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Chronotype Influences Diurnal Variations in the Excitability of the Human Motor Cortex and the Ability to Generate Torque during a Maximum Voluntary Contraction

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Abstract The ability to generate torque during a maximum voluntary contraction (MVC) changes over the day. The present experiments were designed to determine the influence of an individual's chronotype on this diurnal rhythm and on cortical, spinal, and peripheral mechanisms that may be related to torque production. After completing a questionnaire to determine chronotype, 18 subjects (9 morning people, 9 evening people) participated in 4 data collection sessions (at 09:00, 13:00, 17:00, and 21:00) over 1 day. We used magnetic stimulation of the cortex, electrical stimulation of the tibial nerve, electromyographic (EMG) recordings of muscle activity, and isometric torque measurements to evaluate the excitability of the motor cortex, the spinal cord, and the torque-generating capacity of the triceps surae (TS) muscles. We found that for morning people, cortical excitability was highest at 09:00, spinal excitability was highest at 21:00, and there were no significant differences in TS EMG or torque produced during MVCs over the day. In contrast, evening people showed parallel increases in cortical and spinal excitability over the day, and these were associated with increased TS EMG and MVC torque. There were no differences at the level of the muscle over the day between morning and evening people. We propose that the simultaneous increases in cortical and spinal excitability increased central nervous system drive to the muscles of evening people, thus increasing torque production over the day. These differences in cortical excitability and performance of a motor task between morning and evening people have implications for maximizing human performance and highlight the influence of chronotype on an individual's diurnal rhythms.

Key words chronotype, diurnal rhythm, human, motor cortex, transcranial magnetic stimulation, reflex, central nervous system, spinal cord

It is well documented that the ability to generate torque during maximum voluntary contractions (MVCs)

changes over the day. These diurnal rhythms in torque production have been shown for a variety of muscles,

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including the triceps surae (TS; Castaingts et al., 2004; Guette et al., 2006; Guette et al., 2005a; Lagerquist et al., 2006), quadriceps femoris (Callard et al., 2000; Guette et al., 2005b; Sedliak et al., 2008), biceps brachii (Freivalds et al., 1983; Gauthier et al., 1996; Gauthier et al., 2001), and adductor pollicis (Martin et al., 1999). Although diurnal rhythms in maximum torque production are well known, there are discrepancies in the reported amplitude and time course, and the underlying physiological mechanisms are poorly understood. Most human studies report that torque produced during MVCs peaks in the evening (Callard et al., 2000; Castaingts et al., 2004; Gauthier et al., 1996; Guette et al., 2005b; Lagerquist et al., 2006; Martin et al., 1999); however, 2 studies have shown the opposite, with the acrophase of torque production occurring in the morning (Guette et al., 2005a; Guette et al., 2006). Often overlooked in the design of such studies is an individual's chronotype. Chronotype refers to the attributes of a person that define him or her as either a "morning person" or an "evening person" (Horne and Östberg, 1976), and it influences diurnal rhythms in body temperature (Foret et al., 1982), free cortisol levels (Kudielka et al., 2006), self-reported alertness (Kerkhof et al., 1980), sleep behavior (Lehnkering and Siegmund, 2007; Mongrain and Dumont, 2007), and performance of some tasks (Brown et al., 2008; Carrier and Monk, 2000; Schmidt et al., 2007). A few studies designed to investigate diurnal rhythms in torque production have considered chronotype as a possible confounding variable (Castaingts et al., 2004; Gauthier et al., 1996; Guette et al., 2006; Martin et al., 1999; Sedliak et al., 2008), but to our knowledge, only 4 studies tried to control for it. Castaingts et al. (2004) tested only subjects who were intermediate between morning and evening types ("neither types"), while Gauthier et al. (1996) and Martin et al. (1999) tested a majority of neither types with a few morning types. These studies found that torque produced during an MVC increased from morning to evening. Only Sedliak et al. (2008) studied the ability of morning and evening people to generate maximum torque. However, data from the morning people and evening people were not compared to one another but rather to data from neither types. Although they found no influence of chronotype on the ability to generate torque (Sedliak et al., 2008), the influence of chronotype was not the focus of their study, and the comparison to the "neither" group may have been underpowered due to the limited number of morning ($n = 5$) and evening ($n = 4$) types. Thus, it is still unclear whether chronotype influences the ability

to generate torque during an MVC. We suggest that the variability in amplitude and time course of the diurnal rhythm in torque production could be explained by the chronotype of the participants, as different studies may have had different proportions of morning people and evening people.

The ability to generate torque during an MVC depends on the force-generating capacity of the muscle as well as the ability of the central nervous system (CNS) to activate the muscle maximally. It has been suggested that elevated body temperatures over the day will increase the force-generating capacity of the muscle and that this may be responsible for diurnal variations in torque generation (Bernard et al., 1998; Reilly and Down, 1992). However, this is unlikely as diurnal changes in body temperature (~ 0.8 °C in trough-to-peak variation; Gauthier et al., 1996; Reilly and Down, 1992) are much smaller than the temperature changes needed to alter isometric muscle function (>5 °C; Bergh and Ekblom, 1979; Ranatunga et al., 1987). Changes in body temperature can also affect neural function (Abrams and Pearson, 1982; Bigland-Ritchie et al., 1992), although it is not yet established how such diurnal rhythms in temperature may affect the control of human movement. In summary, evidence thus far suggests that diurnal variation in performance is affected by factors other than body temperature alone (Reilly et al., 2007). While there is evidence that changes in muscle contractile properties—namely, inorganic phosphate levels—lead to changes in torque production (Guette et al., 2005b; Martin et al., 1999), there is also evidence that changes in CNS drive to the muscle account for diurnal changes in torque (Callard et al., 2000; Guette et al., 2005a; Guette et al., 2006; Lagerquist et al., 2006).

The goals of the present experiments were 2-fold. First, we wanted to assess the influence of chronotype on diurnal rhythms in maximal torque production. Thus, we compared the peak torque generated during plantar-flexion MVCs performed throughout the day between subjects classified as morning people and evening people. We hypothesized that morning people would produce more torque in the morning (09:00) than in the evening (21:00) and that the converse would be true of evening people. Second, we sought to investigate mechanisms that underlie diurnal patterns in plantar-flexion torque production and determine whether they were different for people of different chronotype. We used magnetic stimulation of the motor cortex, electrical stimulation of the tibial nerve, electromyographic

(EMG) recordings of muscle activity, and torque measurements during MVCs to evaluate cortical excitability, spinal excitability, and the torque generated by the TS muscles. We hypothesized that changes in the excitability of the motor cortex and spinal cord would mirror patterns in torque production (i.e., increased excitability at 9:00 for morning people and at 21:00 for evening people). We did not expect to find changes at the level of the muscle over the day since previous studies have found no such changes for the muscles that plantar-flex the ankle (Guette et al., 2006; Lagerquist et al., 2006).

METHODS

Subjects and Chronotype Assessment

Twenty-three healthy volunteers free of neurological deficits participated after providing informed written consent. All procedures were approved by the Human Research Ethics Board at the University of Alberta. Subjects (7 female, 16 male; aged 19-54 years) completed a self-assessment morningness-eveningness questionnaire (MEQ; Horne and Östberg, 1976) to determine their chronotype. The MEQ consists of 19 questions and generates a score between 16 and 86. Scores above 58 classify individuals as morning type, scores below 42 classify individuals as evening type, and scores from 42 to 58 classify individuals as neither type. MEQ scores for our subjects ranged from 27 to 69. Subjects classified as "neither type" ($n = 5$; MEQ score 48 ± 1 ; mean \pm SE) were excluded from further participation. The rest of the subjects were split into 2 groups: morning types ($n = 9$; MEQ score 64 ± 2) and evening types ($n = 9$; MEQ score 36 ± 2). The morning group consisted of 6 males and 3 females (age 28 ± 4 years), while the evening group had 8 males and 1 female (age 24 ± 2 years). The ages of the subjects in the 2 groups were not significantly different (Student's t test, $p > 0.05$).

Protocol

All experimental procedures were performed on the right leg. Subjects were seated in the chair of a Biodex System 3 Dynamometer (Biodex Medical Systems, Shirley, New York) with the right hip, knee, and ankle at 90, 120, and 90 degrees, respectively (Figure 1A). The right ankle and foot were tightly secured to the footplate of the Biodex to measure

isometric plantar-flexion torque. Surface EMG was recorded from the right soleus (SOL), lateral gastrocnemius (LG), medial gastrocnemius (MG), and tibialis anterior (TA) muscles using bipolar (2.25 cm²) recording electrodes (Vermed Medical, Bellows Falls, Vermont), as shown in Figure 1B. Electrodes were outlined on the skin with a felt marker at the beginning of each experiment and were replaced throughout the day when necessary (i.e., due to drying or loss of adhesion). EMG signals were preamplified (500-2000 \times) and band pass filtered at 30 to 3000 Hz (NeuroLog system; Digitimer, Hertfordshire, England). All data were sampled at 2000 Hz with a 12-bit A/D converter (PCI-MIO-16E-4, National Instruments, Austin, Texas).

One or 2 days prior to the main data collection day, subjects participated in a 2-hour familiarization session (Figure 1C). On the main data collection day, data were collected over four 1.25-hour testing sessions (Figure 1D) starting at 09:00, 13:00, 17:00, and 21:00. Subjects were asked to sleep for their normal amount of time and to wake up at least 2 hours prior to the familiarization session and the first testing session at 09:00. Subjects were also asked to avoid caffeine consumption for 12 hours prior to and throughout the experiments to eliminate the possible effects of caffeine on CNS excitability (Walton et al., 2003). On the day of testing, subjects verbally confirmed their adherence to the above guidelines and limited their activity to nonstrenuous activities such as walking, typing, and writing.

Maximum Voluntary Isometric Contractions with Interpolated Twitches

Subjects performed 3 MVCs of the right plantar-flexors at the beginning of the familiarization session and each testing session on the main data collection day. Each MVC lasted approximately 3 sec and was separated from the previous maximal effort by at least 3 min. Subjects were provided with visual feedback of their torque production and received verbal encouragement to perform maximally. The interpolated twitch technique (ITT) was used to estimate the degree of voluntary muscle activation during the MVCs (Merton, 1954). Pulses of electrical stimulation (1 msec duration; Digitimer DS7A, Hertfordshire, England) were delivered to the tibial nerve in the popliteal fossa (Figure 1B) prior to ($n = 3$), during ($n = 2$), and after ($n = 3$) each MVC. Stimulus intensity was set at 1.5 times the threshold current required to elicit a maximal

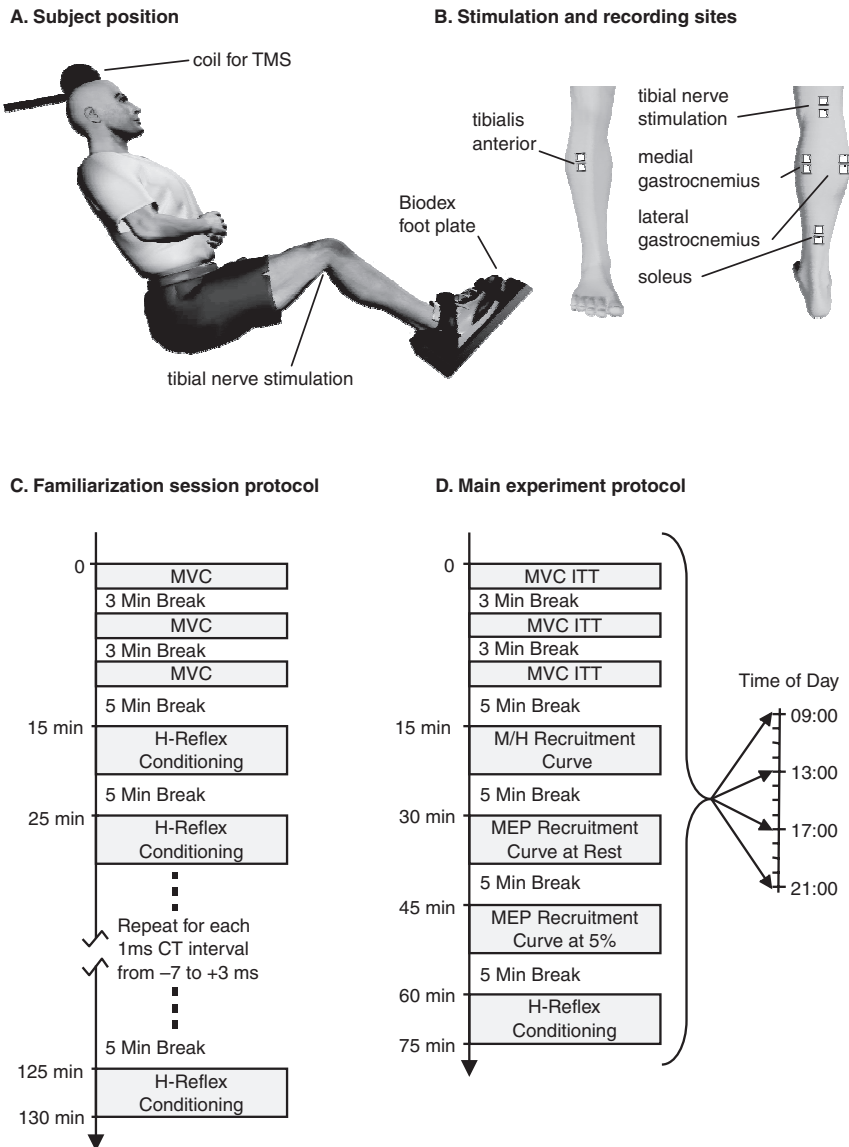


Figure 1. Schematic of experimental protocol. Panel A shows the position of the subject in the Biodex system and the stimulation sites. Panel B shows the location of the electrodes for electromyographic (EMG) recordings and tibial nerve stimulation. In Panel C, the order of trials for the familiarization session is shown, where MVC is maximum voluntary contraction and CT interval is conditioning-test interval. Panel D shows the experimental protocol for the main data collection day, where MVC ITT is maximum voluntary isometric contraction with interpolated twitch technique, and an MEP is a motor-evoked potential. Times shown are approximate.

M-wave (M_{max}) in SOL, and the interstimulus interval was approximately 1 sec.

H-Reflex versus M-Wave Recruitment Curves

SOL H-reflex versus M-wave recruitment curves were constructed from responses to 60 stimuli delivered to the tibial nerve in the popliteal fossa. The

interstimulus interval was varied randomly between 3 and 5 sec, and the stimulation intensity varied from below threshold for both M-wave and H-reflex responses to 2 to 3 times the minimum intensity required to evoke M_{max} . Stimuli were delivered while subjects maintained a contraction that was 5% of their maximal SOL EMG to ensure a consistent activation of the motor pool across sessions. The 5% background EMG was determined from the average EMG in the 3 preceding MVC trials. SOL EMG was rectified, low pass filtered at 0.3 Hz, and displayed on a monitor to provide feedback to the subjects so they could hold the 5% MVC contraction.

Motor-Evoked Potential Recruitment Curves and Threshold

Motor-evoked potentials (MEPs) were elicited using a transcranial magnetic stimulator (TMS; Magpro R30; Medtronic Inc., Minneapolis, Minnesota, Minnesota) with a figure-of-8 coil (Medtronic MC-B70, Minneapolis, Minnesota). The position and orientation of the coil (Figure 1A) were adjusted to find the location at which clear ($\sim 50 \mu\text{V}$) SOL MEPs were generated at the lowest stimulus intensity while subjects held a tonic 5% of maximal

SOL EMG background contraction. This coil position and orientation were guided and recorded by a magnetic resonance image-guided TMS system (Brainsight; Rogue Research, Montreal, Quebec). Using this system, we were able to place the TMS coil to within 3 mm of this optimal position during every trial. Two MEP recruitment curves, one with the subject at rest and one with the subject holding a

5% SOL contraction, were collected during each testing session (Figure 1D). However, MEP recruitment curves could not be constructed for 14 of 18 subjects as maximal MEPs could not be evoked at maximum stimulator output. Therefore, these data were excluded from the present study, and the methodology is not described further here. MEP threshold was determined while subjects held a contraction of 5% of SOL MVC as described above. Stimulator output was adjusted manually in steps of 1% of maximal output.

TMS H-Reflex Conditioning

Subthreshold TMS was used to condition (facilitate) the SOL H-reflex while subjects held a SOL contraction of 5% maximal EMG as described above. The intensity of the TMS was set to $0.95 \times$ MEP threshold (Petersen et al., 1998), and the tibial nerve stimulation was delivered to evoke an H-reflex of 15% to 20% M_{\max} . The earliest conditioning-test (CT) interval at which the TMS significantly facilitated the H-reflex was determined during the familiarization session when CT intervals from -7 to $+3$ msec were examined in 1-msec increments (Figure 1C). Negative CT intervals indicate that the TMS was applied after tibial nerve stimulation. At each CT interval, 15 control H-reflexes (no TMS) and 15 conditioned H-reflexes were collected. The interstimulus interval was varied randomly between 6 and 8 sec. On average, the earliest CT interval that facilitated the H-reflex was -3.4 ± 0.4 (range, -6 to -1 msec), consistent with previous studies (Carroll et al., 2006; Morita et al., 2000; Petersen et al., 1998).

For each subject, the earliest CT interval that facilitated the H-reflex during the familiarization session was used on the main data collection day to ensure that the H-reflex was being facilitated via the fast-conducting monosynaptic corticomotor neuronal pathway as described by Morita et al. (2000) and Nielsen et al. (1993). During each testing session, 20 control and 20 conditioned H-reflexes were collected. The order of the control and conditioned trials was randomized, and the interstimulus intervals varied randomly between 6 and 8 sec. Since the influence of the conditioning volley varies with the size of the control H-reflex (Crone et al., 1990), we ensured that the control H-reflex was the same relative size in all subjects (15% - 20% M_{\max}), occurred on the ascending limb of the H-reflex versus M-wave recruitment curve, and was not maximal. If necessary, tibial nerve

stimulation intensity for a given subject was adjusted to evoke a control H-reflex of the same amplitude (as a percentage of M_{\max}) during each testing session.

Data Analyses

Torque during Plantar-Flexion MVCs

Maximal torque was calculated from each MVC by averaging the torque produced over a 0.5-sec period centered on the maximum that was not contaminated by small deviations in torque associated with the ITT stimulation. The average of the 3 MVC trials performed at each time of day was taken as the maximum torque production.

General Measures of Muscle Activation

Using the ITT, percent activation (ACT %) was calculated using the equation described by Folland and Williams (2007): $ACT (\%) = MVF/TMF \times 100$. MVF is the maximum voluntary force generated during the MVC. TMF (true maximum force—the theoretical maximum force the muscle can generate) was calculated as the MVF multiplied by the reciprocal of 1 minus the ratio of “extra” force evoked by the supra-maximal stimuli delivered during the MVC to the force evoked when the same stimuli were delivered after the MVC (i.e., at rest; Gandevia et al., 1998).

The amount of EMG activity recorded during the MVCs was calculated for each of the 3 components of the TS (LG, MG, SOL). For each muscle, the average rectified EMG recorded during each MVC was quantified over a 0.5-sec period at a point when the torque was maximal and the EMG was not contaminated by a stimulus artifact associated with the ITT stimulation. Data for each muscle were normalized to the amplitude of the corresponding M_{\max} to account for the potential changes in impedance at the recording site over the day. The sum of the values obtained for each muscle was calculated and used as the total TS EMG. TA EMG during the plantar-flexion MVCs was quantified as an indicator of antagonist muscle activation.

Cortical Excitability

H-reflex facilitation was expressed as the ratio of the average amplitude of conditioned H-reflexes to control H-reflexes. This way, values greater than 1 indicate facilitation of the H-reflex, and values

less than 1 indicate inhibition of the H-reflex. MEP threshold was defined as the lowest stimulation intensity at which MEPs of greater than 50 μ V were evoked in response to 4 of 8 stimuli (Carroll et al., 2001).

Spinal Excitability

M-waves and H-reflexes were measured peak-to-peak and were normalized to each subject's M_{\max} . Two measures of spinal excitability were calculated from each H-reflex versus M-wave recruitment curve: $H_{\max}:M_{\max}$ ratio and H versus M recruitment curve slope. H_{\max} was calculated by averaging the 3 largest H-reflexes, and M_{\max} was taken to be the single largest M-wave. The slope of the ascending limb of the recruitment curve was calculated by fitting a sigmoid curve through the data between H threshold and the first occurrence of H_{\max} . The slope of the linear portion of the curve was used for the slope of the recruitment curve.

Peripheral Measures

M_{\max} was calculated as the average peak-to-peak EMG amplitude of the M-waves evoked by 9 supra-maximal stimuli applied before each MVC at each time of day. Peak torque produced during each of these M_{\max} twitches was also measured and averaged. Neuromuscular efficiency (NME) was calculated as the ratio of maximum torque during MVCs to TS EMG, as described by Castaingts et al. (2004).

Statistics

Data were tested for normality using Kolmogorov-Smirnov and Lilliefors tests. Separate 2×4 (Chronotype \times Time of Day) repeated-measures analysis of variance (ANOVA) tests were used to examine dependent variables that were normally distributed (plantar-flexion torque, H-reflex facilitation, MEP threshold, $H_{\max}:M_{\max}$, H-reflex versus M-wave recruitment curve slope, M_{\max} amplitude, M_{\max} twitch torque, EMG, and NME). Tukey's HSD tests were used for post hoc comparisons when appropriate. We were interested in the main effect of time (combining morning and evening people) to assess trends that were common to both groups and to enable comparisons to studies that did not account for chronotype. We were also interested in the Chronotype \times Time interaction to test the hypotheses outlined earlier. We

do not report in the Results on the main effect of chronotype as this was not part of our research question. However, there was never a significant main effect of chronotype for any of the ANOVAs that were performed. A Friedman test was used to evaluate the percent activation data because the data were not normally distributed. All data are presented as means \pm standard errors. The significance level for all tests was set at $p < 0.05$.

RESULTS

Data collected at 09:00 and at 21:00 from a subject identified as an evening person (MEQ score of 37) are shown in Figure 2. Panel A shows the average plantar-flexion torque and EMG recorded from MG, LG, and SOL during the 3 MVCs performed at 09:00 and 21:00. This subject generated 34% more torque during the evening session than the morning, and this was associated with an increase (26%) in total TS EMG. Panel B shows that the amount of facilitation of the H-reflex induced by the subthreshold TMS (a measure of cortical excitability) was larger in the evening (59%) than in the morning (25%). The same subject showed an increase in the slope of the H-reflex versus M-wave recruitment curve (a measure of spinal excitability) from morning to evening (panel C). Panel D shows the average torque produced from 9 M_{\max} stimulations and the peak-to-peak EMG amplitude of these M-waves.

Torque Produced during Plantar-Flexion MVCs

The ANOVA analyses identified a main effect of time on torque produced during MVCs, $F(3, 48) = 8.2$, $p = 0.0002$, and the post hoc test showed that on average for the group of 18 subjects, there was significantly more (9%; $p = 0.0003$) plantar-flexion torque produced during an MVC at 21:00 (86 ± 9 Nm) than at 09:00 (79 ± 7 Nm), as shown in Figure 3A. Similarly, there was more torque (7%; $p = 0.004$) at 17:00 than at 09:00. There was also a Chronotype \times Time interaction, $F(3, 48) = 4.9$, $p = 0.005$, and when separated by chronotype, only evening people demonstrated a significant diurnal rhythm in torque production (Figure 3B). Evening people generated more torque at 21:00 (13%; $p = 0.0002$) and 17:00 (8%; $p = 0.04$) than at 09:00 and at 21:00 (11%; $p = 0.002$) than at 13:00. In contrast, the torque produced by morning people did not change significantly over the day.

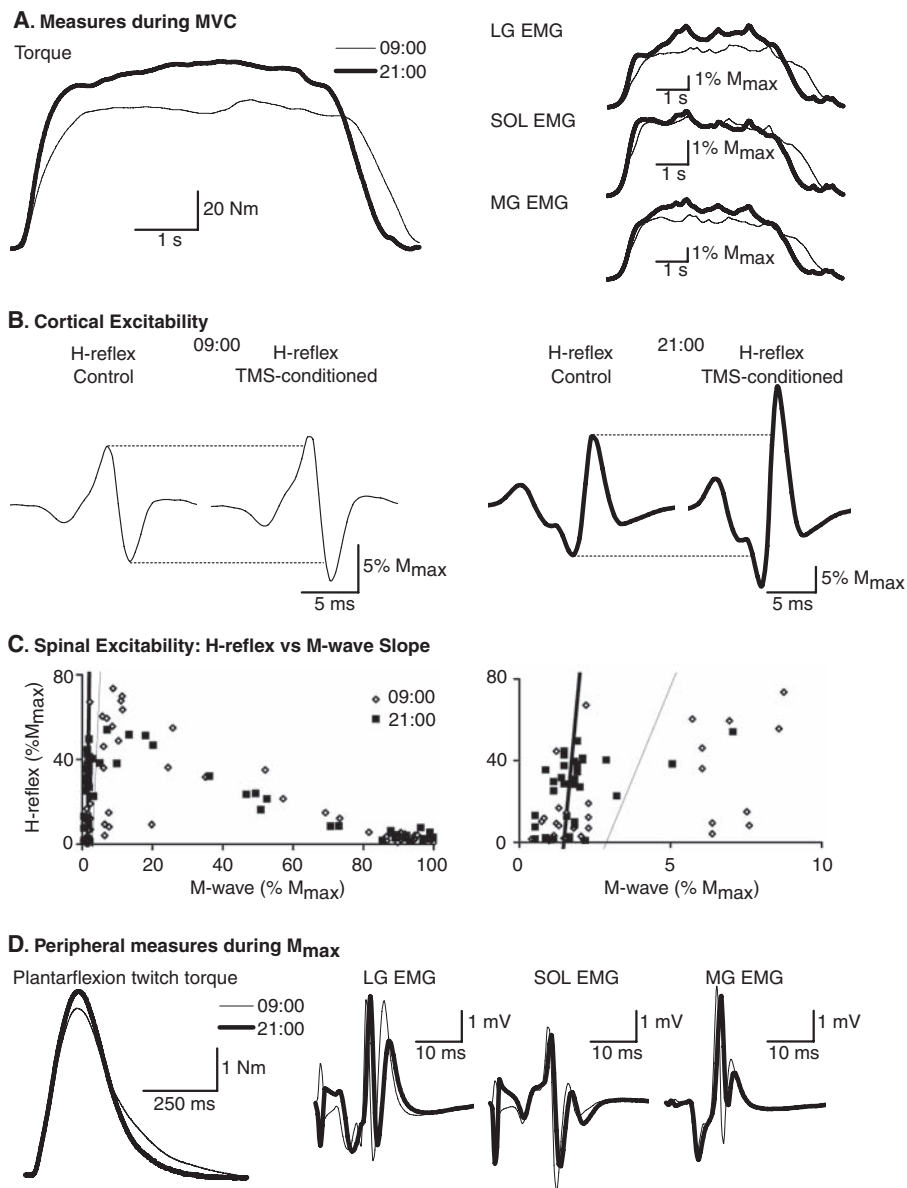


Figure 2. Data collected from an individual subject at 09:00 and 21:00. Panel A shows torque and electromyographic (EMG) measurements made during the maximum voluntary contractions (MVCs) in each session. Panels B to D show measures of cortical, spinal, and peripheral excitability, respectively.

General Measures of Muscle Activation

There was no change in the percent activation of the plantar-flexor muscles over the day, as evaluated by the ITT for the entire group of 18 or when separated by chronotype (Friedman test). The mean percent activation of the entire group varied between $98\% \pm 1\%$ and $99\% \pm 1\%$ over the day. Seven of the

18 subjects (4 evening people, 3 morning people) were fully activated at every testing session throughout the day.

There was no main effect of time on the total TS EMG recorded during the MVCs, $F(3, 48) = 2.7$, $p = 0.06$, indicating that this measure did not change significantly over the day for the group of 18 subjects. There was, however, a significant Chronotype \times Time interaction, $F(3, 48) = 7.3$, $p = 0.0004$. Total TS EMG increased significantly over the day for evening people (Figure 4A), and similar to torque (Figure 3B), TS EMG was larger at both 17:00 ($p = 0.047$) and 21:00 ($p = 0.0003$) compared to 09:00. There were no differences in TS EMG recorded during the MVCs throughout the day for morning people.

The EMG data recorded during the MVCs were also analyzed separately for each of the TS muscles. There was no main effect of time, $F(3, 48) = 1.1$, $p = 0.37$, or Chronotype \times Time interaction, $F(3, 48) = 2.4$, $p = 0.08$, for the EMG recorded from SOL. For LG, there was no main effect of time, $F(3, 48) = 0.2$, $p = 0.92$, but there was a significant Chronotype \times Time interaction, $F(3, 48) = 2.9$, $p = 0.04$; however, no significant differences were identified by the post hoc tests. Thus, EMG recorded from SOL and LG during the MVCs did not

change significantly throughout the day. In contrast, there was a main effect of time on the EMG recorded from MG, $F(3, 48) = 4.8$, $p = 0.005$. MG EMG for the entire group was significantly greater at 17:00 ($p = 0.03$) and 21:00 ($p = 0.02$) than at 09:00. There was also a significant Chronotype \times Time interaction, $F(3, 48) = 4.8$, $p = 0.005$; evening people had more MG EMG at 21:00 compared to 09:00 ($p = 0.0007$) and

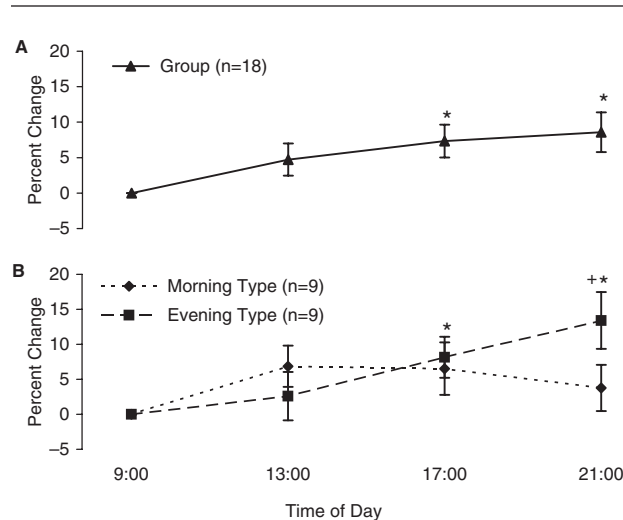


Figure 3. Diurnal changes in maximal torque produced during maximum voluntary contractions (MVCs) over the day. Panel A shows data averaged across the group of 18 subjects, and panel B shows the data averaged across the morning ($n = 9$) and evening ($n = 9$) types. Asterisks indicate significant differences from the 09:00 testing session, and the plus sign indicates a significant difference from the 13:00 testing session.

13:00 ($p = 0.03$), while morning people showed no change over the day (Figure 4B). EMG recorded from the antagonist (TA) during the plantar-flexion MVCs showed a main effect of time, $F(3, 48) = 2.8, p = 0.049$, but the post hoc test did not identify any significant differences. There was also a Time \times Chronotype interaction, $F(3, 48) = 6.3, p = 0.001$. Morning people showed significantly more TA EMG at 09:00 ($67 \mu\text{V}$) than at 17:00 ($54 \mu\text{V}; p = 0.01$) or 21:00 ($53 \mu\text{V}; p = 0.002$).

Cortical Excitability

There was a main effect of time, $F(3, 48) = 7.4, p = 0.0004$, on the amount of facilitation of the H-reflex induced by the TMS conditioning. For the group of 18 subjects, the facilitation at 09:00 (1.27 ± 0.07) was significantly greater ($p < 0.004$) than at 13:00 (1.09 ± 0.05) and 17:00 (1.07 ± 0.002 ; Figure 5A). There was also a Time \times Chronotype interaction, $F(3, 48) = 10.5, p = 0.00002$, and morning and evening people showed opposite trends. Morning people peaked at 09:00, while evening people peaked at 21:00 (Figure 5B). Specifically, the facilitation at 09:00 for the morning group (1.41 ± 0.11) was significantly larger than all other times of day ($p < 0.0008$), and the facilitation for the evening group was larger at 21:00 (1.36 ± 0.08)

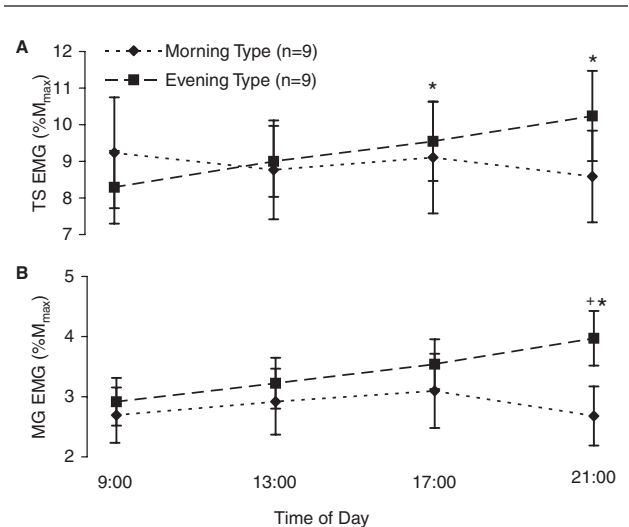


Figure 4. Diurnal changes in triceps surae (TS) and medial gastrocnemius (MG) electromyogram (EMG) recorded during maximum voluntary contractions (MVCs) over the day. Panels A and B show the TS EMG and MG EMG data, respectively, averaged across the morning ($n = 9$) and evening ($n = 9$) types. Asterisks indicate significant differences from the 09:00 testing session, and plus signs indicate a significant difference from the 13:00 testing session.

than all other times ($p < 0.05$). The size of the control H-reflexes did not change significantly throughout the day as there was no main effect of time, $F(3, 48) = 0.54, p = 0.66$, or Time \times Chronotype interaction, $F(3, 48) = 0.37, p = 0.77$.

MEP threshold did not change over the day for the combined group (time: $F(3, 48) = 1.6, p = 0.20$) or either chronotype group (Chronotype \times Time: $F(3, 48) = 0.2, p = 0.88$). For the combined group, threshold ranged from $48\% \pm 2\%$ to $52\% \pm 2\%$ of maximum stimulator output over the day.

Spinal Excitability

There was a main effect of time, $F(3, 48) = 7.2, p = 0.0004$, on the slope of the H-reflex versus M-wave recruitment curve as the slope was significantly steeper at 21:00 compared with all other testing sessions ($p < 0.03$; Figure 6A). There was no significant Chronotype \times Time interaction, $F(3, 48) = 1.7, p = 0.18$, and thus the changes in spinal excitability over the day were not significantly different for the 2 chronotype groups (Figure 6B).

The $H_{\text{max}}:M_{\text{max}}$ ratio did not display a significant main effect of time, $F(3, 48) = 0.2, p = 0.92$, or Time \times Chronotype interaction, $F(3, 48) = 1.0, p = 0.38$. The

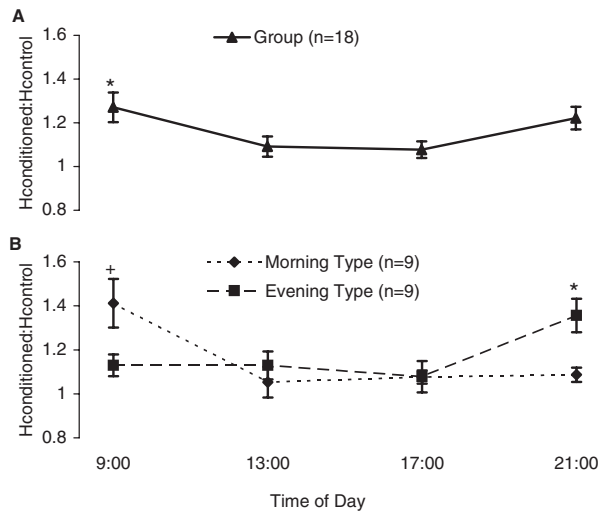


Figure 5. Diurnal changes in cortical excitability measured using transcranial magnetic stimulator (TMS) conditioning of the H-reflex. Panel A shows data averaged across the group of 18 subjects, and panel B shows the data averaged across the morning ($n = 9$) and evening ($n = 9$) types. The asterisk in panel A indicates significant differences from the 13:00 and 17:00 testing sessions. The asterisk in panel B indicates significant differences from the 09:00, 13:00, and 17:00 testing sessions, and the plus sign indicates significant differences from the 13:00, 17:00, and 21:00 testing sessions.

ratio ranged between 0.66 ± 0.04 and 0.67 ± 0.03 over the day for the group of 18 subjects.

Peripheral Measures

SOL M_{\max} EMG amplitude did not change over the day (time: $F(3, 48) = 0.6, p = 0.62$; Chronotype \times Time: $F(3, 48) = 1.1, p = 0.35$) and ranged from 8.4 ± 0.8 mV at 21:00 to 8.7 ± 1.0 mV at 09:00 for the combined group. LG M_{\max} amplitude was also stable across sessions (time: $F(3, 48) = 0.1, p = 0.96$; Chronotype \times Time: $F(3, 48) = 1.6, p = 0.21$) and varied between 7.2 ± 0.5 mV and 7.3 ± 0.6 mV for the group of 18 subjects. There was a significant effect of time, $F(3, 48) = 4.1, p = 0.01$, on MG M_{\max} amplitude but no interaction, $F(3, 48) = 1.6, p = 0.20$. Across the group of 18 subjects, MG M_{\max} was significantly larger at 9:00 (8.3 ± 0.5 mV) compared to 21:00 (7.5 ± 0.6 mV; $p = 0.01$). M_{\max} twitch torque did not change from 8 ± 1 Nm at any time of day, and there was no main effect, $F(3, 48) = 1.1, p = 0.34$, or interaction, $F(3, 48) = 2.6, p = 0.07$. There was no significant main effect of time on NME, $F(3, 48) = 0.1, p = 0.99$ (range, 9.9 ± 1.0 to 10.0 ± 0.9 Nm/% M_{\max}). Although there was a significant

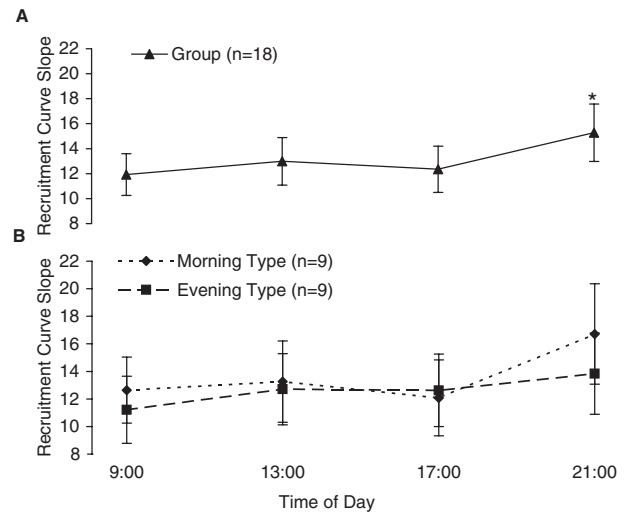


Figure 6. H-reflex versus M-wave recruitment curve slope over the course of the day. Panel A shows data averaged across the group of 18 subjects, and panel B shows the data averaged across the morning ($n = 9$) and evening ($n = 9$) types. The asterisk indicates a significant difference from all other testing sessions.

interaction, $F(3, 48) = 2.9, p = 0.045$, the post hoc test identified no significant differences.

DISCUSSION

In this study, we show for the first time that a person's chronotype—whether he or she is a morning person or an evening person—influences that person's ability to generate torque during an MVC. Evening people generated more torque in the evening than in the morning, while for morning people, torque did not change over the day. We also identify, for the first time, diurnal rhythms in the excitability of the human motor cortex and show that these rhythms are also influenced by chronotype; cortical excitability was highest at 09:00 for morning people and at 21:00 for evening people. Overall, we found that for morning people, cortical excitability decreased and spinal excitability increased from morning to evening, while there were no differences in TS EMG or torque during MVCs. For evening people, concurrent increases in cortical and spinal excitability were associated with increased TS EMG and torque. We propose that for evening people, simultaneous increases in cortical and spinal excitability lead to increased CNS drive to the muscle and an increased ability to generate torque during an MVC.

Torque Produced during Plantar-Flexion MVCs

Most studies report that torque generated during an MVC increases between 3% and 18% from morning to evening (Callard et al., 2000; Castaingts et al., 2004; Gauthier et al., 1996; Guette et al., 2005b; Lagerquist et al., 2006; Martin et al., 1999), while 2 studies have reported decreases of 5% and 7% (Guette et al., 2005a; Guette et al., 2006). Across the group of 18 subjects (combining morning and evening people), our results were consistent with the majority of these studies as torque was greater (by 9%) in the evening than the morning. This increase, however, stemmed from evening types as their torque increased significantly from morning to evening, while torque produced by morning types did not change. Thus, diurnal variations in the ability to generate plantar-flexion torque may become larger with increasing eveningness (i.e., lower MEQ scores). Evening people in our study demonstrated the largest diurnal increase in torque at 13%, while in a previous study, "neither" types increased by 9% (Castaingts et al., 2004), and in our study, morning types did not change. The increased torque we observed for evening people supported our hypothesis, while the lack of a change for morning people did not. Consequently, the previous reports of maximum torque in the morning may not be due to chronotype. Instead, as the authors postulated, torque may have been reduced by fatigue as the physical activity of the participants was not controlled (Guette et al., 2005a; Guette et al., 2006). Sedliak et al. (2008) found no influence of chronotype on torque generated during MVCs, but this was not the focus of the study, and the experiments may have been underpowered.

General Measures of Muscle Activation

Presently, we used the ITT to assess the percent voluntary activation of the TS muscles during the MVC trials. If the stimulus evoked additional torque during the MVC, it would indicate that not all motor units were recruited. We found no change in TS activation over the day as all subjects were completely or nearly completely activated during all sessions. The high percent activation may reflect subject experience from the familiarization session and the fact that the TS is more easily maximally activated than larger muscle groups such as the quadriceps (Behm et al., 2002). This consistent activation contrasts with the decrease in activation over the day reported by Guette et al. (2006), providing further support that

the decline in maximal torque they observed may have been due to subject fatigue.

We also examined EMGs recorded from TS during MVCs as a general measure of CNS drive to the muscle. These data were normalized to the M_{\max} recorded for each muscle in each session to account for changes that might occur at the recording site over the day. Total TS EMG activity closely mirrored maximal torque production as it increased over the day (by 23%) for the evening people but did not change for morning people. Thus, in contrast to the ITT data, the EMG data suggest an increased CNS drive to the TS for the evening group, and this may have contributed to increased torque production. The ITT data suggest that all or nearly all TS motor units were recruited during the MVCs in all sessions; however, this technique may not be sensitive to changes in motoneuron firing frequency. Increased firing frequency, however, would be reflected in a larger EMG signal and could lead to greater torque production. In fact, TS EMG seems to be strongly related to maximal torque production as we show increased TS EMG and torque at 21:00 for evening people and no change in TS EMG or torque over the day for morning people. In addition, Guette et al. (2005a, 2006) showed that lower maximal plantar-flexion torque coincided with decreased TS EMG. When the EMGs recorded from the individual components of TS were examined separately, we found that SOL and LG EMG did not change over the day, while the MG EMG activity increased (34%) for the evening people only. Of the 3 TS muscles, enhanced activation of MG would have the greatest impact on torque as MG is the most powerful contributor to plantar-flexion torque (Kawakami et al., 1998). These EMG data suggest that diurnal rhythms in CNS control can vary between muscles that are close synergists and not only between muscles in the arms and legs as shown previously (Lagerquist et al., 2006). EMG activity recorded from the antagonist muscle (TA) during the MVCs was minimal but was higher for morning people at 09:00 than at 17:00 and 21:00 and did not change over the day for evening people. Thus, the increased plantar-flexion torque in evening people was not due to a concomitant decrease in dorsiflexion torque (see also Castaingts et al., 2004).

Cortical Excitability

The diurnal changes in our measures of cortical excitability reflect changes in the background excitability of the cortex over the day and not changes in

the ability to activate the cortex maximally during MVCs. One such measure was subthreshold TMS delivered over the motor cortex to facilitate the H-reflex. Subthreshold TMS activates corticospinal neurons by depolarizing cortical neurons that project onto corticospinal cells (Edgley et al., 1990, 1997). Since there are no known presynaptic gating mechanisms on corticospinal fibers in the spinal cord (Nielsen and Petersen, 1994), both the conditioned and control H-reflexes will be influenced equally by changes in spinal excitability. Therefore, a change in the amount of H-reflex facilitation has been attributed to a change in the excitability of cells in the motor cortex (Carroll et al., 2006; Mazzocchio et al., 1994; Petersen et al., 1998). The differences we observed in the TMS facilitation of the H-reflex over the day depended strongly on chronotype. Morning people had a peak in facilitation and thus cortical excitability at 09:00, while evening people peaked at 21:00. Whether these diurnal fluctuations are specific to the motor cortex or reflect a more general rhythm for cortical excitability merits further investigation; however, diurnal fluctuations in attention and cognitive performance (Matchock and Mordkoff, 2009; Schmidt et al., 2007) as well as diurnal changes in the electrical activity of the brain (Toth et al., 2007) suggest there may be a more global rhythm in cortical excitability.

We calculated MEP threshold as another measure of cortical excitability. A lower MEP threshold indicates increased cortical excitability, but we found no change throughout the day. This lack of change in MEP threshold, accompanied by the increased TMS facilitation of H-reflexes, may result from decreased intracortical inhibition by altered GABA or NMDA glutamate transmission. Ziemann et al. (1996) report that GABA-controlled circuits in the motor cortex change intracortical inhibition, while changes in ion channel conductivity alter MEP threshold. Hence, drugs that alter GABA (Ziemann et al., 1996) or NMDA glutamate transmission (Liepert et al., 1997; Ziemann et al., 1998) affect some measures of cortical excitability, but not MEP threshold (Teo et al., 2009). A diurnal increase in intracortical inhibition for morning people and a decrease for evening people could account for the change in H-reflex facilitation and the lack of change in MEP threshold presently observed for both groups.

Spinal Excitability

We found that spinal excitability, as measured by the slope of the ascending limb of the SOL H-reflex

versus M-wave recruitment curve, increased over the day regardless of chronotype. Hence, our data suggest that the previously identified diurnal rhythm in spinal excitability (Lagerquist et al., 2006) is independent of chronotype. We also used the $H_{\max}:M_{\max}$ ratio as a measure of spinal excitability and found that it did not change over the day. This is consistent with the findings of Castaingts et al. (2004) and Guette et al. (2005a) but contrasts with the findings of Lagerquist et al. (2006), who showed that the $H_{\max}:M_{\max}$ ratio increased over the day. While the H-reflex versus M-wave recruitment curve slope represents the sensitivity of the H-reflex to a given input, the $H_{\max}:M_{\max}$ ratio represents the maximum number of motor units that can be recruited by the electrically evoked afferent volley in the presence of antidromic block in some motor axons. Consequently, our data suggest that over the day, the gain (input-output relationship) of the H-reflex pathway increases regardless of chronotype, but the maximum number of motor units that can contribute to the H-reflex does not change (cf. Lagerquist et al., 2006). Whether these diurnal changes in reflex transmission are due to presynaptic changes in the gating of the afferent volley or postsynaptic changes in motoneuron excitability is currently unknown. Notably, 2 animal studies suggest that diurnal changes in the H-reflex are mediated by the corticospinal tract (Dowman and Wolpaw, 1989; Chen et al., 2002). If this were the case, we would expect our measures of spinal and cortical excitability to mirror one another as in the evening group. Since the morning group showed opposing trends, we suggest that humans may have a more complex regulation of the H-reflex.

Peripheral Measures

Despite increases in torque produced by evening people throughout the day, there were no measurable changes at the level of the muscle that could account for this increase. We used the peak-to-peak EMG amplitude of M_{\max} , the torque produced by these twitches, and NME as measures of muscle function. The amplitude of M_{\max} in the MG EMG was larger at 09:00 than at 21:00 for the group of 18 subjects, but there was no difference between morning and evening people, and thus this could not account for the differences in torque between these groups. The consistent peak torque generated by the twitch associated with M_{\max} shows that the torque-generating capacity of the muscle remained stable. We also used NME, the ratio of maximum torque to total TS EMG during the

MVCs, as another measure of the torque-generating capacity of the muscle. Despite increases in torque produced during MVCs, NME did not change over the day, which is consistent with previous studies examining the TS (Castaingts et al., 2004) and knee extensors (Sedliak et al., 2008). These data suggest that mechanisms responsible for increased torque in evening people are not at the level of the muscle but rather reside within the CNS. Diurnal changes within the adductor pollicis (Martin et al., 1999) and quadriceps femoris muscles (Guette et al., 2005b) have been reported to account for changes in torque production. Both studies found a change in the twitch force evoked at M_{\max} without a change in M_{\max} amplitude throughout the day. As a result, they proposed that changes in diurnal torque from morning to evening were due to changes in the muscle, specifically changes in inorganic phosphate concentration. Our data and other studies of the TS (Castaingts et al., 2004), on the other hand, show no changes in peripheral measures of muscle activation, suggesting that central mechanisms underlie changes in torque throughout the day.

Implications

On average, torque produced by evening people during an MVC increased 13% over the day and as much as 34% in 1 subject. As we did not detect any diurnal changes at the level of the muscle that could account for such an increase, we propose that increases in torque for evening people resulted from increased CNS drive to the muscle due to concomitant increases in spinal and cortical excitability. Similarly, we propose that torque produced by morning people did not change over the day due to opposing rhythms in cortical and spinal excitability. Our data suggest that evening people demonstrate the greatest diurnal fluctuations in performance of MVCs, while morning people perform more consistently but may never reach their true physiological maximum. Therefore, it may be advantageous for people to alter their diurnal rhythms (see Chen et al., 2008) depending on whether they wish to achieve maximum performance or greater consistency.

The extent to which our results can be generalized to other motor behaviors is not clear. Presently, it is well established that diurnal rhythms affect the ability to generate torque during simple isometric contractions (Callard et al., 2000; Castaingts et al., 2004; Gauthier et al., 1996; Guette et al., 2005b; Guette et al., 2006; Lagerquist et al., 2006; Martin et al., 1999). The evidence for diurnal rhythms in the performance of

more complex motor behaviors is less clear, with some studies showing no changes in performance over the day on a treadmill (Burgoon et al., 1992), cycle ergometer (Hill et al., 1988), or rowing ergometer (Forsyth and Reilly, 2004) and others finding diurnal rhythms in reaction time (Geetanjali and Sushma, 2006; Kerkhof et al., 1980) and sports performance (Brown et al., 2008; Atkinson and Reilly, 1996). Interestingly, chronotype and maximal oxygen consumption display a similar relationship (Hill et al., 1988), as was found for isometric torque production in the present study. In that study, maximal oxygen consumption peaked in the evening for evening people and did not change over the day for morning people (Hill et al., 1988). Taken together with our present results, one would predict that performance in complex tasks that require strength and cardiovascular performance would follow these patterns for people of different chronotypes. However, performance of morning people on a rowing ergometer peaked in the morning and that of evening people did not change over the day (Brown et al., 2008). Hence, the relationship between chronotype and diurnal rhythms in performance of complex tasks is likely to be multifaceted involving factors yet to be identified. Regardless, the emerging evidence highlights the importance of considering chronotype when examining diurnal rhythms. From a methodological standpoint, our data suggest that chronotype should be considered when evaluating human performance or CNS excitability.

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