however, because it would be competing against a contralateral pathway with the added advantage of more patterned stimulation.

A knowledge of the mechanisms underlying the visual field deficit of the less experienced eye may help us understand the basis of a similar deficit seen in certain amblyopic human patients, in whom responsiveness to stimuli in the nasal visual field is reduced relative to responsiveness to stimuli in the temporal visual field (*13*).

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5. Although the person who held the animal knew the experimental condition of the animal being tested, the person who scored the response did not. Further, our results are sufficiently unexpected that it is unlikely that experimenter bias contributed to them.
6. In order to more carefully determine the boundaries of the visual field of the 1-hour eye, we retested the AMD 8/1's, presenting novel stimuli just to either side of the fixation object. The animals approached the novel stimulus whenever it appeared in the temporal field, but they approached the fixation object whenever the novel stimulus appeared in the nasal field. We conclude that the visual field of the 1-hour eye extends to the midline and no farther.
7. The visual field of the 1-hour eye resembles the visual fields of a BD cat in two respects. (i) The fields of BD cats are restricted to the temporal hemifield. (ii) The BD cats show a relative reduction in responsiveness to targets presented at 90° (*4*). However, BD cats respond at reduced levels throughout their visual fields, whereas the AMD 8/1's responded normally throughout the temporal hemifield except at 90°.
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Rebound Insomnia

Kales *et al.* (*1*) recently presented evidence for rebound insomnia, a "worsening of sleep" occurring subsequent to the withdrawal of three benzodiazepine hypnotics—flunitrazepam, nitrazepam, and triazolam. The report by Kales *et al.* raised an important question: Is rebound insomnia a consideration that would preclude the use of these three benzodiazepines, and possibly others, in the symptomatic relief of insomnia?

In addition to the six sleep laboratory studies cited by Kales *et al.* (*2-4*), at least nine additional sleep laboratory studies of flunitrazepam, nitrazepam, and triazolam in both normal and insomniac populations have included a baseline, drug, and withdrawal period (*5-7*). In none of this additional literature are the three objective parameters used by Kales *et al.* to define rebound insomnia—sleep latency, number of awakenings, or wakefulness after sleep onset—significantly elevated above the baseline during drug withdrawal. These studies, which used drug administration periods ranging from 2 (*5*) to 21 (*6*) days, raise the question of whether rebound insomnia may be considered a generalized phenomenon occurring after short- and intermediate- as well as long-term periods. Furthermore, even within a single study, the generalizability of rebound insomnia is at issue. Bixler *et al.* (*3*) found that withdrawal of 1 mg of flunitrazepam produced a significant increase in sleep latency and wakefulness after sleep onset, but withdrawal of a 2-mg dose did not produce these changes. Also, within a single study, sleep parameters do not consistently demonstrate exacerbation of the insomnia during drug withdrawal. For example, Roth *et al.* (*4*) showed a significant increase above the baseline during the withdrawal period in the percentage of total time spent awake but not in sleep latency, number of awakenings, or minutes of wakefulness occurring during the sleep period.

Additionally, the mechanism of rebound insomnia must be reconsidered. Kales *et al.* attributed rebound insomnia to a "lag in the production and replacement of endogenous benzodiazepine-like compounds" (*1*, p. 1040), which is a consequence of the short action of flunitrazepam, nitrazepam, and triazolam. There are, however, major differences in the half-lives of these three compounds. Triazolam has a half-life of 4 to 5 hours (*8*), whereas nitrazepam has a half-life of about 30 hours (*9*). Other short-acting benzodiazapines—for example, temazepam, which has a half-life of 8 to 10 hours (*10*)—also do not cause drug-withdrawal insomnia (*11*).

The report by Kales *et al* has drawn our attention to a potentially important clinical phenomenon which has direct implications for the physician who prescribes drugs for the symptomatic relief of insomnia. More complete data are needed, however, before either the generalizability or specificity of rebound insomnia can be determined. Issues that must be considered include the type of insomniacs who exhibit rebound insomnia, the severity of the insomnia before the drug was prescribed, the specificity of drug-withdrawal insomnia to different drug classes, the relationship between rebound insomnia and drug half-lives, and the critical duration of drug administration necessary to produce rebound insomnia upon withdrawal.

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We are pleased that Hartse *et al.* have noted the clinically significant potential of our findings of rebound insomnia following withdrawal of certain benzodiazepine drugs. They also raise a number of points that need clarification. They are incorrect when they imply that rebound insomnia has not consistently occurred following the withdrawal of specific benzodiazepine drugs. The studies in their references 5 to 7 and 11 were not included in our paper for one or more of the following reasons: (i) the data were based on normal subjects rather than insomniacs (*1-3*); (ii) publication was in abstract form without sufficient data for accurate analysis and comment (*4-6*); (iii) there were methodological shortcomings, such as the use of nonconsecutive laboratory nights, which may introduce readaptation effects (*2, 7*); and (iv) the length of the drug administration, withdrawal periods, or both, was too brief to provide conclusive data (*1, 8-10*). In spite of such factors, however, two of these studies showed rebound insomnia in the form of statistically significant increases in sleep difficulty following withdrawal (*3, 10*), and three presented data that suggested the same finding (*4, 6, 7*). Two other published studies (*11, 12*), which also demonstrated rebound insomnia, rebound anxiety, or both, were not included in our report (*13*) for similar reasons.

Much of the data we reviewed in our report (*13*) and in a subsequent, more extensive publication (*14*), were from other sleep laboratories and were presented by the investigators as mean values for the total withdrawal condition rather than on an individual-night basis. Thus, we were limited in most cases to using a conservative criterion for rebound insomnia—a significant increase in one or more measures of sleep difficulty when these values were averaged for the total withdrawal period. Despite this stringent criterion, rebound insomnia consistently followed drug withdrawal in all studies of triazolam and nitrazepam and in one of the three studies of flunitrazepam (*13, 14*). For rebound insomnia to be present, it need only occur on any one of the individual withdrawal nights. In our two flunitrazepam studies in which data for individual nights were available, rebound insomnia occurred on the third withdrawal night (*14, 15*).

Nitrazepam and flunitrazepam should be considered as intermediate-acting benzodiazepines (*14*). In addition to rebound insomnia occurring in our short-term studies with flunitrazepam (*14, 15*), rebound insomnia was also clearly demonstrated in two recent studies evaluating the long-term effects of flunitrazepam (*16, 17*).

Hartse *et al.* also state that rebound insomnia does not occur with temazepam, a short-acting drug. The data, however, show an approximate 50 percent increase in total wake time during the total withdrawal period (*6*). This large increase would be even more marked if presented on a night-by-night basis. When one considers the intersubject variability in factors such as drug metabolism and the night-to-night sleep of insomniacs, as well as the small number of subjects studied in the sleep laboratory, the consistency of rebound insomnia following the withdrawal of certain benzodiazepine drugs is striking.

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