edge or line type contours produced by luminance or color differences. Responses in area 18 showed several other parallels to perception, such as the relation between the responses to a figure and to its parts and the dramatic effect of small elements added to the figure.

Gregory (*4*) formulated an antithesis between physiological and cognitive explanations of illusory contour effects. According to his cognitive approach, the contours are perceived because an illusory object is "postulated" as a perceptual hypothesis to account for the sensory data. The explanation suggested by the present experiment is physiological, but it differs from the one stated in Gregory's antithesis (and criticized by him) that "feature detector cells of the striate cortex are activated by the disk sectors [scilicet of the Kanizsa triangle] . . . to give the appearance of continuous lines, though only their ends are given by stimulation" (*4*, p. 51). Our results do not support this idea. With stimulus configurations like those of B or G in Fig. 2, cells in area 17 did not respond, some of them not even when the gap was narrowed so that the ends of the bar entered the response field. The responses in area 18 on the other hand cannot be interpreted simply as suboptimal excitation due to partial stimulation of the response field, since they can be evoked by stimuli well outside that field and are affected by small changes in configuration that are negligible in terms of luminous flux. Also the responses to stimuli with lines perpendicular to the cell's preferred orientation reveal an unexpected new receptive field property. The way widely separated picture elements contribute to a response resembles the function of logical gates. The important elements in our stimuli seem to be corners on opposite sides of the response field (Fig. 2, B and G) and line ends arranged in a row (Fig. 2, I and J). Line ends and corners are in fact emphasized in certain signals of area 17 (*8*), and a number of such signals might converge on neurons of area 18. Corners and line ends play a role in the formation of contours because these picture elements are frequently produced by interposition of objects, that is, when an object partially occludes others. Thus, several such elements aligned in a row are likely to mark an object boundary.

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2. Illusory contours are known also as "Scheinkanten," as "quasi perceptive," "anomalous," "subjective," and "cognitive" contours, or "contours without gradients." See (*3*) for a discussion of the terminology.
3. For a review see G. Kanizsa, *Organization in Vision. Essays on Gestalt Perception* (Praeger, New York, 1979).
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5. The range of orientations was obtained from the orientation tuning curve by determining the points where the regression lines fitted to the flanks of the curve crossed the level of spontaneous activity. The length of response field, *L*, was similarly determined from a response curve obtained by scanning the field with the appropriate edge of a bar, taking as *L* the distance between the bars in the two limiting positions. The correctness of this determination was confirmed by the fact that the stimuli in Fig. 2, C and D, singly did not produce a response; because of the choice of the gap width (1.3°) they were outside the response field ($L = 0.9°$).
6. Most of the cells assigned to area 18 were recorded in the posterior bank of the lunate sulcus. The cortical area was judged also from physiological criteria such as the presence of the typical activity of layer IVc in area 17 [G. F. Poggio, R. W. Doty, Jr., W. H. Talbot, *J. Neurophysiol.* **40**, 1369 (1977)] and the topography of receptive fields; it has been confirmed histologically for part of the data. A few cells recorded near the 17-18 border were not counted.
7. The orientation tuning curves obtained with the illusory contour stimulus in area 17 typically showed a single peak corresponding to the orientation of the grating lines.
8. D. H. Hubel and T. N. Wiesel, *J. Physiol. (London)* **195**, 215 (1968).
9. Part A and D are reproduced from figures 4.2 and 12.12 in (*3*); parts B and C are figures 1, C and D, in A. T. Smith and R. Over [*Percept. Psychophys.* **20**, 305 (1976)].
10. To simplify the figure, stimuli have been reproduced in reversed contrast; the parts shown in black were actually lighter than the background (about 2.5 versus 1 foot lambert). To avoid confusion, the text has been made consistent with the figure.

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Treatment of a 12-Hour Shift of Sleep Schedule with Benzodiazepines

Abstract. *Normal sleepers underwent sleep recordings and daytime tests of sleep tendency, performance, and mood while being shifted 180° in their sleep-wake schedule. After two baseline 24-hour periods, subjects postponed sleep until noon. For the next three 24-hour periods, they were in bed from 1200 to 2000 and received triazolam, flurazepam, or placebo at bedtime in parallel groups. Placebo subjects showed significant sleep loss after the shift. Active medication reversed this sleep loss. Despite good sleep, flurazepam subjects appeared most impaired of the three groups on objective assessments of waking function; triazolam subjects were least impaired.*

Many people are familiar with the insomnia, disturbed mood, and reduced daytime alertness that often accompany rapid travel across time zones ("jet-lag") or sudden changes in sleep schedule (for example, shift work). Laboratory studies have documented impairments of sleep and performance that accompany such alterations in sleep-wake schedule (*1*). In particular, Weitzman *et al.* (*2*) shifted the bedtime of normal subjects 12 hours by having them stay awake for a single night. Sleep at the shifted time in bed was disturbed, and function during the nocturnal waking hours was judged impaired. The results were interpreted as the effect of attempting to sleep and to be awake in opposition to the underlying circadian rhythm. The same group carried out a related study (*3*). After a sudden 12-hour phase shift of scheduled time in bed, subjects were given a widely prescribed hypnotic (30 mg of flurazepam) at bedtime. Sleep time and continuity significantly improved; the quality of subsequent wakefulness, however, was not improved. This result was interpreted as evidence that the underlying circadian rhythm of sleep and wakefulness is more important in facilitating daytime alertness than the total amount of sleep one has had recently.

Flurazepam has a long-lived active metabolite (*4*). More recent studies have shown that bedtime ingestion of flurazepam is followed by daytime sedation and performance decrements even in the absence of a shift in the sleep-wake schedule (*5, 6*). Thus, the impaired wakefulness following treated sleep may have been a carry-over of the sedative effect of the drug rather than a circadian effect. Elsewhere, we have suggested that if a hypnotic drug were free of carry-over into the next day, daytime functioning should improve as a result of better sleep (*6*).

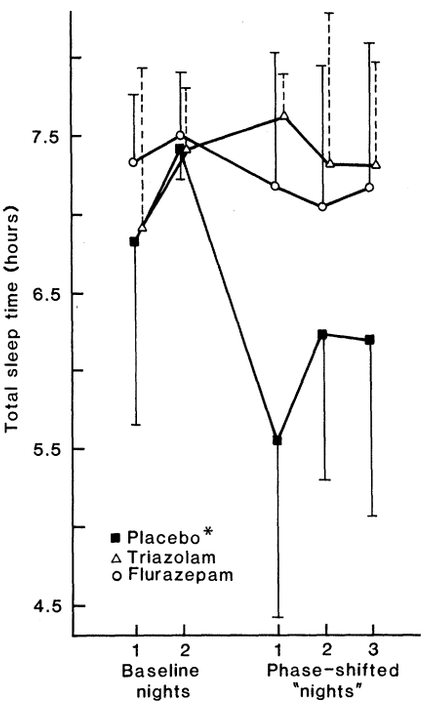
The difficulties in assessing daytime function with any of the myriad available performance tests have been evaluated in recent reviews (*7*) and will not be considered here. The multiple sleep latency test (MSLT) (*8*) may be useful as a primary measure of improved daytime functioning in hypnotic efficacy studies because (i) it is a direct measure of an electroencephalographic (EEG) state associated with reduced alertness and (ii) it seems relatively unaffected by practice, learning, or fluctuating motivation. This

technique has been validated in a wide variety of experimental and medical conditions that affect alertness (*9*) and, in particular, has been used to assess drug carry-over (*6, 10*).

In this study, two sleep laboratories using identical protocols compared long-acting flurazepam (*4*), short-acting triazolam (*11*), and placebo as a bedtime treatment after a 12-hour shift of sleep-wake schedule.

Each sleep laboratory used newspaper advertisements to recruit 12 young, healthy volunteers who reported regular sleep habits. They received a screening polysomnogram and MSLT, and only subjects who slept well (over 430 minutes of sleep out of 480 in bed and nocturnal sleep latency under 30 minutes) and who were not sleepy during the day (MSLT mean > 10 minutes) were eligible. Subjects were randomly assigned to parallel groups to receive double-blind 0.5 mg of triazolam (six males and two females, 21 to 30 years old), 30 mg of flurazepam (seven males and one female, 20 to 30 years), or placebo (six males and two females, 21 to 33 years).

Subjects slept and were tested for two consecutive nights and days on a baseline sleep schedule (0000 to 0800), with a 12-hour transition period (sleeping 0000 to 0200, awake 0200 to 1200) followed by three consecutive 24-hour periods of sleep recordings and testing during phase-reversed sleep (1200 to 2000). Electrodes were attached to allow monitoring and standard sleep scoring (*12*) of monopolar EEG (central and occipital), electrooculogram (EOG) from right and left outer canthi, and chin electromyogram (EMG). After a preliminary adaptation night in the lab, the 24-hour testing routine went as follows. Placebos were taken 30 minutes before each baseline 8-hour sleep period, and triazolam, flurazepam, or placebo before the phase-reversed sleep periods. A profile of mood states (POMS) (*13*) was administered just before bedtime and upon awakening from each sleep period. Daytime (waking) measures included the MSLT, Stanford sleepiness scale (SSS) (*14*) immediately before each sleep laten-



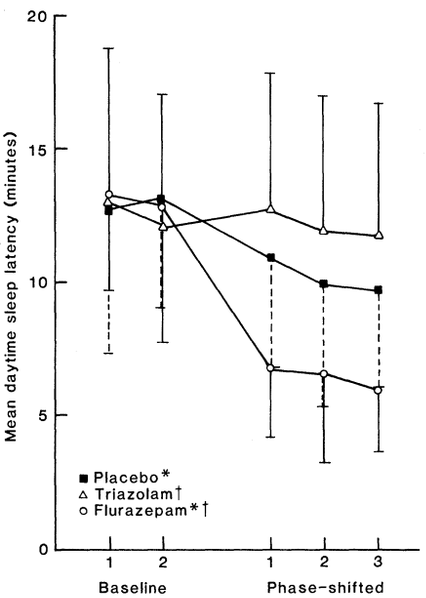


Fig. 1 (left). Mean total sleep time (and standard deviation). Time spent in bed was 8 hours for all sleep periods. *Significant within-group change from baseline sleep ($P < 0.05$). Fig. 2 (right). Daily mean of seven sleep latency tests. *Significant within-group change from baseline sleep tendency ($P < 0.05$). †Significant between-group difference ($P < 0.05$).

Table 1. Nocturnal sleep and performance before and after a 12-hour shift of sleep period. Data are given as means and standard deviations and were evaluated by analysis of variance. REM, rapid eye movements.

Measure	Flurazepam		Triazolam		Placebo	
	Baseline	Phase-shifted	Baseline	Phase-shifted	Baseline	Phase-shifted
			Nocturnal sleep			
Latency to stage 1 (minutes)	11.0 (9.9)	6.4 (6.7)	17.2 (16.1)	4.2 (2.0)*	13.1 (12.9)	5.5 (2.2)
Wake interrupting sleep (minutes)	17.6 (15.2)	25.0 (26.5)	24.1 (15.8)	17.1 (15.8)†	15.6 (14.3)	44.7 (21.1)
Wake at end of night (minutes)	4.8 (11.4)	20.0 (40.5)	0.5 (0.8)	12.5 (31.1)	15.0 (25.0)	68.4 (48.3)*†
Number of wakenings	10.1 (11.0)	8.8 (10.9)	12.5 (10.6)	8.4 (8.8)*	7.4 (6.2)	10.6 (8.3)
Stage 1 (minutes)	54.9 (17.5)	41.3 (16.7)*	47.5 (24.6)	41.7 (27.3)	48.3 (21.7)	54.6 (27.1)
Stage 2 (minutes)	221.6 (43.8)	244.0 (34.9)	227.8 (21.9)	248.9 (16.0)*	203.9 (23.2)	155.3 (38.2)*†
Stages 3 + 4 (minutes)	60.3 (20.8)	58.9 (23.0)	57.4 (40.9)	59.1 (46.4)	83.7 (39.7)	75.5 (29.0)
Stage REM (minutes)	107.8 (16.5)	83.2 (29.2)*	96.5 (19.5)	94.2 (20.2)	91.0 (12.3)	73.2 (20.1)
			Performance tests			
Vigilance visual tracking error (log of arbitrary distance units)	3.37 (0.21)	3.53 (0.27)*	3.39 (0.38)	3.39 (0.39)	3.46 (0.24)	3.52 (0.23)
Vigilance reaction time (arbitrary units)	256 (26)	297 (54)	245 (49)	256 (64)	278 (65)	312 (85)*
Digit symbol substitution (number attempted)	201 (33)	186 (25)*	202 (45)	211 (45)*	176 (28)	179 (29)
Symbol copying (number)	435 (102)	438 (73)	442 (130)	466 (122)	405 (77)	438 (79)
Card sorting (seconds)	126 (26)	121 (18)	112 (23)	105 (17)	123 (21)	117 (25)

*Statistically significant within-group change from baseline value, $P < 0.05$. †Significantly different from both other groups, $P < 0.05$.

cy test, and performance batteries at 1000, 1400, and 2200 during baseline days and at 2200, 0200, and 1000 on phase-reversed "days." The MSLT began 2 hours after lights on in each condition and occurred every 2 hours until bedtime (*15*). A sleep latency test was scored for minutes from lights out to the first 30-second epoch during which a subject was not awake; a score of 20 was assigned tests with no sleep.

Each performance battery included a 40-minute computer-generated visual-tracking and reaction-time test of vigilance, a card-sorting task, and two paper-and-pencil tests (*16*). Repeated measures of analysis of variance were performed on all variates to examine differences over time across drug conditions. Post hoc contrasts (*17*) revealed the direction of significant main effects.

Baseline total sleep time did not differ significantly between groups. Figure 1 illustrates the drastic disruption of phase-reversed sleep in subjects treated only with placebo. (Other sleep variables are summarized in Table 1.) Sleep in subjects treated with triazolam or flurazepam remained near baseline levels.

The mean MSLT scores across baseline days were stable (mean difference from day 1 to day 2 was 1.7 ± 0.8 minutes). During the phase-reversed waking periods, the flurazepam subjects, despite efficient sleep, evidenced sleepiness during their waking periods similar to that seen in pathological states such as narcolepsy (*18*). Placebo subjects showed a significant but less severe change from baseline, while the triazolam group did not show a significant increase in sleep tendency (Fig. 2).

As with alertness measured by the MSLT, performance deteriorated during the phase-reversed waking period for the groups receiving flurazepam (vigilance visual tracking and digit-symbol substitution were significantly impaired) and placebo (impaired vigilance reaction time), while triazolam subjects maintained or improved baseline performance on all tests (Table 1).

In contrast to the differences between treatment groups on objective measures of daytime function, subjective measures were the same for all three groups during the phase-shifted period. All groups showed an overall increase in subjective sleepiness and mood disturbance. The small number of subjects in each group and the large variance in these measures may have contributed to the lack of between-group differences. In addition, subjective impairment correlates poorly with objective measurements in subjects receiving benzodiazepines (*19*).

The behavior of the placebo group confirms that sleep and subsequent alertness are significantly impaired for at least 3 days after a sudden 12-hour shift of the sleep-wake schedule. Ingestion at bedtime of medications (except placebo) before the shifted sleep periods reversed the sleep loss. By facilitating good sleep, the short-half-life hypnotic was able to preserve objectively measured waking function despite the 12-hour shift in bedtime, whereas subjects receiving the long-half-life hypnotic demonstrated decrements in alertness and performance that exceeded those of the placebo-treated group. These findings point to the limitations of considering only the sleeping phase of the 24-hour cycle when evaluating hypnotic medications. In terms of daytime (waking) alertness and performance, triazolam is preferable to flurazepam in the treatment of transient insomnia associated with a sudden sleep schedule change such as occurs in transmeridian travel and shift-work rotation. The data from this study suggest that a short-acting benzodiazepine may completely reverse the insomnia and daytime effects in such instances.

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15. Subjects lay in bed in a dark, quiet room and were asked to have their eyes closed and to try to fall asleep while EEG and EOG were recorded (four channels). Tests were ended after 2 minutes of consecutive nonwakefulness or after 20 mintues otherwise. Thus, significant sleep did not accrue during these tests.
16. In the 40-minute computer-generated vigilance task, subjects sat in a dark, quiet room tracking a randomly moving circle with cross hairs controlled by a joystick, while error was continuously measured (vigilance visual tracking); they pressed a button whenever a small light flashed on the screen (vigilance reaction time). The card-sorting task is described in (*6*). The paper-and-pencil tests were a digit-symbol substitution test adapted from the Wechsler Adult Intelligence Scale for repeated 5-minute testing and a related symbol-copying test, in which similar symbols were simply copied; the number of items attempted on each test was scored.
17. The Ryan-Einot-Gabriel-Welsch multiple F test ($\alpha = 0.05$) [T. A. Ryan, *Psychol. Bull.* **56**, 26 (1959)] was used for between- and within-groups comparison of means. The three groups had similar age and weight.
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