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RESEARCH ARTICLE

# Excitability and recruitment patterns of spinal motoneurons in human sleep as assessed by *F*-wave recordings

**Farid Salih · Saskia Steinheimer · Pascal Grosse**

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**Abstract** This study examines the excitability and recruitment of spinal motoneurons in human sleep. The main objective was to assess whether supraspinal inhibition affects the different subpopulations of the compound spinal motoneuron pool in the same way or rather in a selective fashion in the various sleep stages. To this end, we studied *F*-conduction velocities (FCV) and *F*-tacheodispersion alongside *F*-amplitudes and *F*-persistence in 22 healthy subjects in sleep stages *N*2, *N*3 (slow-wave sleep), REM and in wakefulness. Stimuli were delivered on the ulnar nerve, and *F*-waves were recorded from the first dorsal interosseus muscle. Repeated sets of stimuli were stored to obtain at least 15 *F*-waves for each state of vigilance. *F*-tacheodispersion was calculated based on FCVs using the modified Kimura formula. Confirming the only previous study, excitability of spinal motoneurons was generally decreased in all sleep stages compared with wakefulness as indicated by significantly reduced *F*-persistence and *F*-amplitudes. More importantly, *F*-tacheodispersion showed a narrowed range of FCV in all sleep stages, most prominently in REM. In non-REM, this narrowed range was associated with a shift towards significantly decreased maximal FCV and mean FCV as well as with a trend towards lower minimal FCV. In REM, the lowering of mean FCV was even more pronounced, but contrary to non-REM sleep without a shift of minimal and maximal FCV. Variations in *F*-tacheodispersion between sleep stages suggest that different supraspinal inhibitory neuronal circuits acting on the spinal motoneuron pool may contribute to muscle hypotonia in human non-REM sleep and to atonia in REM sleep.

**Keywords** *F*-waves · Sleep · Spinal motoneuron · Inhibition · Conduction velocity · Tacheodispersion

## Introduction

In non-REM sleep, inhibition of the spinal motoneuron pool physiologically reduces the number of movements and leads to progressing muscle hypotonia. REM sleep is characterised by a further reduction of movements and almost complete muscle atonia (Dement and Kleitman 1957; Rechtschaffen and Kales 1968). While it seems commonplace that humans barely move in sleep, most of the evidence on the neuronal circuits involved in the inhibition of spinal motoneurons in sleep relies on animal experiments alone (for review see e.g. Chase and Morales 2005; Siegel 2005). Yet, it has not been entirely settled whether identical inhibitory neuronal circuits also contribute to muscle hypotonia in human and animal sleep given the ample variations of sleep patterns in mammals (Lesku et al. 2009). From a clinical perspective, abnormal movements in human sleep such as, e.g., REM sleep behaviour disorder (Schenck et al. 1986) or periodic limb movements in non-REM sleep (Symonds 1953; Lugaresi et al. 1965) are mostly bound to specific sleep stages so that it might be assumed that distinct supraspinal and spinal circuits are involved in the generation of movements in sleep, be they physiological or pathological. Thus, it might be assumed that inhibition of spinal motoneurons in human sleep does not affect the entire pool of spinal motoneurons

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F. Salih (✉) · S. Steinheimer · P. Grosse
Neurologische Klinik und Poliklinik,
Charité-Universitätsmedizin Berlin,
Augustenburger Platz 1, 13353 Berlin, Germany
e-mail: farid.salih@charite.de

equally and to the same extent across all sleep stages, but rather in a distinctive fashion leading to, e.g., different phenomenologies of movements. Hence, it seems to be of importance to assess the physiological effects of supraspinal inhibition in human sleep on spinal motoneurons as the final pathway of the motor system.

Electrophysiological studies using stimulation paradigms to investigate the excitability of spinal motoneurons in human sleep have been generally very sparse, mostly because subjects often wake up before a sufficient number of stimuli can be delivered. Pivik and Mercier (1979) demonstrated reduced excitability of spinal motoneurons in human non-REM sleep using the H-reflex technique, a finding that seems to correspond with muscle hypotonia observed at the behavioural level. Ichikawa and Yokota (1994) reproduced this finding using conventional *F*-wave parameters. The latter study showed a marked reduction in *F*-wave persistence (i.e. percentage of elicited *F*-waves in relation to the number of stimuli delivered), reduced amplitudes and prolonged latencies of *F*-waves. These parameters were more prominently altered in REM compared with non-REM sleep. However, the latter study did not address the question whether inhibition affects different populations of the compound spinal motoneuron pool equally.

To further investigate the recruitment patterns of the spinal motoneuron pool in non-REM and REM sleep, we used advanced *F*-wave measures such as *F*-conduction velocities (FCV) and *F*-tacheodispersion (i.e. distribution of *F*-wave responses in relation to conduction velocities) alongside conventional *F*-wave parameters. The *F*-wave is the antidromically elicited motor response following the orthodromic M-wave upon supramaximal electrical stimulation of peripheral nerves (Magladery and McDougal 1950; Dawson and Merton 1956). *F*-waves are considered to be a general measure of excitability of the spinal motoneuron pool (Espiritu et al. 2003), which is under the influence of segmental reflex activity as well as supraspinal modulation. So far, it has not been shown that reduced excitability of spinal motoneurons in sleep is due to intraspinal circuits so that all changes of *F*-wave parameters in sleep must be generated supraspinally alone (Chase and Morales 2005). As a major asset, *F*-wave recordings provide insights into the heterogeneous spinal motoneuron pool with its slower and faster conducting motoneurons if appropriately assessed. Even under identical recording conditions, consecutively recorded *F*-waves vary in latency, amplitude and morphology. Thus, individual *F*-waves represent different individual or small groups of motor units of the same nerve (Chroni and Panayiotopoulos 1993). *F*-tacheodispersion is a measure to assess the distribution of *F*-conduction velocities (FCVs) of these individual or small groups of nerve fibres estimated from significant numbers of consecutively recorded *F*-waves (Chroni and Panayiotopoulos 1993). In disease, *F*-tacheodispersion has proved to be a reliable measure of how subpopulations of the entire compound spinal motoneuron pool may become selectively affected, e.g., in neuropathies or radiculopathies (Chroni and Panayiotopoulos 1993).

Based on the evidence from naturally sleeping animals, different supraspinal systems reduce the excitability of spinal motoneurons in non-REM and in REM sleep (Chase and Morales 2005; Chase 2008; Lai et al. 2001; Kodama et al. 2003). Basically, inhibition of the spinal motoneuron may be through postsynaptic inhibition or disfacilitation (i.e. a reduction in the discharge of presynaptic excitatory neurons). Here, we hypothesised that the effects of different inhibitory systems in non-REM and REM sleep are reflected in different recruitment patterns of *F*-waves. We further assumed that a general shift of mean FCV ($FCV_{mean}$) without affecting the range ($FCV_{range}$) between minimal ($FCV_{min}$) and maximal FCV ($FCV_{max}$) would be indicative of a non-selective inhibition of the entire spinal motoneuron pool. Alternatively, alterations in the range of FCVs and changes in *F*-tacheodispersion would imply selective inhibition of distinct spinal motoneuron populations (e.g. those which conduct fastest or more slowly).

## Methods

### Ethical approval

The study was approved by the Charité-Medical University Berlin Ethics Committee and conforms to the standards set by the *Declaration of Helsinki*. All subjects signed informed consent after complete information about the nature of the experiment.

### Subjects

We examined 22 healthy drug-free, right-handed volunteers (11 men, 11 women) aged between 21 and 39 years (mean: 27.3 years) at the Department of Neurology, Charité-University Medicine Berlin. Subjects had no history of neurological disease, psychiatric disorder or sleep disturbances. Further, they did not show symptoms of peripheral nerve disease.

### Sleep stage assessment

To determine sleep stages, polysomnography (F1, F2, Fz, Cz, O1, O2, A1 and A2 according to the 10–20 system, EOG and submental EMG) was continuously recorded during the experiment on a mobile device (Nihon Koden). Thus, sleep stage assessment was continuously feasible while performing *F*-wave recordings. Time constant of the EEG recording was set at 0.3 s, low-pass-filter at 70 Hz,

and the sampling rate was 256 Hz. Sleep stages were scored in accordance with the modified criteria proposed by the American Academy of Sleep Medicine (2007). The assessment of sleep stages during the experiment was controlled off-line by one of the investigators experienced with sleep stage assessment (FS, PG), but who was not participating in the respective trial.

### *F*-wave recording

Recordings were performed using a Neuropack 8 electromyography (Nihon Koden®, band-pass from 3- to 3,000-Hz sampling frequency 5,000 Hz) and stimulating surface electrodes with the cathode placed distally. We fixated stimulating surface electrodes at right wrist level to deliver electrical stimuli on the ulnar nerve. Electric stimuli were of supramaximal intensity (1.2 times of that producing a maximal M-response in each state of vigilance, respectively). The evoked muscle responses were recorded from the 1DI muscle using surface Ag-/Ag-electrodes according to the belly–tendon technique. We opted for a hand muscle to record *F*-waves, because electrodes are less prone to get compromised in sleep compared with those of a leg muscle. Further, the level of excitability in hand muscles is somewhat intermediate between that of different leg muscles (Espiritu et al. 2003) and is therefore more representative for the overall population of spinal motoneurons. Frequency of stimuli application was set at 0.1 Hz which allowed us to interrupt stimulation as soon as arousal activity changed the EEG sleep pattern. Once an arousal occurred, stimulation was discontinued for at least 3 min. Only after 3 min of stable sleep stage-specific EEG activity, we continued *F*-wave recording. We used a square current of 0.1-ms duration (Chroni and Panayiotopoulos 1993). In order to investigate *F*-persistence, 50 consecutive electrical stimuli were stored. *F*-persistence was then expressed as percentage of elicited *F*-waves during this series of consecutive 50 stimuli. For subsequent analysis of *F*-amplitudes and different measures of *F*-conduction velocity, repeated sets of electrical stimuli were stored to obtain at least 15 *F*-waves in each sleep stage free of artefacts. To obtain this number of *F*-waves for each sleep stage, *F*-wave recordings had to be performed across all the NREM/REM-cycles of the entire sleep period. All subjects in whom the experiment could successfully be completed in at least one sleep stage were also investigated in wakefulness the next morning according to the same protocol. The temperature of the sleep laboratory was kept constant at 25°C.

We defined *F*-waves as muscle compound action potentials of at least 20-μV peak-to-peak amplitudes (Puksa et al. 2003). *F*-latencies were measured at the onset of the first deflection from baseline. For each sleep stage and wakefulness, *F*-persistence, mean *F*-amplitude, different measures of *F*-conduction-velocities ($FCV_{mean}$, $FCV_{max}$, $FCV_{min}$ and $FCV_{range}$) and *F*-tacheodispersion (distribution of FCV of all *F*-waves) were calculated. So-called *F*-wave repeaters (following *F*-waves with same size, configuration and latency) were included for *F*-persistence assessment only. $FCV_{max}$ was calculated by the formula according to Kimura (1974):

$$FCV_{max} = \text{Distance}/[(F\text{-Latency}_{min} - \text{CMAP-Latency} - 1)/2].$$

As Chroni and Panayiotopoulos (1993) suggested FCV of fibres other than the fastest ($FCV_x$) was calculated using a modified formula:

$$FCV_x = \text{Distance}/[(\text{F-Latency}_{min} - \text{CMAP} - \text{Latency} - 1)/2]^{*}(F\text{-Latency}_{min} - 1)/(F\text{-Latency}_{x} - 1)$$

$FCV_{range}$ was defined as difference between maximal and minimal FCV ($FCV_{max} - FCV_{min}$). $FCV_{mean}$ was the average FCV-value of all 15 *F*-waves included for each state of vigilance in each subject.

### Statistics

To test for significant differences between the different sleep stages and wakefulness, the grand mean results for each *F*-wave parameter (i.e. *F*-persistence, *F*-amplitudes, $FCV_{mean}$, $FCV_{min}$, $FCV_{min}$ and $FCV_{range}$) were entered into a general linear model. *F*-wave parameters were used as dependent factor whereas states of vigilance (*N*2, *N*3, REM and wakefulness) were entered as fixed factors. When states of vigilance proofed to influence *F*-parameters significantly ($p < 0.05$), *post hoc* multiple comparisons using the Tukey test were performed between sleep stages and wakefulness as well as between individual sleep stages.

## Results

Assessment of *F*-persistence in a single sleep stage was feasible when at least 50 electrical stimuli could be delivered (see "Methods"). Accordingly, we were able to calculate *F*-persistence in 19 subjects in at least one sleep stage (*N*2: $n = 17$; *N*3: $n = 14$; REM: $n = 17$). *F*-amplitudes and FCV-measures were calculated based on the average of 15 elicited *F*-waves. Thus, *F*-amplitudes and FCVs could be assessed in 18 subjects in at least one sleep stage (*N*2: $n = 13$; *N*3: $n = 13$; REM: $n = 9$). In one subject, *F*-persistence could be assessed in *N*2, *N*3 and REM, but the number of *F*-waves was too low to reach the

number needed to calculate *F*-amplitudes and FCVs. In three subjects, electrical stimulation led to recurrent awakenings prior to reaching maximal M-response. In order to collect a sufficient number of *F*-waves during sleep, 14 subjects agreed to participate in a second night, and 2 subjects were investigated during three nights.

Although group sizes may be equal (e.g. for *F*-persistence, 17 subjects were included for *N*2 and REM), the composition of involved subjects varies in the respective sleep stages. As results for *F*-parameters slightly vary between subjects, minor differences occur in the averaged results for wakefulness even in groups of equal size (e.g. *F*-persistence during wakefulness was 69% for those 17 subjects who could be investigated in *N*2, but 70% for those 17 subjects who could be investigated in REM).

## Conventional *F*-parameters (Figs. 1, 2)

Figure 1 shows *F*-wave responses to sets of 20 electrical stimuli in a subject in whom *F*-waves could be obtained in each state of vigilance (i.e. wakefulness, *N*2, *N*3, REM). *F*-persistence in this individual was reduced in all sleep stages compared with that of wakefulness with the most prominent decrease in REM sleep (22%).

The averaged data (Fig. 2a) show that *F*-persistence differs significantly depending on the state of vigilance ($F_{(3,17)} = 38.26$; $p < 0.005$). *Post hoc* comparisons revealed that *F*-persistence was significantly reduced in all sleep stages as compared to wakefulness and between REM and all other states of vigilance.

Also, *F*-amplitudes differed significantly relative to the state of vigilance ($F_{(3,17)} = 8.98$; $p < 0.005$; Fig. 2b). *Post hoc* comparisons showed a significant reduction in mean *F*-amplitudes in all sleep stages by about a half compared with those of the wakefulness, but not among the different sleep stages. The decrease in *N*3 was more pronounced than in *N*2 and equalled that in REM (*N*2: ratio = 0.59, $p = 0.049$; *N*3: ratio: 0.49, $p = 0.044$; REM = 0.51, $p = 0.035$).

## *F*-conduction velocities and *F*-tacheodispersion (Figs. 3, 4)

Figure 3 shows the distribution of conduction velocities (*F*-tacheodispersion) in steps of 2 m/s for each sleep stage

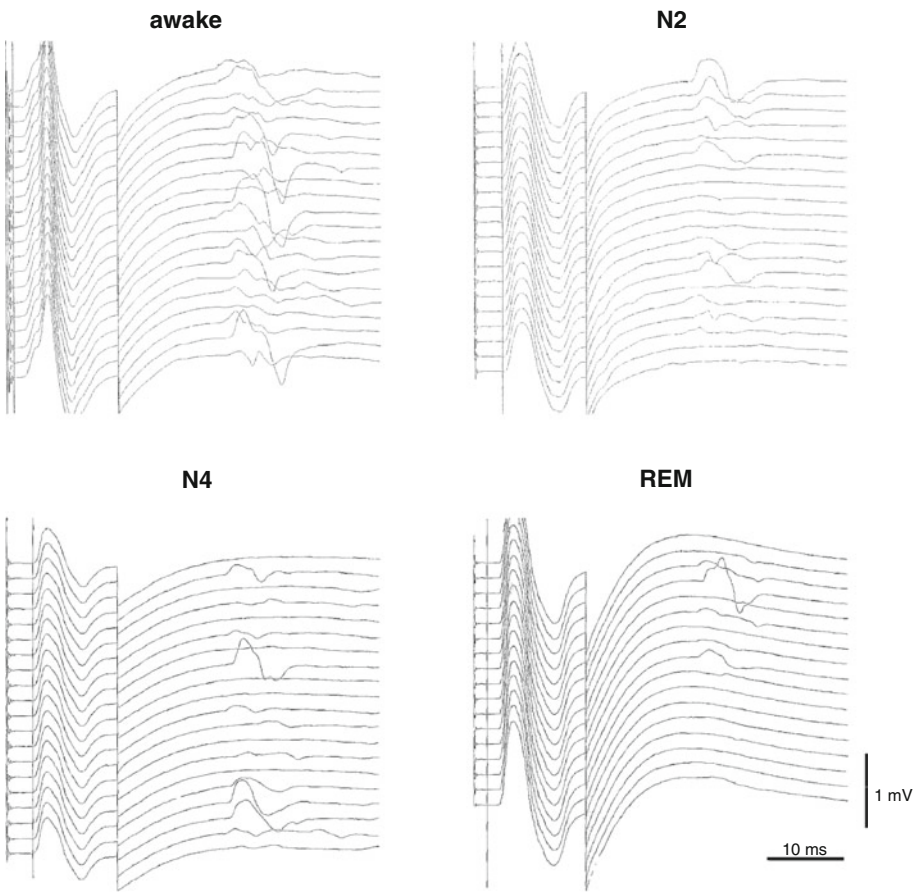


**Fig. 1** *F*-wave responses to sets of 20 electrical stimuli in a single subject in whom *F*-waves could be recorded in all sleep stages (*N*2, *N*3, REM) and wakefulness. In this single subject, *F*-persistence (based on 50 consecutive stimuli) was most markedly reduced in REM (22%). *F*-persistence was 66% in *N*2, 56% in *N*3 and 94% in wakefulness, respectively

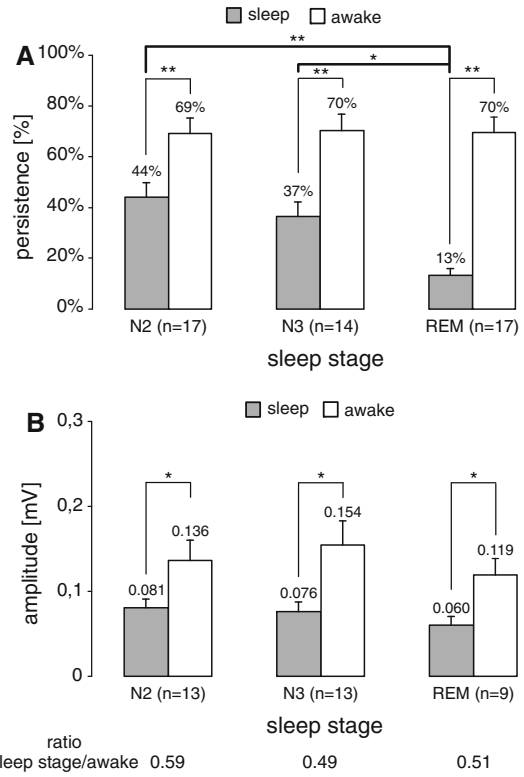


**Fig. 2** **a** *F*-persistence in different sleep stages compared with that in wakefulness (sleep stages correspond to *grey bars*, wakefulness to *white bars*). *F*-persistence was significantly reduced in all sleep stages as compared to wakefulness (REM vs. wakefulness: $p < 0.0005$; *N*2 vs. wakefulness: $p < 0.005$, *N*3 vs. wakefulness: $p < 0.0005$). In REM, *F*-persistence was also significantly reduced compared with *N*2 ($p < 0.005$) and *N*3 ($p < 0.005$). *$p < 0.05$, **$p < 0.005$. **b** *F*-amplitude in different sleep stages compared to wakefulness (sleep stages correspond to *grey bars*, wakefulness to *white bars*). As amplitudes recorded in wakefulness varied between the three groups, ratios are inserted below the figure. *F*-amplitudes were significantly decreased in all sleep stages (*N*2: ratio = 0.59, $p < 0.05$; *N*3: ratio: 0.49, $p < 0.05$; REM = 0.51, $p < 0.05$; Fig. 1a). *$p < 0.05$

compared with that of wakefulness across all subjects (*N*2: $n = 13$; *N*3: $n = 13$; REM: $n = 9$). Variation coefficient in *N*2 was 0.047 (vs. 0.056 in wakefulness), in *N*3 0.054 (vs. 0.057) and in REM 0.051 (vs. 0.054). In wakefulness, the main share of *F*-waves (83.1–86.0% of all *F*-waves) had conduction velocities between 62 and 72 m/s, if >10% of all *F*-waves is taken as cut-off (dotted line); 10.0–10.8% were below and 4.0–6.1% above this range. Also, in *N*2, a similar proportion of *F*-waves as in wakefulness (87.7%) were between 62 and 72 m/s. Conversely, in *N*3, only 74.6% of all *F*-waves were between 62 and 72 m/s. Different to wakefulness in *N*2, only 0.8% of all *F*-waves had velocities above that range, and in *N*3, no *F*-wave was recorded above 72 m/s. In *N*2, 12.3% were below 62 m/s as were 24.6% in *N*3. In REM, only 75.0% of all *F*-waves had velocities between 62 and 72 m/s, whereas 24.0% were below and only 1.0% was above that range.

In order to describe the recruitment patterns of spinal motoneurons more precisely, $FCV_{mean}$, $FCV_{min}$, $FCV_{max}$ as well as the range ($FCV_{range}$) between $FCV_{max}$ and $FCV_{min}$ were taken into account. Apart from $FCV_{min}$ ($F_{(3,17)} = 1.12$; $p = 0.35$), all FCV-measures differed significantly in relation to the state of vigilance ($FCV_{mean}$: $F_{(3,17)} = 6.00$; $p < 0.05$; $FCV_{max}$: $F_{(3,17)} = 10.18$; $p < 0.005$; $FCV_{range}$: $F_{(3,17)} = 6.48$; $p < 0.05$). Inserted boxplots in Fig. 3 show that $FCV_{mean}$ was significantly reduced in all sleep stages compared with wakefulness. Differences to wakefulness were most pronounced in REM (*N*2 = −2.03 m/s, $p < 0.05$; *N*3 = −2.31 m/s, $p < 0.05$; REM = −2.45 m/s, $p = 0.05$). There were no significant differences between individual sleep stages.

Boxplots in Fig. 4a show sleep stage-specific differences of $FCV_{max}$ (i.e. highest FCV) compared with wakefulness. Boxplots in Fig. 4b show sleep stage-specific differences of $FCV_{min}$ (i.e. lowest FCV) compared to wakefulness. $FCV_{max}$ was significantly reduced in all sleep stages, but differences to wakefulness were most pronounced in non-REM sleep, in particular during slow-wave sleep (*N*2 = −4.15 m/s, $p < 0.005$; *N*3 = −4.39 m/s, $p < 0.0005$; REM = −2.30 m/s, $p < 0.005$). There were no significant differences of $FCV_{max}$ when sleep stages were compared directly. Alterations in $FCV_{min}$ showed different trends comparing non-REM and REM stages; however, results were not statistically significant. In non-REM sleep, $FCV_{min}$ was reduced compared with wakefulness (*N*2 = −1.09 m/s; *N*3 = −1.24 m/s). In REM sleep, $FCV_{min}$ was almost equal to wakefulness, showing a trend towards higher values (REM = 0.77 m/s).

Figure 4c illustrates $FCV_{range}$. $FCV_{range}$ was significantly reduced in all sleep stages compared to wakefulness, most prominently in REM sleep (*N*2 = 7.34 m/s, $p < 0.05$; *N*3 = 7.16 m/s, $p < 0.05$; REM = 6.02 m/s, $p < 0.005$) without significant differences between individual sleep stages.

## Discussion

Our study shows generally reduced excitability of spinal motoneurons in non-REM and REM sleep compared with wakefulness. On confirming the only previous data by Ichikawa and Yokota (1994), *F*-persistence was significantly decreased in all sleep stages, however, not to the same extent as in Ichikawa and Yokota (1994) who showed *F*-persistence of 18% in *N*2, of 14.2% in *N*3 and of 7.1% in REM. The reduction of *F*-persistence in REM as well as in non-REM sleep shows that a high number of spinal motoneurons is completely inhibited during the entire sleep period and cannot be recruited to produce *F*-waves at all.

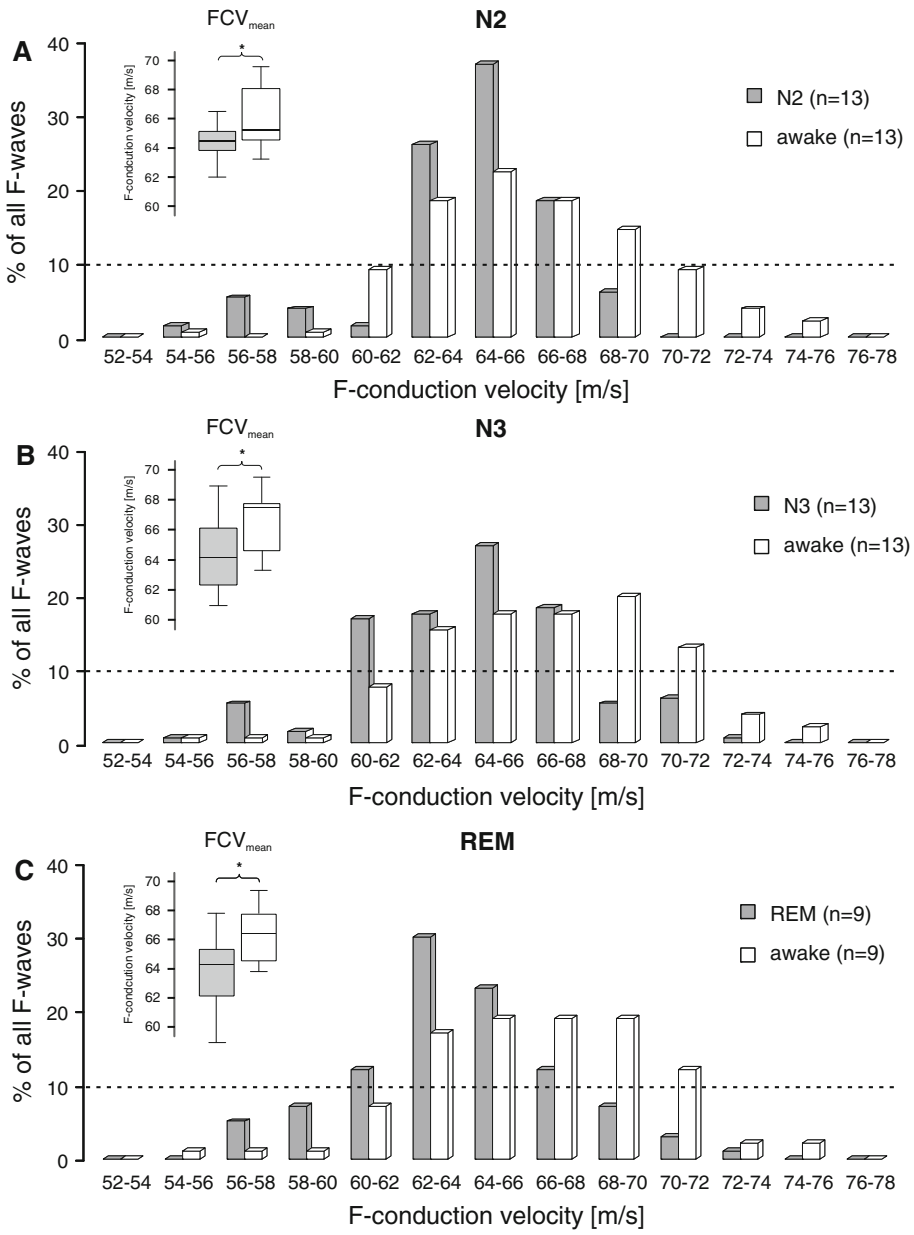


**Fig. 3** *F*-tacheodispersion in different sleep stages compared to wakefulness (**a**: *N*2, **b**: *N*3, **c**: REM). In wakefulness, the main share of *F*-waves had conduction velocities between 62 and 72 m/s, if >10% of all *F*-waves is taken as cut-off (*dotted line*). In wakefulness, between 83.1 and 86% of all *F*-waves fell into this range. *N*2 and *N*3 had a different distribution as 87.7% in *N*2, but only 74.6% in *N*3 of all *F*-waves were in the range between 62 and 72 m/s. In REM, only 75% of all *F*-waves had velocities between 62 and 72 m/s. *Boxplots* in each figure compare $FCV_{mean}$. In all sleep-stages, $FCV_{mean}$ was significantly reduced compared to wakefulness ($N2 = -2.03$ m/s, $p < 0.05$; $N3 = -2.31$ m/s, $p < 0.05$; REM $= -2.45$ m/s, $p < 0.05$). $^{*}p < 0.05$

The latter finding has major methodological implications for the use of *F*-waves in sleep. Especially in REM sleep, the number of *F*-waves that can be used for further analysis is limited. For *F*-wave studies of the ulnar nerve in wake subjects, Panayiotopoulos and Chroni (1996) stated a consensus among different authors to evaluate at least 20 *F*-waves. Nevertheless, other authors relied on 10 *F*-waves or even less in studies on healthy subjects and patients with peripheral neuropathies and radiculopathies with reduced *F*-persistence in wakefulness (Marra 1987; Shivde and Fisher 1988; Olney and Aminoff 1990; Ropper et al. 1990). To collect 15 *F*-waves in each subject as in our study should therefore allow a representative assessment of spinal excitability and recruitment of spinal motoneurons in sleeping humans. The number of 50 electrical stimuli to evaluate *F*-persistence in our study was even higher than that usually recommended (Panayiotopoulos and Chroni 1996). To obtain the required numbers of stimuli and *F*-waves, we had to record during different NREM-/REM-cycles across the entire sleep period. Given these limitations due to the cyclic nature of NREM/REM, variations in *F*-wave responses due to circadian or intra-stage variations of muscle tone, in particular in *N*2, might have escaped our assessment (Tinguely et al. 2006; Werth et al. 2002). As none of our subjects had exclusively been investigated during the first or last NREM-/REM cycles, our data might have potentially omitted variations due to the circadian regulation of NREM-hypotonia (Tinguely et al. 2006).

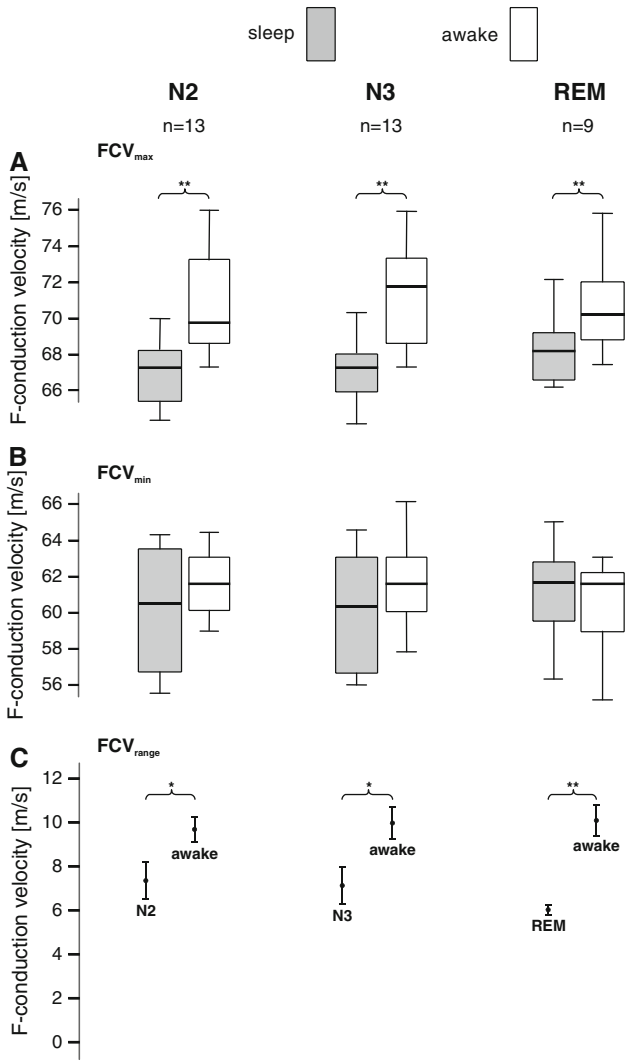


**Fig. 4** **a** $FCV_{max}$ (*highest FCV*) was significantly reduced in all sleep stages compared with wakefulness but most pronounced in non-REM ($N2 = -4.15$ m/s, $p < 0.005$; $N3 = -4.39$ m/s, $p < 0.005$, REM $= -2.30$ m/s, $p < 0.005$). **b** $FCV_{min}$ (*lowest FCV*) showed different trends comparing non-REM and REM stages; however, results were not significant. In non-REM, $FCV_{min}$ was reduced compared to wakefulness ($N2 = -1.09$ m/s; $N3 = -1.24$ m/s). In REM, $FCV_{min}$ showed a trend towards higher values (REM $= 0.77$ m/s). **c** $FCV_{range}$ was significantly reduced in all sleep stages compared to wakefulness, most prominently in REM ($N2 = 7.34$ m/s, $p < 0.05$; $N3 = 7.16$ m/s, $p < 0.05$; REM $= 6.02$ m/s, $p < 0.005$). *$p = 0.05$; **$p = 0.005$

However, our study design to begin with *F*-wave recordings only after a minimum of 3 min of stable sleep stages in each individual sleep stage should have minimised systematic influences of NREM-onset muscle hypotonia (Werth et al. 2002).

The reduction of recruitable motoneurons in sleep leads to differences in the recruitment patterns of spinal motoneurons compared with that of wakefulness. *F*-tacheodispersion and FCV-measures indicate that different inhibitory mechanisms act differently upon the compound spinal motoneuron pool in non-REM and REM sleep. In both non-REM sleep stages, the narrowing of $FCV_{range}$ correlates with a significant reduction in $FCV_{max}$ as well as $FCV_{mean}$ and a trend towards lower $FCV_{min}$. Therefore, alterations in *F*-tacheodispersion in non-REM sleep are mainly indicative of reduced excitability of faster conducting spinal motoneurons. In REM, the reduction in $FCV_{range}$ was even more pronounced. However, differences were seen regarding the results for $FCV_{max}$ and $FCV_{min}$. Whereas $FCV_{max}$ in REM sleep was not reduced to the same extent as in both non-REM sleep stages, $FCV_{min}$ in REM even showed a trend towards higher values compared to wakefulness. This finding suggests that not only faster but also more slowly conducting spinal motoneurons get specifically inhibited in REM.

Advanced *F*-parameters confirm that reduced excitability of spinal motoneurons does not merely follow a gradual decline of excitable spinal motoneurons from *N*2 to *N*3 to REM. Rather different inhibitory mechanisms seem to critically regulate the recruitment of spinal motoneurons in a sleep stage-specific manner. These findings parallel evidence from animal models that different modes of inhibition act upon spinal motoneurons in non-REM and REM sleep (Chase and Morales 2005; Kodama et al. 2003; Lai et al. 2001). Electrophysiological studies in naturally sleeping cats show a slight increase in small-amplitude IPSPs from wakefulness to non-REM sleep acting on spinal motoneurons (Chase and Morales 2005). These small-amplitude IPSPs are accompanied by an increase in membrane hyperpolarisation, rheobase current and input resistance as well as a frequency reduction in soma-dendritic and axonal action potentials and a reduction in Ia monosynaptic EPSPs (Chase et al. 1980; Chase and Morales 2005). In REM sleep, unique large-amplitude IPSPs act additionally on spinal motoneurons leading to the transition from muscle hypotonia during non-REM to muscle atonia during REM sleep. Immunohistochemical techniques have identified glycinergic inhibitory interneurons located in the ventromedial medulla (Chase 2008; Holstege 1996; Soja et al. 1986), which discharge selectively during REM sleep to generate these large-amplitude IPSPs. Glycinergic inhibition during REM sleep is also accompanied by GABAergic inhibitory drives as well as disfaciliation of norepinephrine and serotonin neurons that usually impinge EPSPs on spinal motoneurons (Kodama et al. 2003; Lai et al. 2001).

Based on our findings, it might be reasonable to assume that REM-specific inhibitory drives act on a more extended motoneuron population. In comparison, non-REM-related inhibitory mechanisms predominantly target faster conducting spinal motoneurons. The fact that *F*-waves can be recorded at all during REM sleep may be explained by

sustained excitatory drives on motoneurons that should also account for phasic REM sleep phenomena like muscle twitches and rapid eye movements (Evarts 1964; Marchiafava and Pompeiano 1964).

In summary, we describe two different patterns of how inhibition of spinal motoneurons may operate in non-REM and REM sleep, respectively. These findings might contribute to further insights into the pathophysiology of sleep-related motor disorders that may involve abnormal patterns of motor inhibition in NREM and REM including their potential responsiveness to pharmacological agents (e.g. REM sleep behaviour disorder, periodic limb movements in sleep).

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**Conflict of interest** The authors have no conflicts of interests.

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