Journal Scan

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Is it possible to study sleep-wake patterns in adolescent borderline personality disorder? An actigraphic feasibility study.

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Borderline Personality Disorder (BPD) is characterized by severe instability in mood, impulse control, relationships and sleep patterns, alongside with mild cognitive disturbances in some patients. Although research on adolescent BPD has developed over the last decade, little is known about circadian sleep-wake patterns in this population. Low compliance and cooperation frequently reported in these patients impede data collection. Therefore, research had to introduce non-invasive objective measurements such as actigraphy while minimizing attrition and resurgence of suicidal ideation. This article examined the feasibility of an actigraphic study with BPD adolescents. Eighteen BPD adolescents (13-17 years old) were recruited from a specialized outpatient mood disorders clinic and asked to wear an actigraph for nine days including two weekends. Twelve (66.7%) of the 18 BPD patients who consented kept the actigraph for an average of 11.00 days (SD: 2.04), thus completing the required 9-day period. The reasons surrounding difficulties during the experiment, such as aversive emotions during interviews, dermal irritation, fragile alliance with the research assistant, are described. The factors that contributed the most to our satisfactory compliance rate included stabilized mood before inclusion, close ties between the research and the clinical teams, rapid access to an emergency psychiatric assessment if needed.

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Adolesc Med State Art Rev. 2010 Dec;21(3):446-56, viii.

Sleep and headaches during adolescence.

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Adolescence is a complex period of life with hormonal, physiologic, and psychological modifications that affect headache and sleep. Because of the well-documented association between sleep and headache, it is reasonable to expect that changes in sleep would be reflected in the onset, duration, and frequency of headache. The sleep structure changes and the presence of poor sleep hygiene in adolescence could be responsible for the appearance of headache in adolescents or could contribute to the increased chronicity of headaches. It is essential in adolescence to perform a careful analysis of sleep habits, patterns, and disturbances to develop adequate treatment methods for both sleep and headache.

Sleep Med Clin. 2010 Dec;5(4):701-715.

Therapeutics for Circadian Rhythm Sleep Disorders.

Dodson ER, Zee PC.

The sleep-wake cycle is regulated by the interaction of endogenous circadian and homeostatic processes. The circadian system provides timing information for most physiological rhythms, including the sleep and wake cycle. In addition, the central circadian clock located in the suprachiasmatic nucleus of the hypothalamus has been shown to promote alertness during the day. Circadian rhythm sleep disorders arise when there is a misalignment between the timing of the endogenous circadian rhythms and the external environment or when there is dysfunction of the circadian clock or its entrainment pathways. The primary synchronizing agents of the circadian system are light and melatonin. Light is the strongest entraining agent of circadian rhythms and timed exposure to bright light is often used in the treatment of circadian rhythm sleep disorders. In addition, timed administration of melatonin, either alone or in combination with light therapy has been shown to be useful in the treatment of the following circadian rhythm sleep disorders: delayed sleep phase, advanced sleep phase, free-running, irregular sleep wake, jet lag and shift work.

Front Neurol. 2010 Nov 1;1:137.

Timing of sleep and its relationship with the endogenous melatonin rhythm.

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While much research has investigated the effects of exogenous melatonin on sleep, less is known about the relationship between the timing of the endogenous melatonin rhythm and the sleep-wake cycle. Significant inter-individual variability in the phase relationship between sleep and melatonin rhythms has been reported although the extent to which the variability reflects intrinsicand/or environmental differences is unknown. We examined the effects of different sleeping schedules on the time of dim light melatonin onset (DLMO) in 28 young, healthy adults. Participants chose to maintain either an early (22:30-06:30 h) or a late (00:30-08:30 h) sleep schedule for at least 3 weeks prior to an overnight laboratory visit. Saliva samples were collected under dim light (<2 lux) and controlled posture conditions to determine salivary DLMO. The 2-h difference between groups in the enforced sleep-wake schedule was associated with a concomitant 1.75-h delay in DLMO. The mean phase relationship between sleep onset and DLMO remained constant (~2h). The variance in DLMO time, however, was greater in the late group (range 4.5 h) compared to the early group (range 2.4h) perhaps due to greater effect of environmental influences in delayed sleep types or greater intrinsic instability in their circadian system. The findings contribute to our understanding of individual differences in the human circadian clock and have important implications for the diagnosis and treatment of circadian rhythm sleep disorders, in particular if a greater normative range for phase angle of entrainment occurs in individuals with later sleep-wake schedules.

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Experimental 'jet lag' inhibits adult neurogenesis and produces long-term cognitive deficits in female hamsters.

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BACKGROUND: Circadian disruptions through frequent transmeridian travel, rotating shift work, and poor sleep hygiene are associated with an array of physical and mental health maladies, including marked deficits in human cognitive function. Despite anecdotal and correlational reports suggesting a negative impact of circadian disruptions on brain function, this possibility has not been experimentally examined.

METHODOLOGY/PRINCIPAL FINDINGS: In the present study, we investigated whether experimental 'jet lag' (i.e., phase advances of the light:dark cycle) negatively impacts learning and memory and whether any deficits

observed are associated with reductions in hippocampal cell proliferation and neurogenesis. Because insults to circadian timing alter circulating glucocorticoid and sex steroid concentrations, both of which influence neurogenesis and learning/memory, we assessed the contribution of these endocrine factors to any observed alterations. Circadian disruption resulted in pronounced deficits in learning and memory paralleled by marked reductions in hippocampal cell proliferation and neurogenesis. Significantly, deficits in hippocampal-dependent learning and memory were not only seen during the period of the circadian disruption, but also persisted well after the cessation of jet lag, suggesting long-lasting negative consequences on brain function.

CONCLUSIONS/SIGNIFICANCE: Together, these findings support the view that circadian disruptions suppress hippocampal neurogenesis via a glucocorticoid-independent mechanism, imposing pronounced and persistent impairments on learning and memory.

J Biol Rhythms. 2010 Dec;25(6):460-8.

Partial sleep deprivation reduces phase advances to light in humans.

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Partial sleep deprivation is increasingly common in modern society. This study examined for the first time if partial sleep deprivation alters circadian phase shifts to bright light in humans. Thirteen young healthy subjects participated in a repeated-measures counterbalanced design with 2 conditions. Each condition had baseline sleep, a dim-light circadian phase assessment, a 3-day phase-advancing protocol with morning bright light, then another phase assessment. In one condition (no sleep deprivation), subjects had an 8-h sleep opportunity per night during the advancing protocol. In the other condition (partial sleep deprivation), subjects were kept awake for 4 h in near darkness (<0.25 lux), immediately followed by a 4-h sleep opportunity per night during the advancing protocol. The morning bright light stimulus was four 30-min pulses of bright light (~5000 lux), separated by 30-min intervals of room light. The light always began at the same circadian phase, 8 h after the baseline dim-light melatonin onset (DLMO). The average phase advance without sleep deprivation was 1.8 ± 0.6 (SD) h, which reduced to 1.4 ± 0.6 h with partial sleep deprivation ($p < 0.05$). Ten of the 13 subjects showed reductions in phase advances with partial sleep deprivation, ranging from 0.2 to 1.2 h. These results indicate that short-term partial sleep deprivation can moderately reduce circadian phase shifts to bright light in humans. This may have significant implications for the sleep-deprived general population and for the bright light treatment of circadian rhythm sleep disorders such as delayed sleep phase disorder.

Science. 2010 Dec 3;330(6009):1349-54.

Circadian integration of metabolism and energetics.

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Circadian clocks align behavioral and biochemical processes with the day/night cycle. Nearly all vertebrate cells possess self-sustained clocks that couple endogenous rhythms with changes in cellular environment. Genetic disruption of clock genes in mice perturbs metabolic functions of specific tissues at distinct phases of the sleep/wake cycle. Circadian desynchrony, a characteristic of shift work and sleep disruption in humans, also leads to metabolic pathologies. Here, we review advances in understanding the interrelationship among circadian disruption, sleep deprivation, obesity, and diabetes and implications for rational therapeutics for these conditions.

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Postoperative circadian disturbances.

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An increasing number of studies have shown that circadian variation in the excretion of hormones, the sleep wake circle, the core body temperature rhythm,

the tone of the autonomic nervous system and the activity rhythm are important both in health and in disease processes. An increasing attention has also been directed towards the circadian variation in endogenous rhythms in relation to surgery. The attention has been directed to the question whether the circadian variation in endogenous rhythms can affect postoperative recovery, morbidity and mortality. Based on the lack of studies where these endogenous rhythms have been investigated in relation to surgery we performed a series of studies exploring different endogenous rhythms and factors affecting these rhythms. We also wanted to examine whether the disturbances in the postoperative circadian rhythms could be correlated to postoperative recovery parameters, and if pharmacological administration of chronobiotics could improve postoperative recovery. Circadian rhythm disturbances were found in all the examined endogenous rhythms. A delay was found in the endogenous rhythm of plasma melatonin and excretion of the metabolite of melatonin (AMT6s) in urine the first night after both minor and major surgery. This delay after major surgery was correlated to the duration of surgery. The amplitude in the melatonin rhythm was unchanged the first night but increased in the second night after major surgery. The amplitude in AMT6s was reduced the first night after minimally invasive surgery. The core body temperature rhythm was disturbed after both major and minor surgery. There was a change in the sleep wake cycle with a significantly increased duration of REM-sleep in the day and evening time after major surgery compared with preoperatively. There was also a shift in the autonomic nervous balance after major surgery with a significantly increased number of myocardial ischaemic episodes during the nighttime period. The circadian activity rhythm was also disturbed after both minor and major surgery. The daytime AMT6s excretion in urine after major surgery was increased on the fourth day after surgery and the total excretion of AMT6s in urine was correlated to sleep efficiency and wake time after sleep onset, but was not correlated to the occurrence of postoperative cognitive dysfunction. We could only prove an effect of melatonin substitution in patients with lower than median pain levels for a three days period after laparoscopic cholecystectomy. In the series of studies included in this thesis we have systematically shown that circadian disturbances are found in the secretion of hormones, the sleep-wake cycle, core body temperature rhythm, autonomic nervous system tone, myocardial ischaemia and activity rhythm after surgery. Correlation exists between circadian rhythm parameters and measures of postoperative sleep quality and recovery. However, oral melatonin treatment in the first three nights after surgery, cannot yet be generally recommended for improvement of sleep quality or other recovery parameters based on the available results. It may be indicated in subgroups or if other perioperative treatment algorithms were used, but this has to be investigated in future trials.

Sleep. 2010 Dec;33(12):1605-14.

The use of exogenous melatonin in delayed sleep phase disorder: a meta-analysis.

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STUDY OBJECTIVES: To perform a meta-analysis of the efficacy and safety of exogenous melatonin in advancing sleep-wake rhythm in patients with delayed sleep phase disorder.

DESIGN: Meta analysis of papers indexed for PubMed, Embase, and the abstracts of sleep and chronobiologic societies (1990-2009).

PATIENTS: Individuals with delayed sleep phase disorder.

INTERVENTIONS: Administration of melatonin.

MEASUREMENTS AND RESULTS: A meta-analysis of data of randomized controlled trials involving individuals with delayed sleep phase disorder that were published in English, compared melatonin with placebo, and reported 1 or more of the following: endogenous melatonin onset, clock hour of sleep onset, wake-up time, sleep-onset latency, and total sleep time. The 5 trials including 91 adults and 4 trials including 226 children showed that melatonin treatment advanced mean endogenous melatonin onset by 1.18 hours (95% confidence interval [CI]: 0.89-1.48h) and clock hour of sleep onset by 0.67 hours (95% CI: 0.45-0.89 h). Melatonin decreased sleep-onset latency by 23.27 minutes (95% CI: 4.83 -41.72 min). The wake-up time and total sleep time did not change significantly.

CONCLUSIONS: Melatonin is effective in advancing sleep-wake rhythm and endogenous melatonin rhythm in delayed sleep phase disorder.

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Circadian disruption and metabolic disease: findings from animal models.

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Social opportunities and work demands have caused humans to become increasingly active during the late evening hours, leading to a shift from the predominantly diurnal lifestyle of our ancestors to a more nocturnal one. This voluntarily decision to stay awake long into the evening hours leads to circadian disruption at the system, tissue, and cellular levels. These derangements are in turn associated with clinical impairments in metabolic processes and physiology. The use of animal models for circadian disruption provides an important opportunity to determine mechanisms by which disorganization in the circadian system can lead to metabolic dysfunction in response to genetic, environmental, and behavioral perturbations. Here we review recent key animal studies involving circadian disruption and discuss the possible translational implications of these studies for human health and particularly for the development of metabolic disease.

Neurology. 2010 Nov 16;75(20):1780-5.

Modafinil ameliorates excessive daytime sleepiness after traumatic brain injury.

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BACKGROUND: Excessive daytime sleepiness (EDS) and fatigue are common symptoms after traumatic brain injury (TBI), but there is no specific treatment for affected patients. With this pilot study, we aimed at studying the effect of daily modafinil on posttraumatic EDS and fatigue.

METHODS: We conducted a prospective, double-blind, randomized, placebo-controlled pilot study in 20 patients with TBI who had fatigue or EDS or both. After baseline examinations (questionnaires including the Epworth Sleepiness Scale to assess EDS and the Fatigue Severity Scale to assess fatigue, actigraphy, polysomnography, maintenance of wakefulness test, and psychomotor vigilancetest), 10 patients received 100 to 200 mg modafinil every morning, and 10 patients were treated with placebo. After a 6-week treatment period, all examinations were repeated.

RESULTS: EDS improved significantly in patients with TBI who were treated with modafinil, compared with the placebo group. Similarly, the ability to stay awake on the maintenance of wakefulness test improved only in the modafinil group. Modafinil, however, had no impact on posttraumatic fatigue. Clinically relevant side effects were not observed.

CONCLUSION: This study indicates that modafinil is effective and well tolerated in the treatment of posttraumatic EDS but not of fatigue.

CLASSIFICATION OF EVIDENCE: This study provides Class I evidence that modafinil (100-200 mg daily) improves posttraumatic EDS compared with placebo. This study provides Class I evidence that modafinil (100-200 mg daily) does not improve posttraumatic fatigue compared with placebo.

Reprod Biol Endocrinol. 2010 Nov 8;8:138.

The correlation between urinary 5-hydroxyindoleacetic acid and sperm quality in infertile men and rotating shift workers.

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BACKGROUND: Serotonin is a neurotransmitter that modulates a wide range of neuroendocrine functions. However, excessive circulating serotonin levels may induce harmful effects in the male reproductive system. The objective of this study was to evaluate whether the levels of urinary 5-hydroxyindoleacetic acid (5-HIIA), a major serotonin metabolite, correlate with different classical seminal parameters.

METHODS: Human ejaculates were obtained from 40 men attending infertility counselling and rotating shift workers by masturbation after 4-5 days of abstinence. Urinary 5- HIIA concentration was quantified by using a commercial ELISA kit. Forward motility was assessed by a computer-aided semen analysis (CASA) system. Sperm concentration was determined using the haemocytometer method. Sperm morphology was evaluated after Diff-Quik staining, while sperm vitality was estimated after Eosin-Nigrosin vital staining.

RESULTS: Our results show that urinary 5-HIIA levels obtained from a set of 20 volunteers negatively correlated with sperm concentration, forward motility, morphology normal range and sperm vitality. On the other hand, we checked the relationship between male infertility and urinary 5-HIIA levels in 20 night shift workers. Thus, urinary 5-HIIA levels obtained from 10 recently-proven fathers were significantly lower than those found in 10 infertile males. Additionally, samples from recent fathers exhibited higher sperm concentration, as well as better forward motility and normal morphology rate.

CONCLUSIONS: In the light of our findings, we concluded that high serotonin levels, indirectly measured as urinary 5-HIIA levels, appear to play a role as an infertility determinant in male subjects.

Chronobiol Int. 2010 Oct;27(9-10):1930-42.

Habitual moderate alcohol consumption desynchronizes circadian physiologic rhythms and affects reaction-time performance.

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The authors studied longitudinally four healthy young adults to explore if habitual evening intake of a "moderate" amount of wine alters parameters, including period (ô) of circadian rhythms. Subjects, synchronized by diurnal activity from 07.30 h ± 60 min to 23.00 h ± 90 min and nocturnal rest, were studied during a continuous 22-day span: 11 days without alcohol (control) and 11 days with a glass (200 mL) of wine nightly at supper (alcohol). The amount of alcohol ingested with dinner ranged from 0.28 to 0.42 g/kg/24 h/participant and the estimated evening blood alcohol level ranged from 0.02 to 0.10 g/L/participant. Single reaction time (SRT; yellow light signal), three-choice reaction time (CRT) (red, green, and yellow signals) of both hands, related cumulated errors (c-errors), as well as oral temperature (OT) and grip strength (GS) were measured four to seven times/24 h. Time series were analyzed individually to quantify 24-h means (M), circadian ô (power spectra), and cosinor, and correlation, ÷(2), and t tests were performed. The sleep-wake ô (actography) was 24 h in every subject for both conditions. With alcohol, all subjects showed an OT circadian ô shorter than the control one. The SRT circadian M was longer (poorer performance) with wine versus control in three subjects, while CRT was longer with wine versus control in only one subject. Correlation analyses also showed the detrimental effect of alcohol on the same variables. Number of days with <2 c-errors was predominant in control and decreased with alcohol, especially for SRT. The desynchronization of the 10 different documented rhythms was greater with alcohol with reference to control in two of the four studied subjects. This work shows that habitual "moderate" wine drinking at supper reduces the performance of subjects, increases the level of c-errors/24 h, especially for SRT, suggesting a "moderate" amount of alcohol has the potential to increase accident risk, and it can also desynchronize circadian time organization.

Chronobiol Int. 2010 Oct;27(9-10):1895-910.

Estimation of the benchmark duration of shiftwork associated with weight gain in male Japanese workers.

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The authors estimated the benchmark durations (BMDs) and their 95% lower confidence limit (BMDL) for the reference duration of shiftwork for weight gain. A 14-yr prospective cohort study was conducted in male workers at a Japanese steel company (n = 7254) who had received annual health check-ups between 1991 and 2005. The endpoints in the study were either a 5%, 7.5%, or 10% increase in body mass index (BMI) during the period of observation, compared to the BMI at entry. The association between the duration of shiftwork and weight gain was investigated using multivariate pooled logistic regression analyses with stepwise selection of covariates, including age, BMI measured during the study, drinking and smoking habits, and habitual exercise. The BMDL/BMD for shiftwork in subjects aged in their 40s or ≥50 yrs was estimated using benchmark responses (BMRs) of 5% or 10% and parameters for the duration of shiftwork and other covariates. For workers aged in their 40s, the BMDL/BMD for shiftwork with a BMR of 5% was 18.6/23.0 yrs (≥7.5%) and 16.9/19.4 yrs (≥10%). For workers aged ≥50 yrs, the BMDL/BMD with a BMR of 5% was 22.9/28.2 yrs (≥7.5%) and 20.6/23.6 yrs (≥10%). The reference duration of shiftwork that associated with weight gain was shown to be at least 17 yrs in middle-aged workers. Special attention should be paid to prevent weight gain at an earlier stage and not when this increase in weight has become apparent.

Chronobiol Int. 2010 Oct;27(9-10):1797-812.

Evening preference is related to the incidence of depressive states independent of sleep-wake conditions.

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Although evening preference has recently been identified as a risk factor for depression, it has not been substantiated whether evening preference is a direct risk factor for depressive states, or if it is associated secondarily through other factors, such as delayed sleep timing and shortened sleep duration. The objective of this study is to investigate associations in Japanese adult subjects between evening preference and incidence of depressive states, adjusting for various sleep parameters related to depressive states. The Morningness-Eveningness Questionnaire (MEQ), the Pittsburgh Sleep Quality Index (PSQI), and the Center for Epidemiologic Studies Depression Scale (CES-D) were administered to 1170 individuals (493 males/677 females; mean and range 38.5 and 20-59 yrs) to assess their diurnal preferences, sleeping states, and presence of depression symptoms. Subjects were classified into five chronotypes based on MEQ scores. Evening preference was associated with delayed sleep timing, shortened sleep duration, deteriorated subjective sleep quality, and worsened daytime sleepiness. Logistic regression analysis demonstrated that the extreme evening type (odds ratio [OR] = 1.926, p = .018) was associated with increased incidence of depressive states and that the extreme morning type (OR = 0.342, p = .038) was associated with the decreased incidence of depressive states, independent of sleep parameters, such as nocturnal awakening (OR = 1.844, p < .001), subjective sleep quality (OR = 2.471, p < .001), and daytime sleepiness (OR = 1.895, p = .001). However, no significant associations were observed between the incidence of depressive states and sleep duration, sleep timing, and sleep debt (levels of insufficient sleep). Although the findings of this study do not demonstrate a causative relationship between evening preference and depression, they do suggest the presence of functional associations between mood adjustment and biological clock systems that regulate diurnal preference. They also suggest that evening preference might increase susceptibility to the induction of mood disorders.

Chronobiol Int. 2010 Oct;27(9-10):1778-96.

Phase relationship between skin temperature and sleep-wake rhythms in women with vascular dysregulation and controls under real-life conditions.

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The aim of the study was to investigate whether women with primary vascular dysregulation (VD; main symptoms of thermal discomfort with cold extremities) and

difficulties initiating sleep (DIS) exhibit a disturbed phase of entrainment (y) under everyday life conditions. The authors predicted a phase delay of the distal-proximal skin temperature gradient and salivary melatonin rhythms with respect to the sleep-wake cycle in women with VD and DIS (WVD) compared to controls (CON), similar to that found in their previous constant-routine laboratory data. A total of 41 young healthy women, 20 with WVD and 21 matched CON without VD and normal sleep onset latency (SOL), were investigated under ambulatory conditions (following their habitual bedtimes) during 7 days of continuous recording of skin temperatures, sleep-wake cycles monitored by actimetry and sleep-wake diaries, and single evening saliva collections for determining the circadian marker of dim light melatonin onset (DLMO). Compared to CON, WVD showed increased distal vasoconstriction at midday and in the evening, as indicated by lower distal (DIST; hands and feet) and foot-calf skin temperatures, and distal-proximal skin temperature gradients ($p<.05$). WVD manifested distal vasoconstriction before lights-off that also lasted longer after lights-off than in CON. In parallel, WVD exhibited a longer SOL ($p<.05$). To define internal phase-relationships, cross-correlation analyses were performed using diurnal rhythms of wrist activity and foot skin temperature. WVD showed a phase delay in foot skin temperature (CON versus WVD: 3.57 ± 17.28 min versus 38.50 ± 16.65 min; $p< .05$) but not in wrist activity. This finding was validated by additional within-subject cross-correlation analyses using the diurnal wrist activity pattern as reference. DLMO and habitual sleep times did not differ between CON and WVD. The authors conclude that WVD exhibit a phase delay of distal vasodilatation with respect to their habitual sleep-wake cycle and other circadian phase markers, such as DLMO. A full factorial design will have to show whether the finding is specific to primary vascular dysregulation, to DIS, or to their interaction.