a comparable elevation in brain serotonin may result from relatively mild handling stress in mice. Since these results indicate that total brain serotonin content may be confounded with levels of adaptation or arousal, future pharmacological investigations which utilize neurohumour levels as dependent variables should incorporate adequate control procedures to separate possible treatment differences from placebo effects.

The behavioural findings observed in this investigation indicate that psilocin produced consistent decrements in open field exploration parameters and avoidance conditioning running, but did not appreciably influence avoidance acquisition. The data suggest that open field exploration was enhanced following psilocin withdrawal, and that latency decrements persisted. In addition, psilocin treatment was associated with a dose-dependent decrement in spontaneous locomotor activity on the initial day of treatment, with rapid tolerance development by day 2.

The comparison of the biochemical and behavioural findings is noteworthy in several respects. For example, the significant decrease in day 1 activity wheel performance of both psilocin-treated groups was not associated with a corresponding variation in endogenous whole brain serotonin. Thus, psilocin significantly altered behavioural performance without altering serotonin-levels. Conversely, the locomotor performance of mice administered reserpine did not differ from placebo mice on the first day of testing, although brain serotonin-levels were depleted 29 per cent. Thus, a dramatic change in brain serotonin-level was not associated with a concurrent alteration in behaviour. These results indicate a lack of correlated response between brain serotonin content and certain behavioural criteria.

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EVOKED POTENTIALS CORRELATED WITH A VISUAL ANOMALY

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An incoherent succession of randomly patterned optical images ('dynamic visual noise') offers a useful stimulus to probe the visual system and reveal any bias present in perceptual mechanisms[1–3]. The present investigation concerns the physiological correlates of a curious visual anomaly discovered some years ago when using a stimulus of this kind[4]. If each frame of such a visual noise sequence is followed by a short bright flash of light in the same eye, illuminating the same area of the visual field, then with a certain critical time interval between frame and flash, and at frame repetition rates of the order of 5–20 per sec, the random 'Brownian movement' normally perceived in the visual noise field is disrupted. In its place (or in addition), the screen appears to be filled with elongated objects resembling maggots, which seem to wriggle to and fro at random and link up to form long chains or chain-mesh patterns. The critical lag between the onset of each noise frame and the blank flash varies with frame duration, repetition frequency and intensity[5], but is typically of the order of 18–25 msec.

This is not the only visual anomaly that may be observed with such interlaced sequences of stimuli. With a somewhat longer time interval between frame and flash, Dr. J. P. Wilson[6] has reported that spurious impressions of contour motion are produced with stationary stimulus figures. A stationary black disk on a stroboscopically-illuminated white ground, for example, may appear to be continually expanding or contracting according to the time interval between the illuminating flashes and the blank flashes[6]. (Explanations in terms of eye movements are ruled out, for with a more complex field such as a black annulus one may see simultaneously a contraction of the inner edge and expansion of the outer.)

On both scores it seemed worth while to ask whether the occipital evoked potentials, as recorded from scalp electrodes, showed any corresponding anomalies at the inter-stimulus intervals giving rise to these phenomena. The preliminary investigation to be reported here indicates that they do, and appears to give evidence of a specific sensitivity, at the critical phase, to the presence of spatial patterning in the visual stimulus.

In place of the cine projector used in the earlier investigations[4,5] a high-powered electronic stroboscope was used to illuminate an area of 'static visual noise'—an enlarged photograph of sand paper, mounted on a turntable, and viewed through a circular (non-concentric) aperture. The turntable could be rotated asynchronously, so as to present a substantially unrelated sequence of visual noise samples when required[2]. A second stroboscope illuminated a plain white disk of the same size as the exposed area of visual noise, the two being optically superimposed by means of a half-silvered mirror. These fields subtended an angle of about 10° at the observer's eye. The repetition period and relative timing of the two stroboscopes were adjustable in steps of one msec.

Scalp electrodes were positioned as shown in Fig. 1, with the reference electrode 2 cm above the inion and inter-electrode distances of 5 cm, so that longitudinal (A) and transverse (B) components of the electric field could be simultaneously recorded and compared. Conventional electronic computing equipment (a Mnemotron '*CAT*'), triggered synchronously with the visual noise exposure, enabled the two evoked components A and B to be averaged on separate channels; a typical run lasted for 1 min and represented the sum of 500–1,000 responses.

To summarize the results (to be presented more fully elsewhere), the critical phase of our double-flash stimulation was indeed found to be accompanied by anomalies in the evoked potential. A sample run with a repetition period of 63 msec is shown in Fig. 1, where the number on the left of each pair of tracings represents the lag in msec between noise and blank flashes, and that on the right shows the order in which runs were made (subject A. F.). Since the perceptual anomalies in question are visible only at repetition rates above 5 or 6 per sec, their corresponding evoked potentials have a large continuous and oscillatory component, and the waveforms shown represent one complete cycle of a repetitive train. Slow changes in

form occur even under steady conditions, but in view of the order in which runs were made the general trend emerges clearly in Fig. 1. With a cycle period of 63 msec, the most striking change may be seen to occur in the transverse (B) component at values of lag between 13 and 23 msec, where the amplitude grows markedly and the phase also changes more rapidly than elsewhere. Striking also is the change in relationship between the longitudinal and transverse components, reflecting as it does a shift from virtual synchrony into near antiphase, and the appearance of a marked third harmonic in the longitudinal component. The psychophysically observed delay range for the 'maggot' effect in this case was 15–24 msec, with an optimum at 18 m.sec.

In order to disentangle the factors that might be responsible for the electrophysiological anomaly, a series of further experiments were performed. First, the rotating noise field was brought to rest, so that successive noise frames were identical. Subjectively, the effect at the critical phase was to replace the 'maggots' by a (much fainter) impression of a pulsating lace-work structure in the static noise pattern. The corresponding evoked potentials, however, showed remarkably little difference from those of Fig. 1, apart from a suggestion of an increased lag in the longitudinal component at the critical interval of 18 m.sec.

This raised the question whether the anomalies in the evoked potentials were related at all to spatial patterning in the stimulus, or whether only the temporal rhythm of the light entering the eye was responsible. Accordingly, the responses with the visual 'noise' pattern were compared with those obtained with a uniform grey surface of comparable overall reflectance, under two conditions: (1) blank flash following each frame at the critical interval for the 'maggot' effect; (2) blank flash preceding each frame by the same interval.

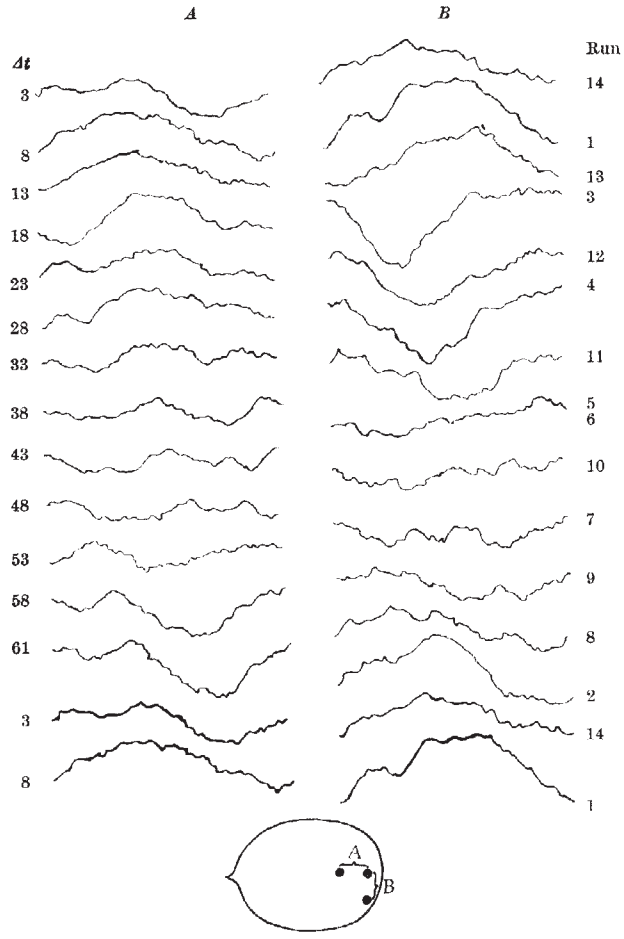

Fig. 1. Longitudinal (A) and transverse (B) occipital evoked potentials as a function of interval Δt between noise frame and blank flash. Intervals are shown on left; run numbers on right. Electrode placements were as indicated, with bipolar connexions. Period of stimulus cycle 63 msec

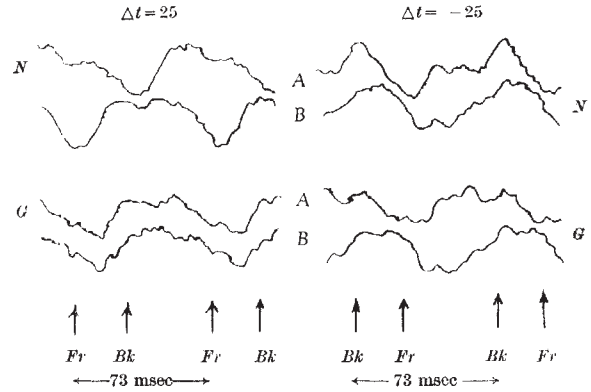

Fig. 2. Effects of stimulus patterning on evoked potentials for $\Delta t = +25$ ('critical interval') and -25 msec. N, With noise field; G, with uniform grey field. Note that almost two complete cycles are shown, with a cycle period of 73 msec

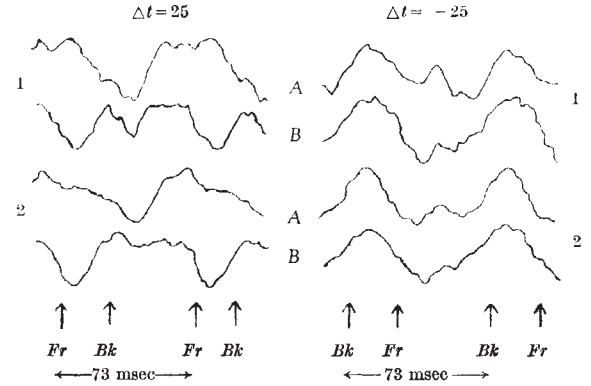

Fig. 3. Control runs showing effects of intensity change on evoked potentials. Intensity for run (1) was greater by 0·5 log unit than for run (2)

The results with a repetition period of 73 msec, for which the critical interval ($\triangle t$) was 25 msec, are shown in Fig. 2, where the longitudinal (A) and transverse (B) response components in each case are presented one above the other. It will be seen that under the critical condition for the 'maggot' effect ($\triangle t = 25$) the change from noise (N) to uniform grey (G) made a marked difference to the phase relationship between the longitudinal and transverse components; but that when the blank flash (Bk) preceded the frame (Fr) by the same time interval ($\triangle t = -25$), the same change from noise to grey had a much smaller effect.

Though care had been taken to match the overall subjective brightnesses of noise and grey fields, the possibility that a brightness difference was responsible for the contrast in evoked potentials was checked by performing two runs with the same noise frame, but at frame brightness levels differing by approximately half a log unit. As will be seen from Fig. 3, the effects of this (subjectively large) change in brightness were both smaller than, and quite different from, those produced by the change from noise to patternless stimulation at subjectively constant brightness. It seems fair, therefore, to conclude that at the critical phase the evoked potentials show an enhanced response to the introduction of patterning as such into the visual field, and that this response takes the form of a change in the relative phase of longitudinal and transverse evoked potentials. Further work is needed, however, with more subjects, to test the generality of this conclusion.

It seems clear from these observations that stimulation of the visual system in specific uneven temporal rhythms calls out anomalous neural responses which are reflected

physiologically in a change of spatial and temporal activity patterns at the cortical level, and perceptually in the imposition of spurious structure on an otherwise incoherent visual field. Unlike the well-known 'stroboscopic patterns'[7] evoked by regularly repetitive flashes, which are most noticeable against a blank background, these perceptual effects are seen most clearly when optical contours are present in at least the first of each pair of stimuli. In this respect they resemble the familiar after-effect of visual image motion, which may be interpreted as due to the activity of a sub-system responsible for signalling motion-as-such, the output of which is perceptually 'attributed' to whatever structure is present in the visual field. In the absence of a structured stimulus the effect has only the residual entoptic irregularities on which to manifest itself.

The suggestion here would be that the spurious contours imposed on incoherent stimuli at the critical phase may result from the excitation of a sub-system the elements of which are normally set to detect local contours in the retinal image[8], but at the critical phase (as the result of a kind of resonant response to the rhythm of the stimulus) become abnormally excitable. A similar temporal rhythm-sensitivity in the motion-detecting sub-system could account for Wilson's effect[6].

The results shown in Figs. 2 and 3, though far from conclusive, seem to be in line with this suggestion, since they indicate that a major change in the sensitivity of cortical activity to temporal rhythm in the stimulus occurs when a spatially patterned stimulus is substituted for a patternless one of similar overall luminance. The fact that no similar effects are observed when the frame and flash are presented to different eyes would suggest that the mechanisms involved are fairly near the periphery of the visual system.

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ACTIVE TRANSPORT OF GLUCOSE BY SUSPENSIONS OF ISOLATED RAT INTESTINAL EPITHELIAL CELLS

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THIS article presents data on the active transport of glucose into the isolated, intact, functioning rat intestinal epithelial cell. Much of our knowledge of the mechanism of amino-acid and sugar transport in the intestine has been derived from observations with various types of *in vivo* and *in vitro* intestinal preparations[1,2]. The use of suspensions of isolated intestinal epithelial cells prepared by the method developed by Harrer, Stern and Reilly[3] affords an advantage over other preparations in that they are uncontaminated by mesenchymal elements and are free of the normal homoeostatic mechanisms that operate when the cells are organized into a tissue. Huang[4] recently reported on the energy-dependent uptake of L-tyrosine and 3-*O*-methyl glucose by intestinal epithelial cell suspensions from the rabbit. Our method appeared to produce much purer cell preparations than did that used by Huang, as his cells were obtained after chopping up the entire intestine, incubating with lysozyme, filtering through gauze and washing. It is likely that his cell preparations were contaminated with other types of cells and debris. With the method we used, only cells from the lumen of the intestine were obtained, and careful microscopic examination revealed that the basement membrane of the intestine was intact.

Suspensions of rat intestinal epithelial cells were prepared as described by Harrer, Stern and Reilly[3] and Stern and Reilly[5] with the following modifications: citrate was used to dissociate the epithelial cells from the mucosa. The composition of the medium was: 0·096 M sodium chloride, 0·008 M potassium phosphate, 0·027 M sodium citrate, 0·0056 M dibasic sodium phosphate, 0·0015 M potassium chloride—final *p*H 7·2. 15,000 U. of penicillin and streptomycin were added per 100 ml. of all solutions used. The lumen of the small intestine was filled with this solution and incubated for 11 min at 33° C. All subsequent operations were carried out at 0°–4° C unless otherwise indicated. This solution was removed following the incubation and either a solution composed of 0·137 M sodium chloride, 0·0115 M potassium phosphate, 0·008 M dibasic sodium phosphate, 0·0022 M potassium chloride—final *p*H 7·2, or 0·2 M sucrose, 0·05 M sodium potassium phosphate, *p*H 7·4 (sodium ion = 0·076 M potassium ion = 0·019 M), was washed through the lumen of the intestine. The cells were released from the mucosa by gently pressing the filled intestine with one's fingers. The cells were suspended in 40 ml. of either the inorganic salt solution or the sucrose phosphate solution and centrifuged at 500*g* for 10 min. 0·4–0·8 ml. of packed cells were suspended in 7·7 ml. of one or other of the foregoing media. To this suspension was added 30 μg of crystalline DNase (Nutritional Biochemical Corp.), 0·07 ml. of 0·25 M D-mannitol-1-^{14}C, 0·02 ml. of 0·4 M $MgSO_4$ to a final volume of 7·82 ml. D-Mannitol-1-^{14}C was used to measure extracellular space since it is not absorbed by the intestine[6]. DNase was added to reduce the viscosity of the reaction mixture. Bare nuclei, and some lysed cells and mucus contributed to the relatively high viscosity. The initial glucose content of the cells, as determined on a portion of the reaction mixture, was negligible. The reaction mixture was transferred to a Warburg flask for the incubation. When glucose uptake was measured in the balanced salt solution, 0·11 ml. of 0·0762 M glucose was added from the side arm. When 4,6-dinitro-*o*-cresol was present, the reaction mixture was pre-incubated for 5 min under argon before the glucose was introduced. The cell suspension was then incubated for 15 min with continuous gassing with oxygen or argon and while shaking slowly. When sucrose phosphate was used as the suspending medium, no glucose was added. After incubation, the suspension was transferred to a McNaught tube (A. S. Aloe Co., St. Louis, Missouri), dispersed by forcing through a 14 gauge needle, centrifuged at 270*g* for 20 min, re-dispersed and centrifuged at 1,100*g* for 15 min. The supernatant was removed and the volume of the cell pellet read with an accuracy

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