

Testosterone Suppresses Circadian Responsiveness to Social Cues in the Diurnal Rodent *Octodon degus*

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Abstract The diurnal, social rodent *Octodon degus* displays a robust sex difference in the ability to use social cues to facilitate reentrainment following a phase advance of the light cycle. Adult females housed with a female social cue donor reentrained 25% to 40% faster than did females reentraining alone. However, reentrainment rates of males were unaffected by exposure to female social cues during reentrainment. The authors hypothesized that males were less sensitive to the reentrainment-enhancing effects of social cues and that their higher threshold to the stimuli could be overcome if the social cues were either increased in strength or salience. Housing a male with two females significantly shortened the time to reentrain following a 9-h phase advance ($p = 0.002$). Housing with a sister had no effect on reentrainment. Therefore, male *degus* are able to respond to social cues but require the stimulus to be stronger than that for females. The effect of testosterone was tested by comparing reentrainment rates of castrated males before and after testosterone replacement both with and without a female social cue donor. Castrated males responded to a single female social cue donor, reentraining 35% faster than when housed alone ($p = 0.006$), whereas the time to reentrainment of intact males and males with testosterone capsule implants did not differ. Intact females were also implanted with testosterone and phase shifted with and without donors. Testosterone treatment eliminated the increase in reentrainment rates in the presence of social cues. The authors conclude that the rate of recovery from odor-enhanced phase shifts is modulated by activational effects of testosterone in male *degus*. Testosterone is also effective in suppressing social cue responsiveness in females, suggesting that testosterone's effects on responsiveness are not sexually dimorphic. This hormonal effect likely occurs by altering sensory system functions or CNS response to sensory information.

Key words jet lag, sex differences, nonphotic, phase shift, circadian rhythms, activity introduction

Circadian rhythms are dependent on environmental temporal cues, or zeitgebers, for steady entrainment to a 24-h cycle. Although the most ubiquitous zeitgeber is photoperiod, a number of nonphotic stimuli have been found to influence circadian rhythms by

resetting the circadian clock, entraining rhythms, or facilitating reentrainment following phase shifts of the light cycle, such as those experienced with transmeridian jet travel (e.g., Mistleberger, 1993; Mrosovsky et al., 1989; Turek, 1989; Antle and

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Mistlberger, 2000; Aschoff et al., 1971; Goel and Lee, 1995a, 1995b; Amir and Stewart, 1996).

Early studies of the effects of nonphotic zeitgebers with human subjects concluded that nonphotic zeitgebers, such as social cues, were also able to entrain human circadian rhythms to a 24-h cycle (Aschoff et al., 1971) and facilitate reentrainment following transmeridian jet travel (Klein and Wegmann, 1974). However, such studies were often confounded with problems related to the types of interactions of the subjects, especially the ability of one subject to select light exposure periods for a group. More recent studies of retinally blind human subjects strongly suggest that nonphotic cues can entrain some humans to a 24-h period (Klerman et al., 1998).

Goel and Lee (1995a) reported that female *degus* housed with an entrained female (hereafter referred to as donors) reentrained faster following a 6-h phase advance of the light cycle than when alone, whereas males did not. This was the first experiment to show that social cues in the presence of a light cycle could influence reentrainment of females. They reported a sex difference in the ability both to respond to and to produce the necessary social cues. This laboratory has also shown that olfactory cues are sufficient to supply the entraining information. Olfactory bulbectomy blocked the effect of a donor on accelerated reentrainment in a phase-shifting female (Goel et al., 1998). In addition, Governale and Lee (2001) routed odors from a housing unit containing entrained donor animals to a box containing phase-shifting animals. Recovery from the phase shift was equivalent to earlier experiments housing the donor in the same cage as the shifting animal.

It is unclear whether males' apparent inability to accelerate reentrainment when exposed to social cues is due to an absolute incapacity for social cue responsiveness or a decreased sensitivity to olfactory social cues relative to females. Kleiman (1975) reported that female *degus* are more sensitive to all odor cues than are males. However, male *degus* are able to distinguish between male and female conspecifics' urine, so they are capable of detecting olfactory social cues.

Experiment 1. We hypothesized that by increasing the strength or salience of the social cue, males would demonstrate enhanced recovery rates following a phase shift. In the first experiment, social cues were made stronger or more salient by increasing the number of female donors or by using sisters of the male

phase shifters as donors. Sisters were thought to possibly be more salient because of their familiarity to the males and possibly through kin recognition.

Experiment 2. We also hypothesized that testosterone inhibits responsiveness to social cues, perhaps by decreasing olfactory sensitivity in the appropriate olfactory central nervous system structures. Alternatively, some studies have shown effects of testosterone directly on the circadian mechanism. For example, castration advances phase angles of entrainment in adult male degus (Jechura et al., 2000) and increases the length of the free-running period in mice (Daan et al., 1975). To test whether adult testicular hormones affect responsiveness to social cues in reentrainment, castrated adult male *degus* were tested with and without testosterone and social cues.

Experiment 3. In addition, the effect of testosterone during the two types of reentrainment was tested in intact females. The aim of this experiment was to determine whether females were also sensitive to the inhibitory effects of testosterone on social cue-enhanced rates of reentrainment. Alternatively, if the neural system involved is sexually dimorphic in its response to testosterone, only the males would probably display sensitivity.

METHODS

Animals were obtained from an outbred colony maintained at the University of Michigan. Prior to use in the experiments, all animals were maintained at $20^{\circ} \pm 1^{\circ}\text{C}$ on a LD 12:12 light schedule, with lights on at 0600 and lights off at 1800. Adult animals were 6 months to 4 years old, with an average life expectancy of 5 to 8 years. Animals were age matched within experiments to provide an approximate age span difference of 2 years. The animals were housed individually in 48 cm \times 26.7 cm \times 20.3 cm Nalgene cages with running wheels (9 cm wide, 34.5 cm diameter). Cages were cleaned weekly at varying times during the light phase of the LD cycle. Rodent chow (Purina 5001) and water were available ad libitum. All procedures involving animals were approved by the Animal Care and Use Committee at the University of Michigan.

Surgical procedures for castration were carried out with Ketamine HCl (30 mg/kg of body weight) and Xylazine (2.5 mg/kg of body weight) anesthesia.

Yohimbine (2.5 mg/kg of body weight) and lactated ringers (3 ml, i.p.) were used to aid recovery. All *degus* were allowed 1 week for recovery before entering the experiment.

During reentrainment, animals were housed in pairs, with the phase-shifting animal and the social cue donor separated by a wire mesh divider in a Nalgene cage with dimensions of 48 cm × 38 cm × 19.5 cm (Goel and Lee, 1995a, 1995b). Data were collected as running wheel rotations per 10-min blocks using Minimitter equipment and software (Minimitter Inc., Sun River, OR). Data collection began 3 days after introduction of the wheels, allowing the animals to become familiar with the apparatus.

Procedures

Experiment 1. Eight adult male *degus* were subjected to three 9-h phase advances in the LD cycle and allowed to reentrain first alone with only photic cues, then in the presence of a sister, and last with two unrelated adult females. A 9-h phase advance was chosen over our more typical 6-h phase shift to prevent any floor effects of reentrainment speed from influencing the data. Since it takes a longer period of time to reentrain after a 9-h phase advance than after a 6-h phase advance, any effects of increased social cues might be more readily observed. Previous counterbalanced design and analysis has demonstrated that there are no order effects on rates of reentrainment as long as complete recovery is achieved between shifts (Goel and Lee, 1995b; Governale and Lee, 2001). Thus, in this experiment, all animals experienced the same order of shifts.

Experiment 2. Eight castrated adult male *degus* were phase advanced 6 h (typical shift used in earlier studies and also used in Experiment 3) and allowed to reentrain with photic cues alone and then with an adult female social cue donor. Silastic capsules containing testosterone with an effective length of 10 mm, presoaked for 24 h in physiological saline, were then implanted in the castrated males, and the phase shifts were repeated with donors and with photic cues only.

Experiment 3. Ten gonadally intact female *degus* were subjected to four 6-h phase advances of the light cycle. Using the same methods as in Experiment 1, the females were phase shifted both with and without a

female social cue donor. Testosterone-filled Silastic capsules with an effective length of 5 mm, presoaked for 24 h in physiological saline, were then implanted, and the sequence was repeated. The effective length of the testosterone capsules was reduced for this experiment because the testosterone levels in the males with 10 mm capsules had about twice the average amount of testosterone found in a typical male *degus* and they were robustly effective at reversing the effects of castration. We wanted to use a dose that was more typical of the average male *degus*' physiological level of testosterone.

Data Analyses

The number of days required to reentrain to a new LD cycle following a phase advance, activity levels, and amplitude of the activity rhythm were obtained from every animal in each of the experimental conditions (with or without donor[s], before and after testosterone replacement, etc.), allowing each animal to serve as its own control. Activity data were collected throughout all phases of the experiment as wheel rotations per 10-min interval with Dataquest III (Minimitter Inc., Sun River, OR) software.

Phase angle of activity onset was determined after an animal displayed at least 2 weeks of entrained rhythms and was calculated by examining 24-h activity frequency histograms for the time of activity onset. Activity onset was measured relative to the onset of the light cue and was defined as at least 40 min of consecutive activity with a minimum of 40 wheel revolutions per 10-min block of activity following a lack of activity of approximately 4 h. The time of activity onset over a period of 4 to 7 days was averaged and compared to the LD cycle to obtain phase angle of activity onset before phase shifts. Reentrainment was operationally defined as the day on which the animal first displayed a phase angle of entrainment similar to the phase angle prior to the phase shift for at least 3 consecutive days. Mean daily activity levels were calculated by averaging activity levels across 10-min bins over a 24-h period. Maximum activity level was defined as the greatest number of wheel rotations per 10-min bin in a 24-h period. Activity rhythm amplitude was obtained by subtracting the activity mean from the maximum activity level.

Two-tailed paired *t* tests were used to compare animals in the donor(s) versus no donor and/or testosterone-treated versus no testosterone conditions for each

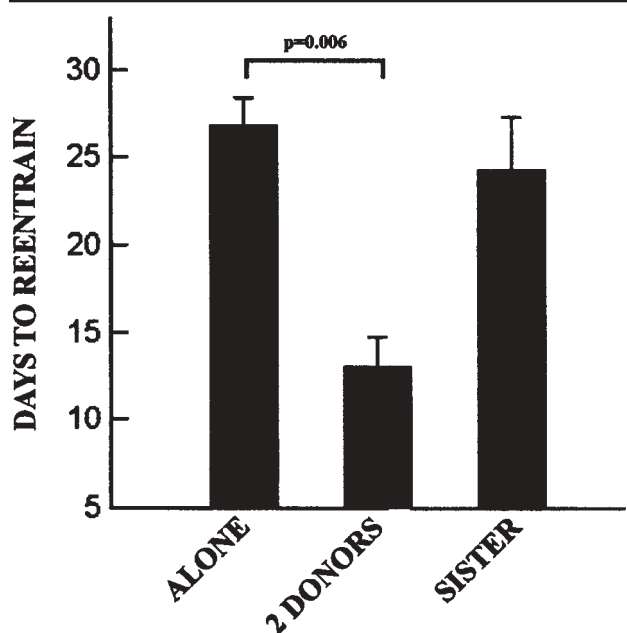


Figure 1. Reentrainment of intact males following a 9-h phase advance of the light cycle while exposed to light cues only (ALONE), two intact female social cue donors (2 DONORS), or an intact sister (SISTER). Note that the y -axis for this figure is larger than in Fig. 2 because the larger phase shift requires far more time for recovery.

parameter examined, with $p < 0.05$ considered significant. Data are presented as means \pm SEM.

RESULTS

Experiment 1. Males responded to increased concentration of social cues (two female donors) by significantly accelerating reentrainment compared to reentraining alone with photic cues ($p = 0.002$), whereas increasing the salience of the social cue by using a sister as donor had no significant effect on males' reentrainment rates (Fig. 1). There was also no difference in mean activity levels, maximum activity levels, or amplitude between groups.

Experiment 2. Castrated males significantly accelerated their rate of reentrainment when housed with a single female relative to their reentrainment rate when housed alone with only photic cues ($p = 0.006$; Fig. 2). Castrated males with testosterone capsule implants did not display facilitated reentrainment rates when in the presence of a female donor. Furthermore, testosterone-treated males required more time to reentrain

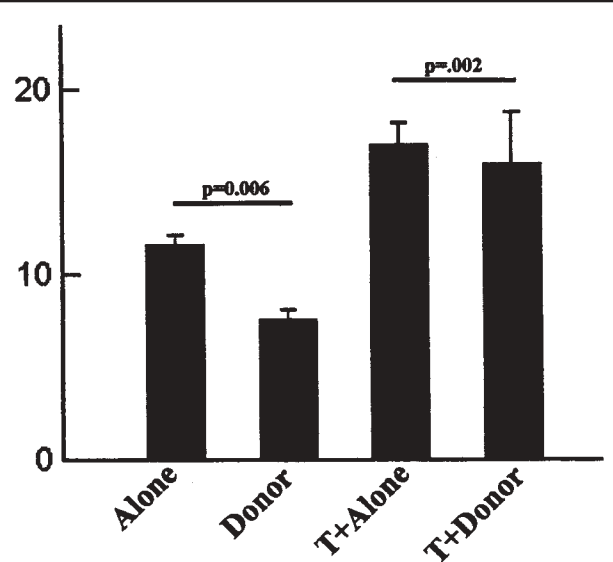


Figure 2. Reentrainment of castrated males following a 6-h phase advance of the light cycle while exposed to light cues only (Alone), a single intact female social cue donor (Donor), light cues while testosterone treated (T+Alone), and in the presence of a single intact female social cue donor while being treated with testosterone (T+Donor). Note that the y -axis is smaller than in Fig. 1 because 6-h phase shifts require less recovery time than do 9-h shifts.

both in the presence of a female donor and with photic cues alone ($p = 0.009$) than when castrated (Fig. 2).

There were no significant differences between groups for maximum activity level or activity amplitude. However, there was a significant ($p < 0.05$) increase in mean activity level in castrates following testosterone replacement (Fig. 3).

Experiment 3. Intact, untreated females significantly improved their rate of reentrainment when housed with a donor as compared to when housed alone (11.30 ± 0.895 days vs. 13.40 ± 1.17 days; $p = 0.029$), replicating previous studies. There was no significant difference in days to reentrain with photic cues only and with a donor when females were testosterone treated (11.13 ± 1.563 vs. 11.1 ± 1.105 days). Testosterone had no significant effect on maximum or mean activity levels or activity amplitude.

DISCUSSION

These experiments offer an explanation for the apparent lack of responsiveness by males to rate-enhancing social cues reported in earlier studies from

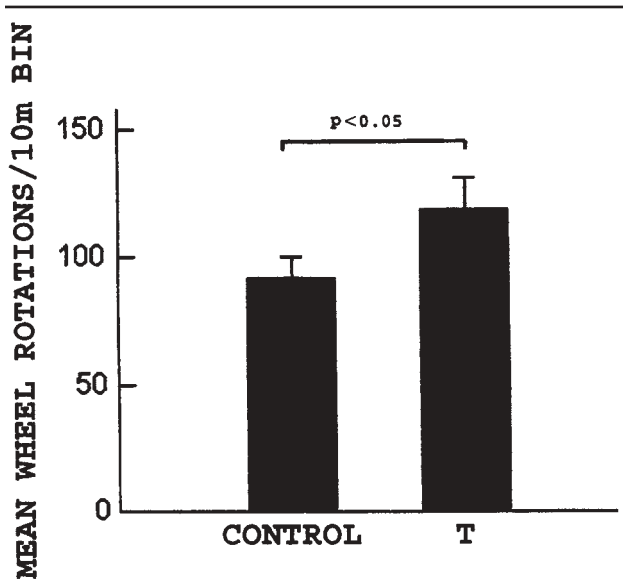


Figure 3. Mean activity levels of castrated males before (Control) and during (T) testosterone treatment.

this laboratory. Experiment 1 shows that males accelerate their reentrainment significantly when the olfactory social cue is made stronger by using two females as social cue donors instead of a single female. Experiment 2 clarifies the role of testosterone in the responsiveness to rate-enhancing social cues. Testosterone suppresses responsiveness in the male, given that castration leads to increased responsiveness and testosterone replacement returns the animals to the less responsive state. The increase in mean activity levels following testosterone replacement replicated earlier data (Jechura et al., 2000) and is consistent with data from other species (voles: Rowsemit, 1986, 1988; hamsters: Ellis and Turek, 1983; mice: Daan et al., 1975; rats: Roy and Wade, 1975). Finally, Experiment 3 demonstrates that both males and females are sensitive to testosterone's inhibiting effects on social cue responsiveness. Thus, the reentrainment-accelerating sex difference in responsiveness to olfactory social cues is a sex difference in gonadal hormones, not a difference in the CNS.

Experiment 1. Although testosterone is effective at suppressing accelerated reentrainment in the presence of a social cue donor, its inhibition is not complete since strengthening the social cue by using multiple females instead of just one enables males to respond. The lack of effect when housed with a sister could have several explanations. First, it was hypothesized that the odors from a familiar female relative would be more salient to the experimental animals. However,

the stimuli from a sister might not be effective at eliciting a response from the male because of an incest-avoidance response between the animals. In the natural environment, it might be best to avoid contact with opposite-sex siblings, and this behavior could translate to factors that would prevent males from responding to their sisters in many ways, including synchronizing their circadian rhythms. Perhaps a female mate would provide more salience. Another explanation is that the sisters are more salient to the males, but the stimulus is not adequate for a significant change in behavior. Perhaps housing with two sisters would increase the rate of reentrainment above that seen with two unfamiliar females. Finally, it may be that the odors relevant for influencing the circadian system are equally salient from relatives and nonrelatives.

Experiment 2. The data show that testosterone reduces the effects of social cues during reentrainment following a phase advance of the light cycle. Since castrating males increases their responsiveness to social cues and reinstating testosterone eliminates the effect, testosterone in adult male *degus* suppresses accelerated reentrainment in the presence of a female social cue donor. The increased length of time needed to reentrain with testosterone replacement capsules (compared with intact males receiving a 6-h phase advance in previous studies [e.g., Goel and Lee, 1995a]) with both photic cues and with a social cue donor is most likely due to a dose-dependent effect of testosterone on both the photic and olfactory systems, since the animals in the experiment were provided with doses of testosterone that were higher than levels found naturally in the animals. Intact male *degus* have testosterone levels of approximately 0.8 ng/ml (Goel et al., 1998), whereas the testosterone capsules used in the study produce approximately 1.6 to 2.0 ng/ml (Lee et al., 1990). It is also notable that the reversal of sensitivity with gonadectomy and testosterone replacement indicates an activational effect of testosterone in the adult male animal.

Experiment 3. Testosterone inhibition of female social cue responsiveness extends and provides additional support for the conclusions in Experiment 2, that is, that testosterone normally suppresses reentrainment-accelerating responsiveness to social cues in males. These data also suggest that males and females have similar neural sensitivity to testosterone for modulation of the use of social cues in reentrainment.

The suppression of responsiveness to olfactory social cues by testosterone most likely occurs within the olfactory system, either at the level of chemosensory stimulus binding in the mucosal layer of the olfactory bulbs or along the olfactory processing pathways in the brain. Halem et al. (2001) reported sex differences in the responsiveness of sensory neurons in the vomeronasal organ to olfactory stimuli and hypothesized that this difference is a result of sexually dimorphic noradrenergic inputs and responsiveness to adult steroid hormones. Beyond the site of chemosensory stimulus binding, the olfactory bulbs project to limbic system nuclei including the medial amygdala (Me), bed nucleus of the stria terminalis (BNST), the medial preoptic area (MPOA), and the hypothalamus. The olfactory processing system of rodents is sexually dimorphic, with males having more cells in brain areas along the olfactory pathways. The areas involved in olfactory processing are also rich in steroid hormone receptors, which could provide several possible sites of action for testosterone's inhibitory effects in the current experiments. Mating behavior in male hamsters is facilitated by the integration of testicular hormones and chemosensory information from the olfactory bulbs within the BNST, MPOA (Wood and Newman, 1995), and Me (Wood and Coolen, 1997). Although testosterone has a facilitative effect on mating behavior, a similar integration of steroid hormones and olfactory stimuli in another neural system could result in inhibitory neural signals in the responsiveness to olfactory social cues during reentrainment for male *degus* and positive neural signals for females.

It is also possible that the main endogenous pacemaker, the suprachiasmatic nucleus (SCN) of the hypothalamus, is responsible for the observed sex differences in reentrainment rates in the presence of olfactory social cues. The SCN receives direct and indirect input from many structures (Abrahamson and Moore, 2001). One or more of these structures could influence the SCN differently in the presence of testosterone. For example, the amygdala might be inhibited in its ability to integrate affective qualities to the olfactory social cues and/or the raphe nuclei might produce less of an arousal response to the social stimuli. Alternatively, testosterone could be acting directly at the SCN. The SCN of male ferrets has been reported to have traditional intracellular androgen receptor-ir (Kashon et al., 1996), although there are no reports for these receptors in adult rodents to date. However, steroid hormones are also able to influence

neural functions and behaviors through cell surface receptors (reviewed by Moore and Evans, 1999). Exactly how testosterone might suppress SCN sensitivity to phase shifts in the presence of odors remains to be determined.

Although the studies herein examined the effects of olfactory social cues on nonhuman diurnal animals, it is entirely possible that the human circadian system could also be responsive to a similar stimulus. As mentioned earlier, nonphotic zeitgebers have been found to be effective in entraining blind individuals and have been used to shorten the length of time needed to recover from jet lag. These studies did not directly use olfactory stimuli (although they have not been excluded), but the human circadian system is very likely responsive to odor cues and might even show a sex difference similar to that found in the *degu* in the ability to use olfactory social cues in an effective manner. Humans have a vomeronasal organ (VNO) that is neuroanatomically sexually dimorphic (Monti-Bloch et al., 1994; Jacob et al., 2000). Behavioral evidence for sex differences in the VNO and/or related brain areas has been found in a number of studies, with females being superior to males in olfactory sensitivity, identification, memory, and recognition (Wysocki and Gilbert, 1989; Koelega, 1994; Koelega and Koster, 1974; Lehrner, 1993). In addition, steroid-derived olfactory stimuli affect the human CNS, as evidenced by electrodermal responses by anosmic subjects (Van Toller et al., 1983), PET brain imaging (Jacob et al., 2001), and fMRI (Levy et al., 1997), although the latter two studies used consciously discernable odors and found no sex difference. Several studies have demonstrated that women's menstrual cycles can be shifted by exposure to odors from other cycling women (Stern and McClintock, 1998; McClintock, 1971; Weller and Weller, 1997). Whether or not olfactory stimuli can speed recovery from phase shifts in humans remains to be tested. However, the implications for possible treatments for jet lag could be tremendous if humans can respond to olfactory cues.

Future research should include identifying the CNS site (or sites) of action by testosterone on the responsiveness to social cues during reentrainment. Also, determining the precise element of the chemosensory stimulus that is being attended to during accelerated reentrainment would be beneficial to future studies so that the effective compound can be quantified and used precisely. It is also important to test whether the same chemosensory stimulus is effective

tive in different species. If the effective compound can be isolated and is effective in species other than *degus*, it could potentially be developed as a reentrainment aid for humans recovering from jet lag. Last, it is important to determine whether steroid hormones might be directly influencing the circadian system (perhaps by altering sensitivity to light), beginning with determining a dose-response curve for circadian effects in response to testosterone.

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REFERENCES

- Abrahamson EE and Moore RY (2001) Suprachiasmatic nucleus in the mouse: Retinal innervation, intrinsic organization and efferent projections. *Brain Res* 916:172-191.
- Amir S and Stewart J (1998) Conditioning in the circadian system. *Chronobiol Int* 15(5):447-456.
- Antle MC and Mistlberger RE (2000) Circadian clock resetting by sleep deprivation without exercise in the Syrian hamster. *J Neurosci* 20(24):9326-9332.
- Aschoff J, Fatranska M, Giedke H, Doerr P, Stamm D, and Wisser H (1971) Human circadian rhythms in continuous darkness: Entrainment by social cues. *Science* 171:213-215.
- Daan S, Damassa D, Pittendrigh CS, and Smith ER (1975) An effect of castration and testosterone replacement on a circadian pacemaker in mice (*Mus musculus*). *Proc Natl Acad Sci U S A* 72:3744-3747.
- Ellis GB and Turek FW (1983) Testosterone and photoperiod interact to regulate locomotor activity in male hamsters. *Horm Behav* 17:66-75.
- Goel N and Lee TM (1995a) Sex differences and effects of social cues on daily rhythms following phase advances in *Octodon degus*. *Physiol and Behav* 58:205-213.
- Goel N and Lee TM (1995b) Social cues accelerate reentrainment of circadian rhythms in diurnal female *Octodon degus* (Rodentia-Octodontidae). *Chronobiol Int* 12:311-323.
- Goel N, Lee TM, and Pieper DR (1998) Removal of the olfactory bulbs delays photic reentrainment of circadian activity rhythms and modifies the reproductive axis in male *Octodon degus*. *Brain Res* 792:229-236.
- Governale MM and Lee TM (2001) Olfactory social cues accelerate entrainment following phase shifts and entrain free-running rhythms in female *Octodon degus* (Rodentia). *J Biol Rhythms* 16:489-501.
- Halem HA, Baum MJ, and Cherry JA (2001) Sex difference and steroid modulation of pheromone-induced immediate early genes in the two zones of the mouse accessory olfactory system. *J Neurosci* 21(7):2474-2480.
- Jacob S, Kinnunen LH, Metz J, Cooper M, and McClintock MK (2001) Sustained human chemosignal unconsciously alters brain function. *NeuroReport* 12:2391-2394.
- Jacob S, Zelano B, Gungor A, Abbott D, Naclerio R, and McClintock MK (2000) Location and gross morphology of the nasopalatine duct in human adults. *Arch Otolaryngology Head Neck Surgery* 126:741-748.
- Jechura TJ, Walsh JM, and Lee TM (2000) Testicular hormones modulate circadian rhythms of the diurnal rodent, *Octodon degus*. *Hormones Behav* 38:243-249.
- Kashon ML, Arbogast JA, and Sisk CL (1996) Distribution and hormonal regulation of androgen receptor immunoreactivity in the forebrain of the male European ferret. *J Comp Neuro* 376:567-586.
- Kleiman DG (1975) Patterns of behaviour in hystricomorph rodents. *Symp Zool Soc Lond* 34:171-209.
- Klein DG and Wegmann HM (1974) The resynchronization of human circadian rhythms after transmeridian flights as a result of flight direction and mode of activity. In *Chronobiology*, LE Scheving, F Halberg, and JE Pauly, eds, pp 564-570, Igaku, Tokyo.
- Klerman EB, Rimmer DW, Dijk D-J, Kronauer RE, Rizzo JF, III, and Czeisler CA (1998) Nonphotic entrainment of the human circadian pacemaker. *Amer J Physiol* 274:R991-R996.
- Koelega HS (1994) Sex differences in olfactory sensitivity and the problem of the generality of smell acuity. *Percept Mot Skills* 78:203-213.
- Koelega HS and Koster EP (1974) Some experiments on sex differences in odor perception. *Ann N Y Acad Sci* 237:234-246.
- Lee TM, Pelz K, Licht P, and Zucker I (1990) Testosterone influences hibernation in golden-mantled ground squirrels. *Am J Physiol* 259:R760-767.
- Lehrner J (1993) Gender differences in long-term odor recognition memory: Verbal versus sensory influences and consistency of label use. *Chem Senses* 18:17-26.
- Levy LM, Henkin RI, Hutter A, Lin CS, Martins D, and Schellinger D (1997) Functional MRI of human olfaction. *J Comput Assist Tomogr* 21(6):849-856.
- McClintock MK (1971) Menstrual synchrony and suppression. *Nature* 229:244-245.
- Mistlberger RE (1993) Effects of scheduled food and water access on circadian rhythms of hamsters in constant light, dark and light:dark. *Physiol Behav* 53:509-516.
- Monti-Bloch L, Jennings-White C, Dolberg D, and Berliner D (1994) The human vomeronasal system. *Psychoneuroendocrinology* 19:673-686.

- Moore FL and Evans SJ (1999) Steroid hormones use non-genomic mechanisms to control brain functions and behaviors: A review of evidence. *Brain Behav Evol* 54: 41-50.
- Mrosovsky N, Reeb SG, Honrado GI, and Salmon, PA (1989) Behavioural entrainment of circadian rhythms. *Experientia* 45:696-702.
- Rowsemitt CN (1986) Seasonal variations in activity rhythms of male voles: Mediation by gonadal hormones. *Physiol Behav* 37:797-803.
- Rowsemitt CN (1988) Activity of castrated male voles: Rhythms of responses to testosterone replacement. *Physiol Behav* 45:7-13.
- Roy EJ and Wade GN (1975) Role of estrogens in androgen-induced spontaneous activity in male rats. *J Comp Physiol Psych* 89:573-579.
- Stern K and McClintock MK (1998) Regulation of ovulation by human pheromones. *Nature* 392:177-179.
- Turek FW (1989) Effects of stimulated activity on the circadian pacemaker in vertebrates. *J Biol Rhythms* 4:135-147.
- Van Toller C, Kirk-Smith M, Wood N, Lombard J, and Dodd GH (1983) Skin conductance and subjective assessments associated with the odour of a 5-a-androstenone-3-one. *Biol Psych* 16:85-107.
- Weller A and Weller L (1997) Menstrual synchrony under optimal conditions: Bedouin families. *J Comp Psych* 111(2):143-151.
- Wood RI and Coolen LM (1997) Integration of chemosensory and hormonal cues is essential for sexual behaviour in the male Syrian hamster: Role of the medial amygdaloid nucleus. *Neuroscience* 78(4):1027-1035.
- Wood RI and Newman SW (1995) Androgen and estrogen receptors coexist within individual neurons in the brain of the Syrian hamster. *Neuroendocrinology* 62:487-497.
- Wysocki CJ and Gilbert AN (1989) National geographic smell survey: Effects of age are heterogeneous. *Ann N Y Acad Sci* 561:12-28.