

Title of Study: Toileting at Night in Older Adults: Light to Maximize Balance, Minimize Insomnia

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Initial protocol

Study Procedures

Subjects will be initially phone screened before being asked to come to the lab for a screening visit. By including the phone screen, we have found that our failure rate during the screening visit is relatively low (around 20%). Our previous experience indicates that relatively few of the randomized subjects will be disempaneled. Subjects will be randomized after passing their lab screening visit; subjects who are disempaneled will be replaced. Subjects will be block randomized in three groups of nine (three in each condition), with drop-outs replaced. In-person screening will consist of discussion and signing of the consent form and completion of the following forms or tests: demographics, medication/health log, Owl and Lark Questionnaire ('morningness'/'eveningness'), Ishihara Color Plate (color blindness), Mini Mental State Exam (dementia), Pittsburgh Sleep Quality Index (sleep disorders), Geriatric Depression Scale, AUDIT (alcoholism), Balance Self-efficacy Scale (self-assessed balance), Nocturia, Nocturnal Enuresis and Sleep-interruption Questionnaire, Octopus 900 (peripheral vision), and ETDRS (visual acuity).

For one week prior to entry into the laboratory, subjects will be required to maintain a regular sleep-wake cycle. The purpose of this schedule is to ensure that subjects have adequate sleep time (i.e., are not significantly sleep deprived) before coming into the laboratory and to regularize exposure to light and dark which should, in theory, help to maximize the amplitude of the oscillation of the circadian pacemaker and to stabilize the phase angle between the circadian pacemaker and the sleep schedule. A regular sleep-wake cycle is defined for these purposes as having nocturnal time in bed being between 7 and 9 hours and going to bed and arising within 30 minutes of target bed and wake times. The prospective timing of sleep during this one-week period will be determined by consensus between the subject and research personnel. Compliance with the schedule will be determined through use of wrist actigraphy (Actiwatch 2, Philips Respironics) and concomitant sleep logs. Wrist actigraphy is a validated, low burden technique for estimating the timing of sleep and wake. The Actiwatch 2 is a small device (16 g) about the size of a standard wrist watch that collects data on three dimensional movement using a piezoelectric accelerometer (sample rate = 32 Hz, sensitivity = 0.025 G). It includes a silicon photodiode for detection of ambient illumination ($\nu\lambda$ filtration for photopic sensitivity, 5-100,000 lux range) and an event marker that the subject will be instructed to press when entering and exiting bed. It has a rechargeable lithium battery and will be set to collect data as the integrated movement occurring during 30 second intervals. On-board memory with these settings is sufficient for 15 days of recording. The Actiwatch 2 is waterproof and subjects will be instructed to wear the Actiwatch continuously, including during bathing. Using the automated sleep scoring software that comes bundled with the Actiwatch 2 (Actiware 5, Philips Respironics), the actigraph illuminance data, and the self-reported sleep diaries, at-home sleep patterns can be accurately assessed. Upon entry to the laboratory at the end of the one-week phase/amplitude stabilization protocol, compliance with the sleep schedule will be verified. Subjects who were unable to maintain the required sleep schedule will be disempaneled or rescheduled. Otherwise, the average bed and wake times will be calculated (removing up to two variant times) and the midpoint calculated. This will be the midpoint of the subject's 8 hour in-lab sleep opportunity in the dark.

After the one-week, at-home protocol, subjects will come to the laboratory three hours before their scheduled bed time. Following confirmation of their at-home sleep schedule, subjects will produce a

urine and saliva sample. Urine will be tested for the presence of common illegal drugs (cocaine, tetrahydrocannabinol, methamphetamine; DrugCheck3, Express Diagnostics; result in 5 minutes) and saliva will be tested for the presence of alcohol (Chematics, Alco-Screen 02; result in 4 minutes). The presence of illegal drugs or alcohol (>0.02% blood alcohol content) will result in dispanelment. Other than indicating in the medical record that the subject was dispaneled for cause, no other record of the drug and alcohol tests will be kept. Cleared subjects will be brought to the Stanford University/VA Palo Alto Health Care System Sleep and Circadian Translational Research Laboratory (SCTRL). During their entire stay at the SCTRL, subjects will remain in a time isolation suite (no windows, no clocks or other time cues, *en suite* bathroom, regulated temperature of 70 °F, all lighting controlled from outside the suite). Upon entry into the SCTRL until the subject leaves the next morning, illuminance is kept at normal room lighting (~150 lux in any angle of gaze) except during hours of scheduled darkness (<0.03 lux) and the 13-minute experimental light stimulus. In the SCTRL, the floors are white and the walls are painted with a white, titanium dioxide-based paint that increases luminosity and ensures a relatively even illuminance across the room.

After entry into the SCTRL, subjects will have a baseline testing sequence: Stanford Sleepiness Scale (subjective sleepiness), visual acuity testing, peripheral vision testing, mobile balance testing (walking on a specialized, pressure-sensing walkway), Karolinska Drowsiness Task (EEG monitoring of drowsiness), mobile balance testing, auditory version of the Psychomotor Vigilance Test (objective alertness), a five minute break while seated, and the sequence repeated. During this testing, brain wave activity (electroencephalogram, electromyogram) and eye movements (wireless eye tracking) will be monitored. This will serve as a baseline test to account for interindividual variability. Subjects will go to sleep at their habitual bed time (calculation described above).

After 2 hours in darkness subjects, will be awakened by the technician into one of the three experimental lighting conditions (dim white light, room light, dim orange light) and be kept awake for 13 minutes. Subjects will be tested with the same sequence as at baseline. Following the 13-minute experimental light exposure, subjects will be allowed to sleep in darkness until their typical wake time. Upon awakening, subjects will be given a subjective test of alertness (Stanford Sleepiness Scale), an objective test of alertness (Psychomotor Vigilance Test), and a questionnaire regarding the previous night of sleep (Groningen Sleep Quality Questionnaire). They will then be provided a standard hospital breakfast and discharged.

Exposure to the experimental light will always start two hours after habitual bedtime and last 13-minutes. The first two conditions, very dim white light (0.5 lux, low mesopic range) and dim white room light (5 lux). The illuminance will be confirmed with a photometer (IL1700, International Light, Peabody MA). The orange light condition will be produced by filtering the fluorescent lamps with an acrylic filter (Roscolux #19 "Fire", Roscolux, Glendale CA) so as to produce 1×10^{13} photons \cdot cm $^{-2}$ \cdot s $^{-1}$ or an equivalent LED light.

As a follow-up to this original protocol, subjects who completed all three of the visits previously described, and who indicated a willingness to be recontacted, will be asked to sign a new consent form and participate in a single overnight visit (with preceding at-home sleep monitoring) identical to the described, except that they will be awoken into normal room light (150 lux).