasing slope going from left to right in each panel. Concave down means constantly decreasing slope. The visual system is presumably responding, then, to the direction in which orientations are changing.

It is interesting that no color reversal occurs as fixation is moved from the center to the edge of the test panel. While the edge is fixated, the half of the fovea that still lies within the test panel is stimulated by strongly sloping lines, yet neither hue predominates in the CAE. Perhaps the factors of curvature and line orientation are opposing one another almost equally at this point, and it is only after the fovea moves entirely outside the test area, with fixation 1° or more away, that the curvature factor becomes so weak that color reversal can occur.

I regard the moving-lights experiment described by Stromeyer in paragraph 7 as something of a red herring (or should I say a green and magenta herring?) dragged across the trail of the CAE. Granted that the 20° eye movements made during inspection do control for the factor of the line orientation by equally exposing each point on the retina with the two colors, the relative time of effective exposure to curvature is very short. An outside estimate is that the fovea occupies a favorable position (that is, centered within 1.5° of the centers of the inspection patterns) during 15 percent of the inspection time. Add to that the possible smearing of the lines on the retina, the possibility that detectors for motion may generate competing responses, and the likelihood that the 85 percent ineffective exposure time may permit the CAE to decay as fast as it is built up, and the prediction must be that if any CAE is obtained under these conditions it will indeed be minimal. The MacKays and Stromeyer report zero CAE's. White and I (*6*), using different experimental conditions (with steady fixation and patterns moving all the way across a restricted aperture) have obtained small but reliable CAE's after long periods of inspection. Inasmuch as a null hypothesis can never be proved, we regard even slight amounts of CAE as evidence that curvature can be effective in these difficult experiments in which the line orientation factor is canceled out. But we rely more heavily on the evidence (see above) of experiments in which stronger CAE's are obtained.

Table 1. Hues of pattern-contingent aftereffects of color.

Direction of curvature	Slope of line: Positive	Slope of line: Negative
Concave up	Pink	Pink
Concave down	Green	Green

The most interesting experiments are reported in paragraphs 8 and 9. Stromeyer verifies my finding (*1*) that "the most vivid aftereffects are seen on test patterns having a stronger curvature" than those used for inspection. His procedure, however, is one in which straight lines are used to build up the effects. In some experiments he tests also with straight-line patterns inclined at various angles to one another. These experiments may be leading in the same direction as those of White and Riggs (*7*). We show that a CAE can be produced by inspection of either curves or angles and tested with either angles or curves, and also that the inspection of nearly straight curves or angles leads to larger CAE's when tested with sharp curves or with angles near 90° than when tested with the ones used for inspection. A reasonable interpretation would seem to be that there are cortical units that receive inputs from more than one set of line orientation units, and that lines at right angles to one another (and curves of radius 3° or less) are particularly effective stimuli for such units. Our tentative hypothesis is that the visual system has some units that respond selectively to direction of change of slope, whether this be an abrupt change as in angles or a continuous one as in curves. We do not hesitate to invoke such constructs in view of present reports that they exist as hypercomplex cells in the cortex of cat and monkey (*8*). We doubt that the Stromeyer hypothesis about the overlapping sensitivities of separate line orientation units over a wide range of orientations is applicable here, since widths up to about ± 15° are characteristic of line orientation channels (*9*), while orientation differences near 90° are required for arousing CAE's of optimal strength.

In summary, McCollough's experiments and many succeeding ones show that CAE's can be established on the basis of line orientation. However, certain other CAE's are based on spatial frequency, direction of motion, and curvature under conditions in which the line orientation hypothesis is not applicable. Admittedly, we cannot yet take the leap of dealing with the perception of little green apples and pink cheeks, but we do wish to take one step in that direction. We maintain, as a working hypothesis, that there are visual units specialized both for color and for the changes in line orientation that define angles and curves.

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Eye-Tracking Patterns in Schizophrenia

The report of saccadic interruptions during ocular pursuit in patients with schizophrenia by Holzman *et al.* (*1*) confirms and replicates a 1908 study by Diefendorf and Dodge (*2*) in which the authors graphically demonstrated similar saccades during ocular pursuit in patients with dementia praecox and compared them with individuals with mania, epilepsy, and dementia paralytica and normal controls. They used the beam of an "electric arc" reflected from the cornea onto a vertically sliding photographic plate (the rate of fall of which was ingeniously contrived by a hydrostatic device) to record results. Both reports are consistent with a number of other extraocular dysfunctions to be found in individuals with schizophrenia, including altered blink rate, glabellar reflex, gaze contact, stare, episodic lateral oscillation of eyes, increased periorbital tone, transient unexplained lateral deviation of eyes, and increased incidence of external strabismus. All of these extraocular disturbances are reported in the old literature concerning schizophrenia but have remained dormant during psychiatry's long flirtation with mythology. The data suggest a mesencephalic locus for the pathology of this disorder, a conjecture consonant with current concepts of disturbed central amine function in schizophrenia (*3*).

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Holzman *et al.* (*1*) contend that schizophrenic patients show patterns of eye-tracking (smooth pursuit) that differ from normals, thereby implicating a primary ocular motor system defect in schizophrenics. We are concerned about major problems in their study with regard to the eye movement recording technique, the selection of control and subject populations, and the interpretation of results.

Only a sketchy account of the electrooculographic recording method is presented in the report, but Holzman kindly provided us with methodological details (*2*). There are many pitfalls in accurate eye movement recording, of which the authors seemingly were unaware. Their instrumentation and methodology were standard and suitable for electronystagmographic studies in a clinical neurootology laboratory, but are inappropriate for quantitative recording of eye movements. The absence of vertical electrodes, essential for detection of blink artifact, was unfortunate. Whereas horizontal electrodes might detect complete eye lid closure during a blink, there are many incomplete blinks without full closure of the lid. These partial blinks are indistinguishable from actual eye movements when monitored with horizontal electrodes and can only be recognized with vertical electrodes. Thus, blink artifact had to be a problem in this study.

Another serious methodological omission was the absence of head restraints. There is a compelling urge to move the head during slow tracking tasks. The simple instruction to keep the head still, even monitored with careful observation by the experimenter, is inadequate for quantitative recording of eye movement. A small head movement in the direction of the pendulum could cancel the eye position and appear to produce a zero eye velocity.

We duplicated the instrumentation of Holzman *et al.* by using the standard Beckman components described, with both the position and the velocity channel switches in the "slow" setting. The bandwidth of the "slow" position channel is 5.5 hertz, which greatly distorts the response to fast eye movements. The "slow" differentiator mode has a bandwidth of 4 hertz and response time of 75 msec, which also precluded a true record of velocity (*3*). Thus, Holzman *et al.* were analyzing distorted and inaccurate eye movement analogs. The authors defined a "positive saccade" as a fast eye movement exceeding the maximum velocity (31.4° per second) of the target by 33⅓ percent (41.9° per second). With the restricted bandwidth recording system employed in their study, the true velocity of eye movements, which they interpreted as just greater than 41.9° per second, was in fact much higher. We compared the velocities derived from such a restricted recording system with those from d-c–coupled electrooculography with a position channel bandwidth of 100 hertz and a differentiator response time of 4 msec. We determined that saccades of less than 2° in amplitude would not meet the authors' own criteria for the identification of "positive saccades." To record peak velocities of small saccades (less than 5°), the bandwidth of this system should be 100 hertz and the response time of the differentiator less than 10 msec (*4*). By merely switching to the "fast" modes, without any system modifications, the authors could have used the existing bandwidth of 25 hertz and significantly improved the technical quality of their analogs.

Faithful analogs are necessary to eliminate artifact and to detect any small corrective saccades that may occur when a normal subject tracks a slowly moving target (½ hertz). The bandwidth deficiency prevented proper differentiation between real eye movement and artifact, and thus confused the data. For this reason it is impossible to evaluate the reported increase in "positive saccades" greater than 2°.

The major conclusions were primarily based on a newly defined ocular motor phenomenon present in the distorted velocity analog: "evlocity arrest," a time when the eyes had no velocity relative to the head as determined by the return of velocity analog to the baseline. Obligate velocity arrests must occur at the end of the pendulum swing, which gives 2 arrests per cycle. The authors stated that normals make 4.5 velocity arrests (2 are expected, leaving 2.5 unexpected arrests) and 0.5 saccade per cycle. Similar values were given in their figure 2 for schizophrenics. This is impossible. People not only do not do this, they cannot. Any real velocity arrest occurring during tracking would cause the eyes to fall behind the target, necessitating a corrective saccade. Therefore, a true velocity arrest could not be independent from a saccade as implied by the authors. The independence of the two phenomena ("velocity arrests" and "positive saccades"), which is essential to their conclusions, remains dubious. We have not observed frequent velocity arrests during tracking in normal subjects and must conclude that those described by Holzman *et al.* in their control population are primarily artifacts. Head movement, as previously mentioned, might be interpreted as a velocity arrest, as could blink artifact. Since a partial blink can cause the velocity tracing to cross the baseline twice, their occurrence every few seconds could be responsible for the abnormally high number of "velocity arrests."

Criticism must be made of the selection of patients who were taking a variety of drugs. Drugs—including barbiturates, minor tranquilizers, and phenothiazines—alter the ability of subjects to pursue targets, causing "saccadic" or "cogwheel" pursuit. The fact that the authors claimed in a separate study that no alterations occurred after withdrawal of phenothiazines, raises questions as to the actual ocular motor function that was being monitored. No other information regarding drug intake by either subjects or controls was given. Drug-induced saccades during slow tracking tasks may be less than 2° in amplitude. These movements would be ignored by the authors and not counted as "positive saccades." This is the only reasonable explanation for the observation that drugs did not alter the tracking performances.

In the control group, two of the four subjects with abnormal patterns were later found to have spontaneous nystagmus. The fact that such an obvious sign as nystagmus was detected only after data analysis indicates that the authors did not clinically examine their controls or schizophrenics for eye movement disturbances. We wonder how many of the schizophrenics had similar problems. While one might justify, on a purely statistical basis, the division of the whole population into those with and without schizophrenia and also the elimination of screening of both patients and controls, the inclusion of two "normals" with nystagmus could only confuse the issue. A nystagmus oscillation of 3 hertz would introduce 6 to 12 velocity arrests per cycle of pendulum swing which would be totally unrelated to tracking ability. Screening all subjects for unrelated eye movement abnormalities would result in more meaningful data. Any such abnormality should be cause for exclusion from the study.

In summary, we believe that Holzman *et al.* have not documented an eye-tracking abnormality in schizophrenics.

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References and Notes

1. P. S. Holzman, L. R. Proctor, D. W. Hughes, *Science* **181**, 179 (1973).
2. Standard Beckman components were utilized for a-c–coupled electrooculography with a time-constant of 3 seconds. Both the nystagmus (position) and velocity couplers were in the "slow" mode. The filter switches on the power amplifiers were in the No. 3 position. The velocity couplers were calibrated in the manner advised in the Beckman instruction manual. Target position analogs were not written out on the paper. Vertical electrodes were not used to detect blink artifacts. Heads were not restrained.
3. D. A. Robinson [*J. Physiol.* (*Lond.*) **174**, 245 (1964)] has criticized electrooculographic eye movement recording systems employing bandwidths as high as 85 hertz used to derive accurate quantitative information.
4. For a discussion of frequency characteristics of saccadic eye movements see B. L. Zuber, J. L. Semmlow, L. Stark, *Biophys. J.* **8**, 1288 (1968).

17 August 1973

We are grateful to Stevens (*1*) for calling our attention to Diefendorf and Dodge's 1908 paper and for providing another clinical dimension to our report. We have avoided formulating hypotheses about the specific significance of the eye-tracking dysfunction until we could investigate the phenomenon further.

Troost *et al.* (*2*) call attention to several ambiguities in our brief report. We reported that schizophrenic patients and a significant number of their first-degree relatives showed deviant patterns of smooth pursuit eye movements (*3*). These deviations are easily seen qualitatively from inspection of the eye position records. A quantitative index of these records is provided in a count of the number of times the eyes stopped their pursuit of the target when they should have been moving if tracking accurately. Although Troost *et al.* stated that we counted obligate velocity arrests as part of our score, we did not do so. Even if we had included obligate velocity arrests, this would be a constant number added to the score of all subjects and would not have changed the results.

The number of positive saccades is, as Troost *et al.* assert, an arbitrary measure. The score represents the number of times the eye moves at a speed at least one-third greater than the maximum velocity of the target. We were not counting, nor did we wish to count, every instance of positive saccades, but only those above a certain arbitrary limit. Our purpose was to show that such positive saccades could come under voluntary control, in contrast to the velocity arrests which are apparently involuntary. Troost *et al.* are thus quite correct in stating that we do not score certain fine eye movements.

In our pilot work we compared records obtained by using the fast and the slow recorder modes. Attempts to analyze such movements in the fast mode were prohibitively contaminated with signal noise. Our settings were thus chosen to exclude a significant amount of signal noise which would have obscured the data. Yet our settings are not as insensitive to eye movements as these critics allege. Although Troost *et al.* state that the 50 percent bandwidth on the slow mode is 5.5 hertz in the direct channel, it is actually 10 hertz on our equipment. In our differentiator channel the 50 percent bandwidth is 6 hertz and not 4 hertz as Troost *et al.* assert. Our figures agree with theirs for the fast mode.

The use of electronystagmographic techniques requires that a certain amount of signal noise be excluded from the position and velocity tracings. Obviously, this means excluding very brief eyeball accelerations. Nevertheless, registration of eyeball velocity has found wide application in clinical vestibular testing since its usefulness was demonstrated by Henriksson (*4*). Gross accelerations can be easily detected in the velocity recording (*4*) and provide the basis for a new method for scoring dysrhythmic nystagmus (*5*).

We concede that our scoring system distinguishes in a somewhat arbitrary way between high frequency and lower frequency eye movements. Further, our scoring system is biased to score more velocity arrests than positive saccades. Velocity arrests of more than 40 msec are scored; these correspond to 1° or less of target motion for a 2.5-second period. Positive saccades of 1°, however, occur in 2.8 msec and therefore are not scored. This is one explanation for the appearance of more velocity arrests than positive saccades, a finding that puzzles Troost *et al.* A further explanation is that subjects may make corrective saccades which are not scored if these saccades are less than our criterion amplitude.

The assertion of Troost *et al.* that they have "not observed frequent velocity arrests during tracking in normal subjects" accords with our findings. That is just the point: our schizophrenic subjects do show them in a frequency significantly greater than that found in normals. But velocity arrests are seen in about 3 percent of normals as documented by Benitez (*6*), Von-Noorden *et al.* (*7*), and Corvera *et al.* (*8*).

Use of a head restraint would have added a dimension of control, and we are currently employing a restraint. But vertical leads are not necessary for accurate eye movement recording since the presence of blink artifacts of sufficient magnitude to affect our scoring system can be ascertained without them.

The selection of schizophrenic subjects who were taking phenothiazines presents a problem for all research involving schizophrenic patients. Many drugs impair smooth pursuit movements, but these effects are dose-related (*9*). To our knowledge, no studies of the effects of phenothiazines on smooth pursuit movements have been published. It is conceivable that long-term treatment with phenothiazines, as is given to schizophrenic patients, may improve rather than impair pursuit movements. We are currently studying this problem in an animal model. But several nonschizophrenic subjects who were taking phenothiazine medication did not show the eye-tracking dysfunction; the relatives of our schizophrenic subjects were not taking these drugs, yet many of them showed the deviant eye-tracking patterns. We thus cannot accept the allegations that the effects we observed were drug-induced.

In our normal group, two of four subjects with abnormal patterns had a gaze nystagmus. Troost *et al.* assert that this indicates "that the authors did not clinically examine their controls or schizophrenics for eye movement disturbances." This is an incorrect conclusion on their part. All of our subjects were examined clinically, and our scoring was done independently of the knowledge of that examination and of the diagnostic status of the patients. The eye-tracking test was part of a larger series of tests which included vestibular examinations. None of our other subjects showed gaze nystagmus. To have excluded these two normal controls from data analysis would not be legitimate, since the purpose of examining a large number of normals was to get some estimation of the expected prevalence of deviant tracking patterns in the nonpatient population.

Since Troost *et al.* did not attempt to replicate our study, their response is exclusively a methodological note. They are apparently used to working with near absolute values of eye position and eye velocity and were therefore understandably irked by our measurement. They would impose a precision of measurement which would not be appropriate to our task; they are not concerned with the reproducibility or the stability of our data.

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1 February 1974

Meetings

Moscow Symposium on Radiation Chemistry of Aqueous Systems

The symposium on radiation chemistry of aqueous systems held in Moscow, 10 to 14 December 1973, was sponsored by the Soviet Academy of Sciences and chaired by Professor A. K. Pikaev of the Institute of Physical Chemistry of the Academy of Sciences. The symposium was attended by 20 radiation chemists from the United States, Great Britain, Yugoslavia, Poland, Norway, Denmark, Sweden, Hungary, West Germany, and East Germany, in addition to about 150 radiation chemists from the Soviet Union. The 55 papers that were presented in nine sessions included 17 papers that were given by the foreign participants. The sessions were devoted to discussions of general problems of radiation chemistry, effects observed in frozen systems, and the radiation chemistry of aqueous solutions of inorganic and organic compounds and of biologically important systems. The presentations were given in either Russian or English. Abstracts of the talks were available in both languages. The presentations themselves were not translated but the discussions were. Slides were presented with English captions. After the symposium visits to the laboratories of the Institutes of Physical Chemistry, Organic Chemistry, and Electrochemistry were arranged for the foreign participants.

The symposium was opened by Academician V. I. Spitzyn with general remarks about the applicability of information gained in radiation chemical studies to many areas of chemical and biological research. Similar emphasis on fundamental research aspects was very much evident throughout the remaining presentations which were devoted entirely to discussions of results of current researches on the mechanistic details of various radiation induced processes. There were no general reviews and very little time was devoted to instrumental methods, although there was a fair amount of informal discussion on those methods. In their individual talks participants emphasized optical pulse radiolysis studies carried out from picosecond through microsecond times, the examination of intermediate radicals by electron spin resonance (ESR) spectroscopy, and determination of the overall chemistry by product analysis. The Soviets have active pulse radiolysis programs in three laboratories in Moscow (the Institutes of Physical Chemistry and Electrochemistry and the Karpov Institute). Stabilized radicals are studied by ESR in many laboratories throughout the Soviet Union. The overall chemistry received somewhat more attention at this symposium than in other recent radiation chemical conferences that I have attended, probably because there is a considerable emphasis on this approach within the Soviet laboratories.

The emphasis of the sessions on frozen systems was on ESR and optical studies. A number of researches that involved examination of products produced in alkaline ices at 77°K were also presented. Work of this type is being carried out at the Institute of Physical Chemistry and at Moscow State University. Attention was paid to the abnormally high local concentrations of radicals produced in the spurs of radiation chemical processes where there is considerable activity in the application of ESR spin-echo techniques at the Institute of Chemical Kinetics and Combustion in Novosibirsk. Scavenging of the initial radicals produced in various ices (mostly at

Science

Eye-Tracking Patterns in Schizophrenia

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