# Fatigue and Discomfort During Spatially Distributed Sequential Stimulation of Tibialis Anterior

Matheus Joner Wiest, Austin J. Bergquist, Matthew G. Heffernan, Milos Popovic, and Kei Masani

***Abstract*— Neuromuscular electrical stimulation is conventionally applied through a single pair of electrodes over the muscle belly, denominated single electrode stimulation (SES). SES is limited by discomfort and incomplete motor-unit recruitment, restricting electrically-evoked torque and promoting premature fatigue-induced torque-decline. Sequential stimulation involving rotation of pulses between multiple pairs of electrodes has been proposed as an alternative, denominated spatially distributed sequential stimulation (SDSS). The present aim was to compare discomfort, maximal-tolerated torque, and fatigue-related outcomes between SES and SDSS of tibialis anterior. Ten healthy participants completed two experimental sessions. The self-reported discomfort at sub-maximal torque, the maximal-tolerated torque, fatigue-induced torque-decline during, and doublet-twitch torque at 10- and 100-Hz before and after, 300 intermittent (0.6-s-ON-0.6-s-OFF) isokinetic contractions were compared between SES and SDSS. SDSS stimulation improved fatigue-related outcomes, whereas increased discomfort and reduced maximal-tolerated torque. SDSS holds promise for reducing fatigue. However, limited torque production and associated discomfort may limit its utility for rehabilitation/training.**

***Index Terms*— Electrical stimulation, sequential, rehabilitation, tibialis anterior, isokinetic, discomfort, fatigue, maximal torque.**

## I. Introduction

TRANSCUTANEOUS neuromuscular electrical stimulation (NMES) is conventionally applied using a single pair of surface electrodes positioned over a skeletal muscle belly or a group of muscle bellies to generate muscle contractions for rehabilitation/training [1], which we call in this paper as a single active electrode stimulation (SES) [2]–[5]. The main limitations of SES are the intense discomfort associated with peripheral stimulation [6] and the non-physiological pattern of motor unit recruitment [1], [7], [8], which limits torque production and leads to premature muscle fatigue expressed as a decline in torque over time (henceforth referred to as fatigue). Together, these limit the effectiveness of SES for rehabilitation purposes [1], [9].

To minimize the premature fatigue associated with SES, researchers have developed a technique involving "sequential" rotation of stimulation pulses between multiple active (cathode) electrodes positioned over a muscle belly or a group of muscle bellies [2]–[5], [10]–[13]. Sequential stimulation (also referred as asynchronous [13], rotary [14], distributed [12], [15], [16] or interleaved [17]–[19]) crudely mimics the asynchronous pattern and firing frequency range of motor unit recruitment associated with voluntary contractions [20]. During sequential stimulation, each electrode is activated at a low frequency (e.g. 10-15 Hz), whereas maintaining a high composite frequency (e.g. 40-60 Hz when four cathodes are used) delivered to the muscle, or muscle group, as a whole. We have developed a method called spatially distributed sequential stimulation (SDSS) to reduce muscle fatigue by distributing the center of an electrical field over a wider area within a single stimulation site and muscle belly, using an array of surface electrodes [2]–[4]. SDSS is unique compared to other sequential stimulation methods in a sense that, whereas the stimulation is interleaved between electrodes [3], it is not applied to different muscle heads. Instead, SDSS is distributed between multiple active surface electrodes that are placed at the same muscle and over approximately the same area as during SES with a single active electrode. In this way, each SDSS electrode activates partially distinct motor unit populations [4] theoretically reducing motor unit discharge rates of each motor unit population and, subsequently, muscle fatigue compared to SES. Further, this method can be applied when it is difficult or not possible to distribute stimulation between muscle heads, such as in the tibialis anterior muscle to induce ankle dorsiflexion.

Despite its success in reducing fatigue, it is currently unknown if SDSS represents an alternative to SES with respect to discomfort and torque production (e.g. maximal-tolerated torque), which are two primary determinants of NMES

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effectiveness [21], [22]. Smaller electrodes tend to produce less discomfort than larger electrodes in the tibialis anterior muscle [23], [24], and lower frequencies per electrode pair (e.g. 10-15 Hz) generates considerably less torque than higher frequencies (e.g. > 30 Hz) [25]. Before SDSS can be considered as a potential alternative to SES for rehabilitation purposes, a detailed assessment of discomfort and torque production is needed.

The purpose of the present study was to compare discomfort and torque related outcomes between SES and SDSS at sub-maximal torque, the maximal-tolerated torque, and fatigue-related outcomes between SES and SDSS of tibialis anterior. We hypothesized that, whereas SDSS can improve fatigue-related outcomes compared with SES, the use of relatively small electrodes and lower frequencies at each pair of electrodes during SDSS would decrease discomfort at sub-maximal torque, and reduce the maximal-tolerated torque. Tibialis anterior was studied because it is a frequent target for NMES-based rehabilitation [26], [27], and the effectiveness of SDSS in reducing muscle fatigue has been shown [3].

## II. Methods

### A. Participants

Eleven participants volunteered for the present experiments. One participant was excluded from the original cohort due to incomplete relaxation between evoked contractions during the fatigue protocol for both SES and SDSS. Thus, 10 participants (nine males, one female) aged 19-34 [mean ± standard deviation (SD): 23.4 ± 4.8 years] were part of the present cohort. No participant had previous history of neuromusculoskeletal disorders. Participants were asked to refrain from strenuous lower limb exercises for at least 24-hours prior to the experiments. The experimental protocols were approved by the local research ethics committee, and all participants signed a consent form.

### B. Joint Torque Measurement

Isometric and isokinetic ankle dorsiflexion torque was measured using an electrical dynamometer (Biodex System 3, Biodex Medical Inc., Shirley, NY). Participants were seated and straps were used to stabilize trunk, hip and legs. The hip and right knee were positioned at approximately 90°. Isometric dorsiflexion torque was measured with the ankle at approximately 100°, where 90° was the neutral position of the ankle. Isokinetic torque was measured at an angular velocity of 90°/s, allowing a range of movement from 50° to 120° (70° range of motion). The dynamometer axis of rotation was aligned with the center of rotation of the ankle joint.

### C. SES and SDSS

Transcutaneous neuromuscular electrical stimulation was delivered to the tibialis anterior muscle using a programmable 4-channel electrical stimulator (Compex Motion 2, Compex SA, Switzerland). Rectangular asymmetric biphasic pulses with duration of 300 $\mu$s were delivered throughout the experiments. The use of asymmetric instead of symmetric biphasic pulses was chosen to avoid muscle recruitment at both pulse phases and increased efficiency during SDSS. Self-adhesive stimulation electrodes were positioned proximally (cathode) and distally (anode) over the tibialis anterior muscle, with the cathode always located over the primary motor point. The primary motor point was identified at the location over the tibialis anterior skin where the lowest-intensity single pulse of stimulation evoked a muscle twitch [28]. This location was recorded and carried between experimentation days using permanent ink.

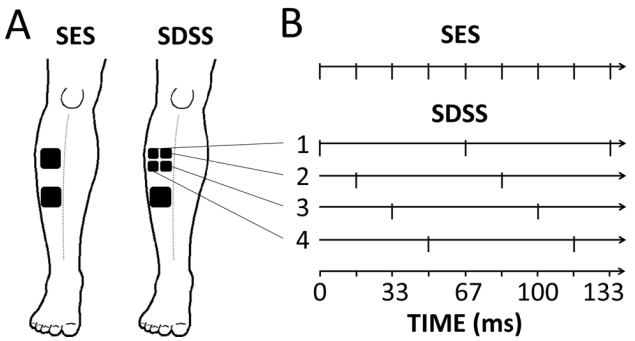


Fig. 1. Electrode location and stimulation pulse timing for SES and SDSS of tibialis anterior.

For SES, two large adhesive gel electrodes (each electrode was 5 × 5 cm, 25 cm$^2$ total area) were placed over the muscle belly, with the cathode positioned over the primary motor point, and the anode positioned distally. The composite frequency was delivered conventionally to this pair of electrodes (i.e. 60 Hz) (Fig. 1A).

For SDSS, four adhesive gel electrodes (each electrode was 2.25 × 2.25 cm – 5 cm$^2$, total area of the four electrodes: 25 cm$^2$) were placed over the same location as the cathode during SES, with the minimum gap possible (∼1-2 mm) aiming to mimic the same area as the SES electrodes. The anode had the same size and was placed in the same location as the SES cathode [3]. The composite stimulation frequency of SDSS was rotated between the four cathodes, one after the other, so that each electrode received 15 Hz with a phase shift of 90°, resulting in a stimulation frequency of 60 Hz (Fig. 1B). A composite frequency of 60 Hz is commonly used in interventions because it ensures torque fusion [26], [29] whereas stimulating each SES electrode at only 15 Hz replicates physiological range of motor unit firing rate during voluntary contractions [20]. Electrode position was also marked using a permanent ink to ensure placement was equal between both days of data collection. Electrode location and stimulation pulse timing are depicted in Fig. 1.

### D. Procedures and Measurements

Each participant visited the laboratory for a two-hour experimental session, on two occasions separated by at least 48 hours. Fig. 2 shows the protocol timelines. At the beginning of each experimental session (PRE), participants performed

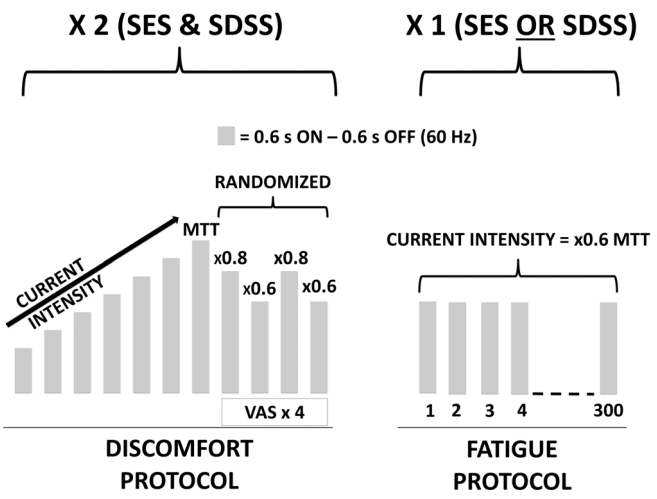


Fig. 2. Discomfort and fatigue protocol timelines. Participants completed two experimental sessions (SES and SDSS). Discomfort during SES and SDSS delivered at 0.6x and 0.8xMTT was measured twice in each experimental session (four times total) using a VAS. Fatigue was induced using either SES or SDSS in a given experimental session. Discomfort and fatigue protocols were delivered under isokinetic condition.

two maximal voluntary isometric contractions (MVIC) of the right ankle dorsiflexors. MVICs consisted of 3- to 5-second maximal contractions, separated by two minutes whereas receiving strong verbal encouragement. Another MVIC was repeated before the fatigue protocol to ensure muscle potentiation.

The initial part of the experiments was designated to test the maximal-tolerated isokinetic torque (MTT) and the self-reported discomfort at submaximal torque during SES and SDSS. The MTT was tested for SES and SDSS using stimulation trains of 60 Hz delivered for 0.6 seconds. The intensity of stimulation was progressively increased to the maximal intensity that the participant could tolerate. In this way, we could record the maximal torque that each stimulation type could produce before being limited by discomfort.

Discomfort was tested for SES and SDSS at two submaximal levels corresponding to 60% (0.6xMTT) and 80% (0.8xMTT) of the current intensity used during the MTT trials. When SES fatigue was randomly selected for Day I, the stimulation intensity of SES and SDSS were adjusted to generate 0.6xMTT and 0.8xMTT of the SES MTT and discomfort was recorded. On Day II – SDSS fatigue, this procedure was reversed: the stimulation intensity of SES and SDSS were adjusted to 0.6xMTT and 0.8xMTT of SDSS and discomfort recorded. We adopted this protocol because the MTT of SES was larger than SDSS, resulting in different torque amplitudes at the 0.6xMTT and 0.8xMTT discomfort trials. In a given day, 10 trains were delivered and recorded during the MTT and discomfort trials: two at MTT intensity, two trains at 0.6xMTT for SES, two trains at 0.6xMTT for SDSS; two trains at 0.8xMTT for SES; and two trains at 0.8xMTT for SDSS, in a randomized manner. Discomfort was measured using a visual analogue scale (VAS), which consisted of a 10 cm horizontal line where the left end was labeled "No pain" and the right end "Maximal tolerated pain." Participants were instructed to make a mark in the VAS corresponding to the level of discomfort produced by the previous stimulation train [18], taking into consideration that MTT corresponded to the far right end (VAS = 10 cm) of the scale. The goal of this protocol was to identify if SES and SDSS produced different levels of discomfort at a given percentage of the MTT, even if MTT and stimulation intensity was different between stimulation types. This information is relevant for clinicians balancing their choice of stimulation type based on maximal torque and discomfort.

Next, the fatigue protocol was delivered using either SES or SDSS in a given session. Isokinetic contractions were used because they are dynamic speed-controlled contractions that are closer to daily functional movements (e.g. walking), compared to isometric contractions. The fatigue protocol consisted of 300 intermittent (0.6-s-ON-0.6-s-OFF; total of six minutes) contractions produced by trains of stimulation delivered at 60 Hz. This pattern of stimulation mimics patterns of tibialis anterior muscle activation and de-activation seen during voluntary walking [30]. The stimulation intensity at the beginning of the fatigue protocol was set at 0.6xMTT for SES and SDSS.

The isometric torque produced by two pulses (i.e. doublets) delivered at short inter-pulse intervals (i.e. 100 ms and 10 ms; 10 Hz and 100 Hz, respectively) was recorded to infer over the mechanisms of electrically-evoked fatigue. A reduction in the ratio of the torque produced by the low- and high-frequency doublets ($Db_{10:100}$) indicates the development of low-frequency fatigue [31]. Low-frequency fatigue is characterized as larger decreases in torque at lower than at higher stimulation frequencies, being attributed to compromised excitation-contraction coupling mechanisms related to sarcoplasmic calcium [32], [33]. Doublets were recorded immediately after the first set of MVICs (PRE) [34] and 30 s after the last train of the fatigue protocol (POST). When delivering doublet stimulation before and after the SDSS fatigue protocol, the four electrodes of the SDSS array were synchronized from a single channel of stimulation.

### E. Data Analyses

Isometric and isokinetic torque was measured peak-to-peak and described as normalized values (% MVIC pre). The fatigue index (FI) was calculated to express the capability of SES and SDSS to maintain torque output over repeated evoked contractions. The FI is calculated by dividing the torque produced during the last 10 trains of the fatigue protocol to the torque produced during the first 10 trains, multiplied by 100, where higher values indicate higher fatigue resistance or less muscle fatigue. We also calculated the peak torque mean (PTM) to characterize the contractile work during the entire muscle fatigue protocol [3]. PTM was calculated as the average peak torque generated across all 300 contractions of the fatigue protocol, normalized to the average torque produced during the first 10 contractions, multiplied by 100. Stimulation efficiency refers to the amount of torque produced by a given current; in this case, we divided the MTT torque (%MVIC) by the current (mA) required to generate MTT for each stimulation site. The clinically meaningful difference for FI, PTM,

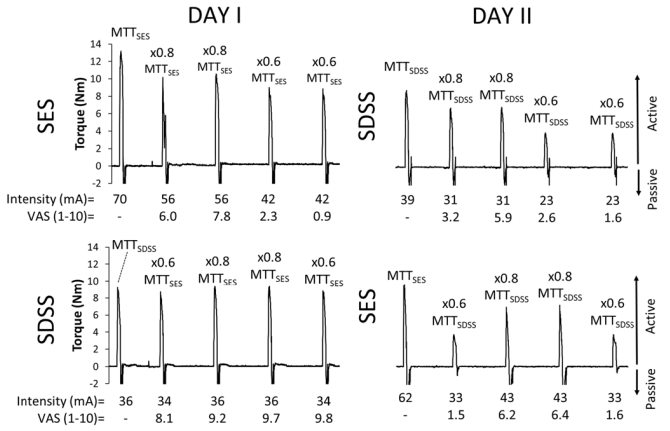


Fig. 3. Maximum tolerated isokinetic torque (MTT) and discomfort protocol during SES and SDSS for a single participant. For this participant, the SES fatigue protocol was performed on Day I and SDSS on Day II. On Day I, the stimulation intensity of SDSS was matched to generate the same torque as SES during the 0.6xMTT and 0.8xMTT. The opposite procedure was performed on Day II where the stimulation intensity of SES was matched to generate the same torque as 0.6xMTT and 0.8xMTT of SDSS. Stimulation intensity (mA) and VAS scores (cm) are reported under the torque-time trace data.

and MTT was assessed by the smallest real difference [40], SRD = 19.6 $\sqrt{}$ 2 x standard error of mean during SES.

### F. Statistical Analyses

All descriptive statistics presented are mean ± SD values. The normal distribution of the data was confirmed using the Shapiro-Wilk tests. Dependent T-tests were used to compare SES and SDSS regarding the stimulation intensity during doublets, MTT stimulation intensity, MTT normalized torque, stimulation intensity during the fatigue protocol, PTM, FI, and stimulation efficiency. Repeated measures ANOVAs were used to compare $Db_{10:100}$ (2 × 2; SES and SDSS vs PRE and POST); and MVICs (2 × 2; Day I and Day II vs PRE vs POST). VAS scores, stimulation intensity and normalized torque during the discomfort protocol were analyzed separately for Days I and II using repeated measures ANOVAs (2 x 2; SES and SDSS vs 0.6xMTT and 0.8xMTT). Bonferroni post-hoc tests with correction were used to test the interactions identified by the repeated measures ANOVAs. To test the discomfort score variability between trials and between days, we calculated the 1) percent change on VAS score between trials at the same intensity (e.g. Day I: SES 0.8xMTT trial 1 vs. SES 0.8xMTT trial 2); 2) correlation coefficient ($R^2$) between VAS scores of trials at the same intensity; and 3) 95% confidence intervals (CI). Similar reporting was provided for between days trials. Significance was set at $\alpha = 0.05$.

## III. Results

### A. Single Participant Data

The results from Day I and Day II of discomfort protocols from the same single participant are shown in Fig. 3.

On Day I, the torque of SDSS was matched to the torque of SES at 0.6x and 0.8xMTT. This participant produced larger MTT during SES (13.2 Nm or 28% MVIC) than SDSS

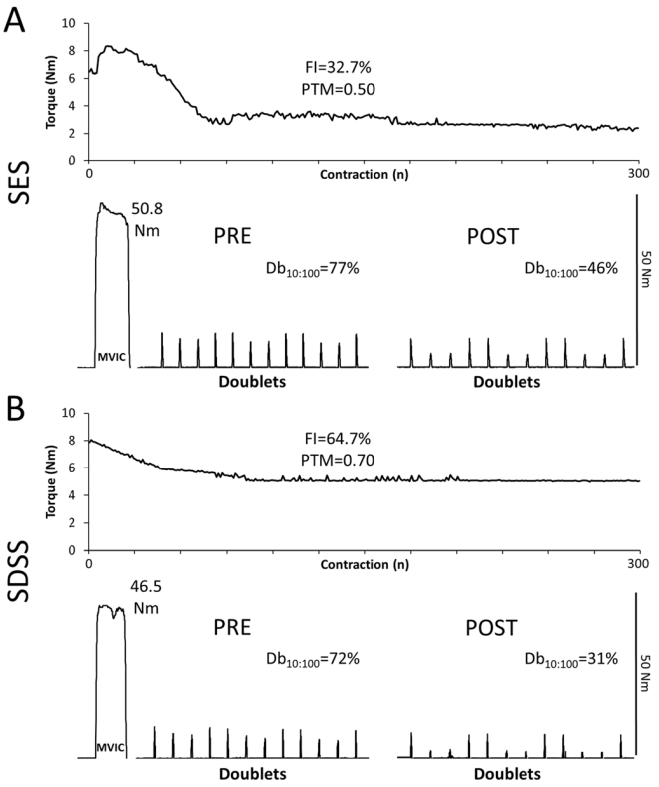


Fig. 4. SES (*A*) and SDSS (*B*) fatigue protocols (top plots), MVICs, Fatigue index (FI), peak torque mean (PTM), and doublets ratio ($Db_{10:100}$; PRE and POST) for a single participant.

(9.2 Nm or 20% MVIC). The torque of SDSS was matched to the torque of SES at 0.6xMTT (SES: 8.9 ± 0.09 Nm; SDSS: 8.9 ± 0.07 Nm) and 0.8xMTT (SES: 10.4 ± 0.3 Nm; SDSS: 9.4 ± 0.002 Nm). On Day II, the torque of SES was matched to the torque of SDSS at 0.6x and 0.8xMTT. MTT was larger during SES (9.3 Nm or 18% MVIC) than SDSS (8.6 Nm or 17% MVIC); MTT current was higher for SES than SDSS.

The torque of SES was matched to the torque of SDSS at 0.6xMTT (SES: 3.7 ± 0.05 Nm; SDSS: 3.9 ± 0.02 Nm) and 0.8xMTT (SES: 6.9 ± 0.1 Nm; SDSS: 6.9 ± 0.02 Nm). Independent of day, SES required larger stimulation current (33-56 mA) than SDSS (31-36 mA), but discomfort scores were lower during SES (VAS = 0.9-7.8) than SDSS (VAS = 8.1-9.8).

During the fatigue protocol (Fig. 4), we recorded torque-time changes that are represented by the FI, PTM and $Db_{10:100}$ (PRE and POST). Torque generated at the beginning of the protocol was similar between SES (7.2 ± 0.8 Nm; 14.1 ± 1.5% MVIC) and SDSS (7.8 ± 0.2 Nm; 15.3 ± 0.3% MVIC). SES stimulation showed lower FI and PTM indicating more fatigue than during SDSS. $Db_{10:100}$ showed a larger decay after SDSS than SES fatigue protocol.

### B. Group Data

Fig. 5 shows the maximal normalized isokinetic torque and stimulation intensity during the MTT trials. SES produced 30% more torque ($t_{(9)}$ = 4.86; $p<0.001$)(Fig. 5A)

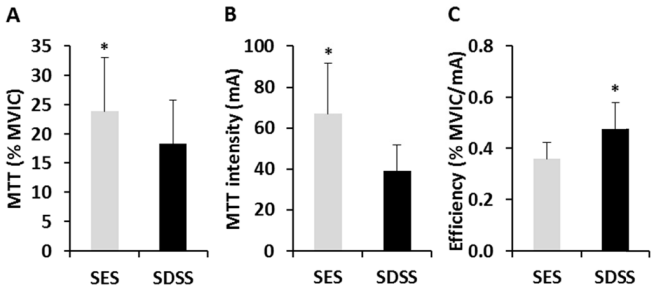


Fig. 5. Normalized torque (*A*), stimulation intensity (*B*), and stimulation efficiency (*C*) during the MTT protocol for SES and SDSS (n=10). ∗p<0.01.

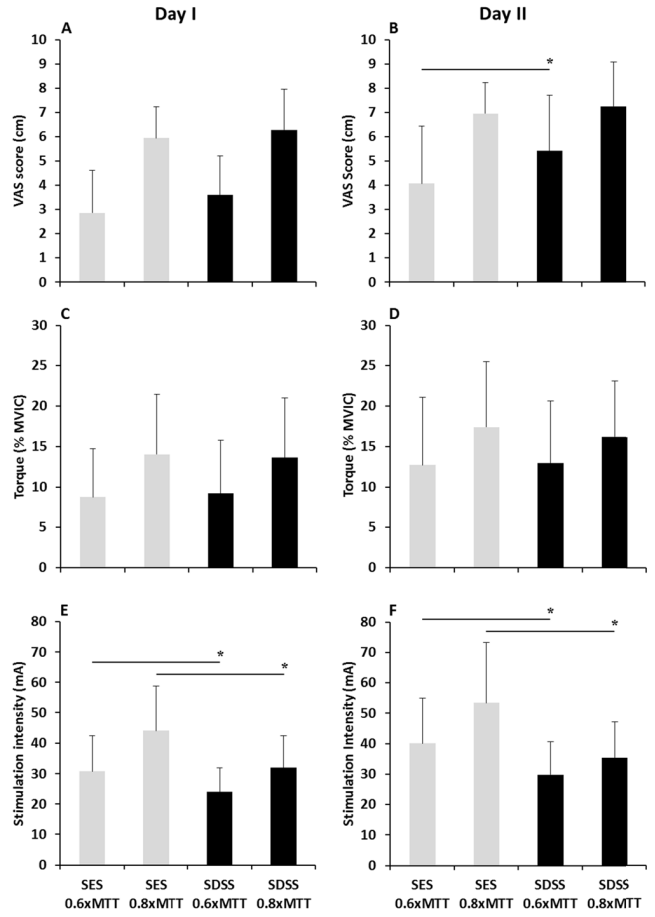


Fig. 6. VAS score (*A, B*), normalized torque (*C, D*), and stimulation intensity (*E, F*) during the discomfort protocol when trains of stimulation were delivered at 0.6x and 0.8xMTT for SES (grey bars) and SDSS (black bars). On Day I (A, C, E), SES was matched to the MTT of SDSS. On Day II (*B, D, F*), SDSS was matched to the torque of SES. (n=10); ∗p<0.01.

using 72% higher stimulation intensity ($t_{(18)}$ = 6.39; p<0.001)(Fig. 5B) than SDSS. Although SES produced larger torque, it was less efficient (0.36 ± 0.07 %MVIC/mA) in generating MTT than SDSS (0.48 ± 0.1 %MVIC/mA) ($t_{(9)}$ = −5.13; p<0.001)(Fig. 5C).

During the discomfort protocol on Day I (Fig. 6A), when the torque of SES was matched to SDSS, there was no interaction in the VAS scores between stimulation intensity (0.6x vs 0.8xMTT) and stimulation types (SES vs SDSS)

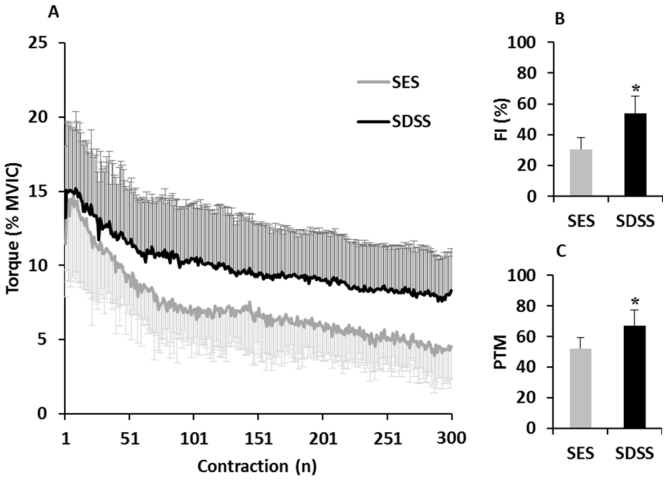


Fig. 7. Fatigue protocol (n=10). Isokinetic torque recorded during the 300 contractions of the fatigue protocol for SES and SDSS (*A*), fatigue index - FI (*B*), and peak torque mean - PTM (C). ∗p<0.01.

($F_{(1,9)}$ = 0.58; p=0.46; $\eta_p^2$ = 0.46). On Day II (Fig. 6B), when the torque of SDSS was matched to SES, SDSS produced more discomfort ($F_{(1,9)}$ = 8.81; p=0.016; $\eta_p^2$ = 0.48) than SES at 0.6xMTT (p=0.003) but not at 0.8xMTT (p>0.05). Larger normalized torque ($F_{(1,9)}$ = 11.2; p=0.008; $\eta_p^2$ = 0.55) (Fig. 6C) was generated at 0.8xMTT than 0.6xMTT for SES (p<0.001) and SDSS (p<0.001).

The variability in the discomfort reported on Day I between the two trials at 0.8xMTT for SES was 12.8 ± 13% ($R^2$ = 0.62; CI: 4.7 to 20.9), and for SDSS was 11 ± 12.9% ($R^2$ = 0.61; CI: 2.9 to19); at 0.6xMTT, the variability in reported discomfort during SES was 32.8 ± 22.5% ($R^2$ = 0.76; CI: 18.9 to 46.9) and for SDSS was 16.5 ± 19.3% ($R^2$ = 0.90; CI: 4.6 to 28.4). During Day II, the variability in the discomfort between the two trials at 0.8xMTT for SES was 26 ± 25.2% ($R^2$ = 0.62; CI: 10.4 to 41.6), and for SDSS was 11.3 ± 11.5% ($R^2$ = 0.76; CI: 4.1 to 18.4); at 0.6xMTT, the variability during SES was 26.5 ± 25.6% ($R^2$ = 0.61; CI: 10.6 to 42.3) and for SDSS was 19.9 ± 16.1% ($R^2$ = 0.82; CI: 10 to 29.9). The variability in the averaged discomfort between Day I and Day II during the SES 0.8xMTT trials was 15.6 ± 14.7% ($R^2$ = 0.60; CI: 6.5 to 24.8), SDSS 0.8xMTT was 9.8 ± 11% ($R^2$ = 0.68; CI: 2.9 to 16.6), SES 0.6xMTT trials was 23.8 ± 24% ($R^2$ = 0.81; CI: 8.9 to 38.8), and SDSS 0.6xMTT was 9.7 ± 5.3% ($R^2$ = 0.91; CI: 6.4 to 12.9).

There was no difference in the normalized torque generated by SES and SDSS when torque was targeted to generate 0.6xMTT and 0.8xMTT (p>0.05) (Fig. 6C and 6D). Stimulation intensity (Fig. 6E and 6F) was higher on Day I ($F_{(1,9)}$ = 9.92; p=0.01; $\eta_p^2$ = 0.54) and Day II ($F_{(1,9)}$ = 15.3; p=0.004; $\eta_p^2$ = 0.76) during SES than SDSS at 0.6xMTT [p<0.001] and 0.8xMTT [p<0.001].

SES and SDSS stimulation were tested regarding their resistance to fatigue (Fig. 7A). Isokinetic torque was measured throughout the 300 contractions of the fatigue protocol. The stimulation intensity required to generate 0.6xMTT at the beginning of the fatigue protocol was higher for SES (38.6 ± 11.8 mA) than SDSS (30 ± 8.9 mA)($t_{(9)}$ = 3.26; p=0.009).

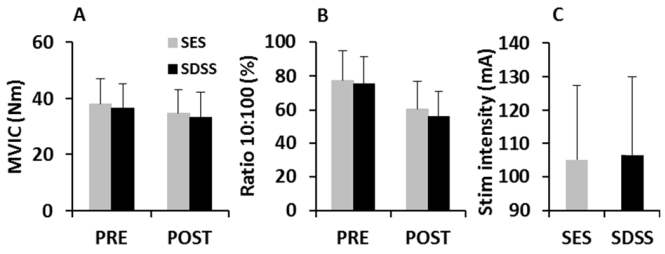


Fig. 8. Maximal voluntary isometric contractions (*A*), doublets ratio (*B*) and doublets stimulation intensity (*C*) recorded pre and post-fatigue protocol (n=10).

TABLE I
SRD OF FATIGUE INDEX (FI), PEAK TORQUE MEAN (PTM), AND MAXIMAL-TOLERATED TORQUE (MTT; %MVIC AND MA)

| | SRD | >SRD[a] n/10 |
|---|---|---|
| FI (%) | 6.47 | 10 |
| PTM | 6.35 | 8 |
| MTT (% MVIC) | 7.93 | 4 |
| MTT Stimulation Intensity (mA) | 21.53 | 6 |

MVIC, maximal voluntary contraction; SRD, smallest real difference.
[a]>SRD rows indicate the number of subjects who showed larger difference from the SRD (n) as well as the total number of subjects within the group (n=10).

There was no significant difference in the normalized torque ($t_{(9)} = -1.99$; p=0.07) generated during the first 10 contractions of the fatigue protocol between SES (12.6 ± 5.1% MVIC) and SDSS (13.9 ± 4.9% MVIC). The normalized torque produced by SES (4.4 ± 2.1 %MVIC) during the last 10 contractions of the fatigue protocol was significantly lower ($t_{(9)} = -5.56$; p<0.001) than during SDSS (7.9 ± 2.8 %MVIC). Higher fatigability during SES was also confirmed by higher FI ($t_{(18)}$ >-6.45; p<0.001)(Fig. 7B) and lower PTM ($t_{(18)}$ >-7.26; p<0.001)(Fig. 7C) after SES than SDSS.

Before and after the SES and SDSS fatigue protocols, we recorded MVICs and doublets (expressed as the ratio of the torque produced by 10 and 100 Hz - $Db_{10:100}$ ratio). MVICs recorded on different days or before and after the fatigue protocols did not differ ($F_{(1,9)} = 0.01$; p=0.91; $\eta_p^2 = 0.01$), where participants produced on average 35.8 ± 8.5 Nm (Fig. 8B). There was a main effect of time where MVICs performed 10 min after the fatigue protocols were lower (34.2 ± 8.5 Nm) than pre-fatigue (37.5 ± 8.5 Nm) [p<0.001]. There was no interaction between torque $Db_{10:100}$ ratios (pre vs post; SES vs SDSS – Fig. 8A) [$F_{(1,9)}$ <0.01; p=0.98; $\eta_p^2$ <0.01]; however, $Db_{10:100}$ ratio was lower post-fatigue (56.8 ± 14.8%) than pre-fatigue (76.4 ± 15.8%) [p<0.001]. The intensity of stimulation used to deliver doublets was not significantly different between SES (105 ± 22.5 mA) and SDSS (106.5 ± 23.3 mA) [$t_{(9)} = -1.0$; p=0.34] (Fig. 8C).

## IV. DISCUSSION

Here we compared maximal-tolerated torque (MTT), discomfort at sub-maximal torque, and fatigue-related outcomes between conventional (SES) and spatially distributed sequential stimulation (SDSS) neuromuscular electrical stimulation of the tibialis anterior muscle. Although SDSS produces significantly less isokinetic fatigue than SES, there was a trend for SDSS to cause more discomfort at submaximal contractions, and clearly generated less torque at maximally tolerated levels (i.e. MTT).

### A. Discomfort at Sub-Maximal Torque

We hypothesized that discomfort would be lower with SDSS than SES during submaximal contractions due to the use of relatively smaller electrodes during SDSS. This hypothesis was based on previous studies that compared discomfort when electrical stimulation was delivered through electrodes of different sizes located over the tibialis anterior muscle [23], [24]. Our hypothesis was not confirmed since there was a trend for SDSS producing more discomfort than SES (Fig. 6B). Although our results disagree with the tibialis anterior literature, they do agree with studies that tested the relationship of discomfort and electrode sizes in other muscles. Larger electrodes produced less discomfort than smaller electrodes in the quadriceps [35]–[37] and triceps surae [38] muscles, these results being attributed to a lower current density in larger than smaller electrodes. Indeed, current density was 2.3x smaller at MTT during SES (2.7 mA/cm$^2$) than SDSS (6.2 mA/cm$^2$), agreeing with previous results from the quadriceps muscle [37]. We believe that this discrepancy between our results and previous tibialis anterior literature are due to the location where the electrodes were positioned by Forrester and Petrofsky [23] and Milner *et al.* [24]. Both studies showed lower discomfort when smaller electrodes were located proximally, close to the common peroneal nerve where most of the motor axons innervating the tibialis anterior muscle are contained, whereas larger electrodes were located on the motor point. The common peroneal nerve trunk has a small diameter (0.3 cm), it concentrates axons in a small surface area (0.8 cm$^2$), and it is located close to the skin surface [39]. The tibialis anterior muscle has on average 16.9 cm in fascicle length, 76.2 cm$^2$ cross-sectional area, and 2.5 cm in thickness [40], a much larger structure with motor axons spread throughout the muscle. Therefore, nerve stimulation requires lower stimulation intensities to generate a given torque than muscle stimulation [18]. Thus, the comparison between smaller and larger electrodes in the previous studies [23], [24] corresponds to a comparison between the nerve stimulation and the motor point stimulation, which is more complicated than a simple comparison of the electrode size. Since we compared the two electrodes at the same motor point location, our results support the theory that larger electrodes tend to reduce discomfort compared to smaller electrodes, giving an advantage for SES over SDSS.

It is important to mention that although discomfort at submaximal contractions (0.6xMTT and 0.8xMTT) was higher during SDSS than SES, neither stimulation type produced discomfort levels towards the far right end of the VAS scale (range 2.8-7.2 cm, average 5.3 cm). The torque produced at 0.6xMTT (10.9% MVIC or 3.9 Nm) was approximately two times higher than the 2 Nm necessary to dorsiflex the ankle

during the swing phase of walking [41], [42]. This demonstrates the functional relevance of the contractions generated by both stimulation types even at low levels of discomfort.

### B. Maximal-Tolerated Torque

Higher discomfort during SDSS also resulted in lower MTT during SDSS than SES. The effectiveness of electrical stimulation for rehabilitation or training depends on a trade-off between torque generating capacity and discomfort. On the one hand, high torque during electrical stimulation is essential to optimize neuromuscular adaptations [37], [43], and it depends on high stimulation intensities to recruit the largest possible number of motor axons located under the stimulating electrodes, using relatively high stimulation frequencies to produce tetanic torque. On the other hand, increases in stimulation intensity result in the activation of progressively larger numbers of skin nociceptive A$\delta$-fibers and, consequently, increased discomfort [44]. Another key factor is current density, especially when comparing electrodes of different sizes such as during SDSS and SES, where A$\delta$-fibers are more sensitive to high current densities [45]. In our case, the higher current density during SDSS generated higher discomfort, limiting MTT compared to SES. The MTT of SDSS can also be limited by 1) the asynchronous activation of different portions of the muscle compared to the synchronous activation during SES; and 2) the potential overlap of motor unit recruitment between different channels [46].

The MTT of the tibialis anterior muscle is notoriously low when stimulation is delivered using conventional stimulation over the muscle belly (i.e. <40% MVIC) [18]. Both SDSS and SES are affected by the same limitation, producing MTT ranging from 13-43% MVIC.

### C. Fatigability

Although the fatigability of SES and sequential stimulation was previously compared during dynamic contractions [47], [48], these experiments are the first to compare the fatigability of the tibialis anterior muscle contractions during SES and SDSS under isokinetic conditions. Previous studies from our group and others have shown that sequential stimulation produces isometric muscle contractions that are more fatigue-resistant than SES in the quadriceps [3], [5], [10], [12], triceps surae [2]–[5], biceps femoris [3], [5] and tibialis anterior [3]. Sayenko *et al.* [3] showed that SDSS was 51% more fatigue-resistant than SES during isometric contractions, which is in line with the results reported here where SDSS produced 56% less fatigue than SES during isokinetic contractions. Moreover, the lack of significant differences between the $Db_{10:100}$ post-fatigue indicates similar exposure to low-frequency fatigue mechanisms during SES and SDSS. These results further strengthen the hypothesis that the localized recruitment of distinct motor unit populations by each stimulating electrode during SDSS contributes to significant reductions in muscle fatigue.

### D. Clinical Implications

In a rehabilitation or training context, the advantages of SDSS and SES are dependent on the relationship of intensity and volume. SES can produce larger maximal torque (i.e. higher intensity) but fatigues more quickly. SDSS produces less maximal torque but has higher fatigue resistance (i.e. higher volume). It should be noted that the majority of the present participants showed lower fatigability during SDSS (10/10 for FI, and 8/10 for PTM), whereas less than half of the present participants showed differences between SDSS and SES reaching SRD in MTT. This suggests that improvements in resistance to fatigability can be expected in more participants compared to increases of MTT when using SDSS. The clinical relevance of SDSS still has to be tested to explore neuromuscular and skeletal adaptations during long-term trials in non-impaired and impaired populations (e.g. spinal cord injury and stroke). However, our results suggest that SDSS has the potential to produce functionally relevant muscle contractions for prolonged periods, offering the possibility for strong neuromuscular adaptations.

The present results also expand the ecological validity of SDSS stimulation since our long-term goal is to implement SDSS to prosthetic devices such as foot-drop stimulators. In these devices, muscle length and joint angles have a wide range of motion, from plantarflexion to dorsiflexion. Thus, demonstrating the capacity of generating functionally relevant torque allied to low fatigability is fundamental to support the appropriate performance of activities of daily living.

## V. Conclusions

SDSS delivered by multiple pairs of electrodes positioned over the muscle belly of the tibialis anterior muscle can produce isokinetic contractions with 56% lower fatigability than SES stimulation delivered through a single pair of electrodes. However, SDSS showed a tendency to produce smaller maximal torque and higher discomfort.

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