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## Growing evidence that some aspects of SCN function differ in nocturnal and diurnal rodents

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THE PRIMARY CLOCK MECHANISM controlling most of the circadian patterns in mammals resides in the suprachiasmatic nucleus (SCN). It appears that the feedback loops that control the ~24-h period of circadian rhythms are the same in diurnal and nocturnal species (6), and yet the timing of daily peaks and nadirs of many circadian rhythms (e.g., activity, sleep, body temperature, corticosteroid release) are completely out of phase. Early studies examining the metabolic activity of the SCN (e.g., 9), as well as behavioral responses to light pulses (e.g., 5), suggested that this circadian mechanism differed very little between nocturnal and diurnal species. As a result, we expected to find the source of diurnality in the interpretation of the SCN signal, rather than in the function of the SCN itself. More recent data, however, suggest that differences may indeed exist in the function of diurnal and nocturnal SCNs. For example, *c-Fos* activation after light pulses is the same in all nocturnal rodents studied, whereas it differs from and among diurnal species (see review, Ref. 10). Similar results are obtained when firing rates of cells in response to light within and around the SCN are examined. Such data are consistent with a hypothesis that evolution of diurnality has occurred multiple times in mammals and may involve changes within the SCN in some species.

The paper by Novak and Albers (8) in this issue of the *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology* poses an interesting hypothesis regarding possible differences in the response of diurnal and nocturnal species to nonphotic signals. They predict that the phase-shifting effects of GABA in the SCN will differ between nocturnal and diurnal species. They note that nocturnal animals are most sensitive to phase-shifting effects of nonphotic signals during subjective day when the signals typically arouse them from sleep. Numerous studies have demonstrated that arousal is necessary and sufficient for most nonphotic signals to have their effect on these species (7). Interestingly, similar studies with diurnal ground squirrels and degus have found that nonphotic stimuli are also most effective during subjective day and are not at all correlated with levels of activity or arousal (1, 4). GABA appears to mediate the effects of nonphotic stimuli on the circadian rhythms of nocturnal mammals (2, 3), but will it act similarly or differently in diurnal species?

Novak and Albers' careful examination of the effects of muscimol on phase shifts of free-running, diurnal grass rats (*Arvicanthus niloticus*) produced dramatic results. This diurnal species produces large phase delays when injected during subjective day with muscimol, whereas hamsters exhibit robust phase advances at the same time of day. During subjective evening, muscimol produces small delays in hamsters, but had

no significant effect in the grass rats. They also demonstrated that tetrodotoxin did not block the effects of muscimol but did diminish the effect of light pulses in the grass rats. These latter data are consistent with the findings in hamsters and suggest that muscimol acts directly on the pacemaker cells in the SCN or through non-sodium-dependent action potentials.

These data are the first to demonstrate a significant difference in a fundamental characteristic of the circadian clock mechanism between diurnal and nocturnal species. It is interesting that both nocturnal and diurnal species are sensitive to the phase-shifting effects of GABA<sub>A</sub> receptor stimulation during subjective day, but the response is in the opposite direction. Interestingly, nonphotic signals produce phase advances in both the tested nocturnal and diurnal species during subjective day, leading one to wonder whether GABA<sub>A</sub> receptor stimulation is relevant to nonphotic signaling in diurnal species. Because the effects of nonphotic cues have not been tested in grass rats, we do not know if grass rats will show phase advances during subjective day, as do ground squirrels and degus, or phase delays consistent with their response to muscimol. Thus it will be very interesting to see the outcome of further research examining the role of GABA<sub>A</sub> receptors in SCN function and whether those actions will differ or be similar between nocturnal and diurnal species. We may find that the role of GABA<sub>A</sub> receptor stimulation varies among diurnal species, just as we have found with the *c-Fos* response to light. Thus it is imperative that a more diverse group of nocturnal and diurnal species be examined to determine the generalizability of these and any results related to SCN function. More diversity of species in testing is needed, even among nocturnal species, because the seeming similarity in function, to date, may be due to the relatively close relationship among the nocturnal species that have been studied.

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